GW RESEARCH DAYS

— WEDNESDAY, MARCH 30, 2016

HEALTH & MEDICINE RESEARCH DAY

THE GEORGE WASHINGTON UNIVERSITY

WASHINGTON, DC

GW RESEARCH DAYS 2016

HEALTH & MEDICINE RESEARCH DAY

WEDNESDAY, MARCH 30, 2016

MARVIN CENTER

800 21ST STREET, NW, 3RD FLOOR

8:00–9:00 a.m. **Posters Setup** *(Grand and Continental Ballrooms)*

JACK MORTON AUDITORIUM

805 21ST STREET, NW

8:00–9:00 a.m. **Registration and Breakfast**

9:00–9:05 a.m. **Welcome to Research Days 2016**

Jeffrey S. Akman, MD
Vice President for Health Affairs and Dean, School of Medicine and Health Sciences

9:05–9:10 a.m. **Introduction of Keynote Address**

Catherine Bollard, MD, FRACP, FRCPA
Professor of Pediatrics and Microbiology, Immunology and Tropical Medicine, School of Medicine and Health Sciences; Director, Program for Cell Enhancement and Technologies for Immunotherapy (CETI), Children's National Health System

9:10–10:00 a.m. **Keynote Address**

Stanley R. Riddell, MD
Fred Hutchinson Cancer Research Center, Clinical Research Division; Professor of Oncology, University of Washington School of Medicine

"Designing Safe and Effective T-Cell Therapy for Cancer"

10:00–10:30 a.m. **Coffee break**

10:30–11:30 a.m. **William Beaumont Research Award Oral Presentations**

Moderators: Ajlan Al Zaki, PhD, and James Boddu

Siyang Chaili
"Efficacy of IV Kinocidins in a Neutropenic Murine Model of Multi-Drug-Resistant Acinetobacter barman (MDRAB) Pneumonia"

Nicole Doria
"Cutaneous Infection with Leishmania major Mediates Heterologous Protection against Visceral Infection with Leishmania infantum"

Angeline Pham
"Hypoxia Results in White Matter Immaturity in a Piglet Model of Congenital Heart Disease"

MARVIN CENTER

800 21ST STREET, NW, 3RD FLOOR

12:00–2:00 p.m. **Distribution of Box Lunches**
(MC 310)

12:30–3:00 p.m. **Poster Presentations and Judging**
(Grand and Continental Ballrooms)

3:00–4:00 p.m. **Awards Ceremony and Oral Presentations**
(includes 10-minute presentations by winners of oral competition awards) (MC 309)

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH BUILDING

950 NEW HAMPSHIRE AVENUE, NW, 1ST FLOOR AUDITORIUM

4:30–4:35 p.m. **Welcome Video & Introduction of Keynote Address**

Lynn R. Goldman, MD, MS, MPH
Michael and Lori Milken Dean, Milken Institute School of Public Health; Professor of Environmental and Occupational Health

Kimberly Horn, EdD, MSW
Associate Dean for Research, Milken Institute School of Public Health; Professor of Prevention and Community Health

4:35–5:15 p.m. **Keynote Address**

Brian A. King, PhD, MPH
Deputy Director for Research Translation, Office on Smoking and Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention

"Public Health Promise or Peril? The rise of e-cigarettes and implications for tobacco control policy, planning, and practice"

5:15–5:30 p.m. **Award Ceremony for the Milken Institute School of Public Health**
Reception to Follow

GW RESEARCH DAYS

MARCH 30, 2016

3:00–4:00 p.m.

AWARDS CEREMONY

SCHOOL OF MEDICINE AND HEALTH SCIENCES, DONALD H. GLEW PRIZE

Moderator: **Lawrence Deyton, MSPH, MD**
Senior Associate Dean for Clinical Public Health, School of Medicine and Health Sciences

Alexa Lean:
"Circulating miRNA Biomarkers in Early Breast Cancer Detection Following Mammography"

INSTITUTE FOR BIOMEDICAL SCIENCES

Moderator: **Linda Werling, PhD**
Associate Dean for Graduate Studies, School of Medicine and Health Sciences; Director, Institute for Biomedical Sciences

Eshini Panditharatna:
"Identification of Driver Mutations in Diffuse Intrinsic Pontine Glioma Using Comprehensive Spatial & Temporal Molecular Studies"

DEPARTMENT OF BIOMEDICAL ENGINEERING

Moderator: **Vesna Zderic, PhD**
Associate Professor of Engineering and Applied Science

Ivan Suarez Castellanos:
"Ultrasound stimulation of insulin release from pancreatic beta cells"

SCHOOL OF NURSING

Moderator: **Pamela Jeffries, PhD, RN, FAAN, ANEF**
Dean, School of Nursing

Ann Hoffman:
"Adverse childhood experiences and binge drinking as an adult"

RESIDENT ORAL PRESENTATION

Moderator: **Robert H. Miller, PhD**
Senior Associate Dean for Research, School of Medicine and Health Sciences

Case Report:
Ivy Haskins, MD
"Exercise-related transient abdominal pain (ETAP)s"

GRADUATE MEDICAL EDUCATION RESEARCH COMPETITION WINNERS

Clinical Science:
Ivy Haskins, MD
"The Use of Mesh in Emergent Ventral Hernia Repair: Effects on Early Patient Morbidity and Mortality"

Basic Science:
Yasmine Assadipour, MD
"Discovery and Characterization of an Immunogenic Mutation in a Patient with Metastatic Triple Negative Breast Cancer"

Quality Improvement:
Joseph Delio, MD
"Improving adherence to the United States Preventive Services Task Force (USPSTF) screening and immunization guidelines among residents at the internal medicine clinic within the GWU MFA group"

2016 DORIS DEFORD SPECK AND GEORGE SPECK, MD ENDOWED PRIZE

Moderator: **W. Scott Schroth, MD, MPH**
Associate Dean for Administration, School of Medicine and Health Sciences

Sarah Himmelfarb:
"Site-Specific Commensal Control of T Effector Function in Human and Non-Human Primate Skin"

Ria Roberts:
"Is there Pandemic Vitamin D Deficiency in the Black Population? A review of Evidence"

POSTER AWARD WINNERS ANNOUNCED

School of Medicine and Health Sciences

Institute for Biomedical Sciences

Biomedical Engineering

School of Nursing

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH POSTER AND ONLINE VIDEO AWARD WINNERS ANNOUNCED

5:15–5:30 p.m.

950 New Hampshire Avenue, NW
1st Floor Auditorium

Reception to Follow

THE GEORGE WASHINGTON UNIVERSITY

WASHINGTON, DC

OVPR_1516_8

TABLE OF CONTENTS

INSTITUTE OF BIOMEDICAL SCIENCES

Endurance exercise as a potential therapy for myositis: Uncovering the genetic basis for functional improvements using gene expression profiling

BACKGROUND

The idiopathic inflammatory myopathies, or myositis, are a heterogeneous group of muscle disorders characterized by proximal muscle weakness, immune cell infiltration and abnormalities in energy metabolism. Recent studies have suggested that endurance exercise increases aerobic capacity and mitochondrial enzyme activity with a general clinical improvement in patients; however, the molecular mechanisms behind this benefit are unknown.

OBJECTIVE

Analyze skeletal muscle from exercised and non-exercised myositis patients to determine changes at the genetic level as a result of endurance exercise.

DESIGN/METHODS

Myositis patients were randomized into a 12-week endurance exercise group or a non-exercised control group. Muscle biopsies from the vastus lateralis were collected before and after the 12-week training program. Gene expression profiling was determined using the Affymetrix platform. Post intervention values were normalized to pre-intervention biopsies and a one-way ANOVA for exercised vs. control patients was used to determine significant changes. Data were filtered on $p<0.05$ with a fold change +/- 1.2. Gene lists were uploaded into Ingenuity Pathway Analysis (IPA) to identify commonly changed pathways due to exercise intervention.

RESULTS/DISCUSSION

Top canonical pathways that were changed in response to exercise include PEDF Signaling, Phosphatidylcholine Biosynthesis I, AMPK Signaling, ILK Signaling and Actin Cytoskeleton Signaling. A majority of these pathways are activated by inflammation and hypoxia and associated genes involved in promoting inflammation were down-regulated in response to exercise. Additionally, genes responsible for inhibiting angiogenesis were down regulated indicating exercise may improve oxygen transport to the muscle. Furthermore, genes involved in ILK and actin cytoskeletal signaling were down-regulated, which could signify a decrease in the cycles of degeneration and regeneration seen in myositis. Changes in gene expression that lead to more efficient oxygen transport to muscle with a decrease in inflammation and muscle degeneration, may explain the functional benefit seen in myositis patients after an endurance exercise intervention.

STATUS

Graduate Student

AUTHORS

Jessica Boehler

Marshall W. Hogarth

Svetlana Ghimbovschi

Li Alemo Munters

Ingela Loell

Yi-Wen Chen

Helene Alexanderson

Ingrid E. Lundberg

Kanneboyina Nagaraju

RESEARCH MENTOR/ DEPARTMENT CHAIR

Kanneboyina Nagaraju

INSTITUTE OF BIOMEDICAL SCIENCES

Elucidating the mechanism of human amylin trafficking in the pancreatic β cells

Type 2 Diabetes Mellitus (T2DM) is a complex metabolic disorder characterized by progressive loss of pancreatic β-cells secretory functions, β-cells death, peripheral insulin resistance and resulting hyperglycemia. Studies showed that, β-cell derived toxic aggregates of pancreatic hormone amylin contribute significantly towards the development of T2DM. The human amylin (hA) is a 37 amino acid hormone, which shares similar biosynthesis mechanism like insulin and is co-secreted with insulin by the pancreatic β-cells upon glucose stimulation. However, the cellular processes that regulate hA mediated cytotoxicity is far from clear. It is known that during T2DM, impaired folding, dysregulated ER to Golgi traffic or increased ER exit of proinsulin contribute to the development of insulin deficiency. It has also been suggested that similar to proinsulin, dysregulated processing and trafficking of pro-amylin contributes significantly towards the β cell failure during T2DM. However, detailed cellular trafficking mechanism of hA is unknown and hence investigated in the current study. In order to achieve the goal, I used lenti virus mediated gene delivery approach and validated hA and rat amylin (rA) overexpression in two rat pancreatic β-cells lines (*RIN-m5f* and *INS 832/13*) as well as in human islet cells. In order to identify the cellular compartments involved in hA trafficking and turnover cytosolic, membrane/organelle and nuclear/cytoskeletal fractions were prepared from the pancreatic β-cells following overexpression of hA and rA. WB analyses revealed the accumulation of hA in cytosol and organelle-enriched (Golgi/ER) fraction of RIN, INS and human islets cells. Interestingly, hA was also frequently found in the nuclear/cytoskeletal fraction of the RIN and human islet cells but not in the INS cells. Co-localization studies using immunofluorescence confocal microscopy confirmed significant accumulation of hA in Golgi, as well as nuclear accumulation of hA in RIN and human islet cells. Accumulation of hA in Golgi region rather than ER resembles trafficking pattern of proinsulin and possibly indicates the rate limiting role of Golgi during hA trafficking. Nuclear accumulation of hA mirrors trafficking pattern of other amyloid proteins and implies possible role/s of nucleus in turnover of hA in pancreatic β cells. This study, as well as future studies focused on determining the hA trafficking under normal and hyperglycemic condition, will help us to understand the strategies by which β-cells distribute and/sequester hA to prevent its toxicity, and if and how this protective mechanism may be altered and/or impaired under stress conditions like diabetes. This knowledge is important for development of new treatments against hA toxicity and T2DM.

STATUS

Graduate Student

AUTHORS

Diti Chatterjee Bhowmick

Aleksandar Jeremic

RESEARCH MENTOR/ DEPARTMENT CHAIR

Aleksandar Jeremic

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Mechanisms involved in the antioxidant properties of azithromycin in lung epithelial cells

Chronic obstructive pulmonary disease (COPD) is a leading cause of mortality world-wide. Macrolide antibiotics, e.g., azithromycin, have antioxidant and anti-inflammatory properties and decrease the frequency of acute exacerbations of COPD. The aim of this study was to identify the molecular mechanisms whereby azithromycin decreases oxidative stress and inflammation. We have reported that azithromycin decreased intracellular Nrf2 protein (-55±6%) and its target gene, downstream phase II detoxifying enzyme NQO1 (-45±4%), suggesting that Nrf2 activity is also decreased; reactive oxygen species (ROS) production (-1.6-fold), pro-inflammatory cytokine interleukin 8 (IL-8) secretion (-2.1-fold), and histone deacetylase 2 (HDAC2) expression are also decreased (-41±4%) in A549 cells (human airway epithelial cells) exposed to cigarette smoke extract (CSE) (200 µg/ml, 24 h). Pretreatment of A549 cells with azithromycin (0.5µg/ml) decreased ROS (-29±4%) and IL-8 (-45±6%) and G protein-coupled receptor kinase 4 (GRK4) expression (-33%). Furthermore, azithromycin promoted Nrf2 nuclear translocation (270±24%), catalyzing the reduction of hyper-oxidized peroxiredoxins (Prx) (-70±3%), leading to the reduction of oxidative stress. H_2O_2 (200 µM/24 h) increased GRK4 (191±4%) and decreased HDAC2 (-29±4%) expressions, suggesting that oxidative stress can regulate these proteins. GRK4 co-localize with surfactant protein-A (marker for alveolar epithelium type II) in human lung tissue and GRK4 and HDAC2 colocalize in human bronchus. Sestrin2, an antioxidant enzyme, was increased after treatment with azithromycin in a time- and concentration-dependent manner. Silencing Nrf2 resulted in suppression of azithromycin-induced sestrin2 expression (-35±3%). Silencing sestrin2 abolished the azithromycin-induced decrease in peroxiredoxin hyper-oxidation and partially attenuated the inhibitory effect of azithromycin on ROS production and IL-8 expression (by 26% and 41%, respectively). Our results suggest that the antioxidant and anti-inflammatory effects of azithromycin in COPD may be, in part, mediated by induction of sestrin2, via Nrf2, involving the GRK4 and HDAC2 pathways.

STATUS

Faculty

AUTHORS

Santiago Cuevas

Yu Yang

Ines Armando

Pedro A. Jose

RESEARCH MENTOR/ DEPARTMENT CHAIR

Alan G. Wasserman

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Lymph Node Activation by PET/CT Following Vaccination with Licensed Vaccines for Human Papillomaviruses

BACKGROUND

Vaccination is known to cause transient inflammation of lymph nodes with visualization from positron emission tomography (PET) using ^{18}F-fluoro-2-deoxy-D-glucose (FDG). PETFDG is most commonly used for imaging malignant tumors and vaccination has induced false positive findings on FDG-PET scans from transient inflammation. The pattern, magnitude and duration of lymph node activation following vaccination have not been clearly defined. The addition of adjuvants to vaccines can further enhance the immune response. The Vaccine Research Center (VRC) 900 study at the National Institutes of Health (NIH) was designed to define tissue specific immune-responses that also visualized lymph node activation following administration of the Food Drug Administration (FDA) licensed human papillomavirus (HPV) vaccines, Cervarix® and Gardasil®. These vaccines contain similar antigens with different adjuvants.

METHODS

Twenty seven women ages 18-25 were randomized to receive either Cervarix® or Gardasil®. We performed PET and computer tomography (CT) of lymph node activation at pre vaccination, “one week” (8 to 14 days), and “one month” (23 to 36 days) after first or third vaccination.

RESULTS

PET/CT scans revealed that all vaccine recipients had ipsilateral axillary lymph node activity. Three out of four Cervarix® recipients also showed contralateral lymph node activity one month after first vaccination. For both Cervarix® and Gardasil® the standardized update value (SUV) activity resolved over time, with activity extended up to day 37 post first and third vaccination.

CONCLUSIONS

Following intramuscular vaccination there were no major differences between duration of uptake and intensity of SUV between Cervarix® and Gardasil® recipients in ipsilateral axillary lymph nodes. Contralateral node activation was detected up to one month post first vaccination in Cervarix® recipients only which possibly reflects differences in vaccine adjuvant formulation.

KEYWORDS:

PET/CT, SUV, FDG, Human Papillomavirus Vaccination

STATUS

Medical Student

AUTHORS

Emily Coates

Pamela Costner

Martha Nason

Douglas Herrin

VRC 902 Study Team

RESEARCH MENTOR/ DEPARTMENT CHAIR

Julie Ledgerwood

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Interferon lambda 4 (IFN-λ4) genotype is associated with fatigue in patients with chronic hepatitis C (CH-C) receiving direct-acting antiviral (DAA) treatment

Fatigue can be a debilitating symptom in patients with CH-C. Endogenous interferons are commonly associated with fatigue. Functional IFN-λ4 is only expressed in patients with HCV who carry the IFNL4-ΔG allele for the rs368234815 locus. The aim of this pilot study is to investigate possible correlation between IFN-λ4 genotype and fatigue-related patient-reported outcome scores (PROs) in patients with CH-C receiving treatment with direct-acting antivirals (DDAs). Following informed consent, patients with CH-C were treated with DAA therapy (sofosbuvir with ledipasvir, simeprevir or ribavirin). Fatigue PROs data was assessed by Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) scoring system at baseline, end of treatment (EOT), and post-treatment week 4 (PTW4). Patient DNA was extracted from buffy coat isolated from blood collected during treatment. Patient IFN-λ4 genotype was determined by TaqMan SNP genotyping. Based on genotype, the three groups were: IFNL4-ΔG/ΔG (N=12), IFNL4-ΔG/TT (N=33), and IFNL4-TT/TT (N=14).

RESULTS

Of the 59 patients, data is available for 36 (72% were Caucasian, 14% were African-American, 56% were male, and the average age was 52.75±11.3 years). At baseline, the fatigue scores of FACIT-F did not differ significantly based on number of ΔG alleles. However, by end of treatment, lower FS scores not only correlated with the number of IFNL4-ΔG alleles (rho=0.458, P=0.01), but those scores were significantly lower depending on the number of IFNL4-ΔG alleles (IFNL4-ΔG/ΔG=27.75±15.17, IFNL4-ΔG/TT=38.68±12.46, and IFNL4-TT/TT= 45.33±10.56, P=0.03). Post treatment, these associations were no longer detected. Conclusion: In this pilot study, the number of IFNL4-ΔG alleles a patient carries increases treatment associated fatigue with DAA therapy compared to baseline. Larger cohort are being investigated to better understand the role of this genotype and fatigue in HCV.

STATUS

Medical Student

AUTHORS

Spencer Frost

James M. Estep

Kellie Perry

Sean Felix

Leo McLaughlin

Brian Lam

Maria Stepanova

Pegah Golabi

Lynn Gerber

Zobair Younossi

RESEARCH MENTOR/ DEPARTMENT CHAIR

Michael Estep

COLUMBIAN COLLEGE OF ARTS AND SCIENCES

Keratinocytes cultured from human chronic wound specimens demonstrate delayed wound closure and differences in apoptosis in an *in vitro* scratch assay

Wound healing is a critically important physiologic process which restores the normal epidermal barrier function of the skin after injury. Chronic wounds that have failed to heal affect approximately 6.5 million people in the US with a prevalence of 1% and costs estimated at $25 billion per year. The purpose of this study was to utilize a keratinocyte scratch assay to investigate molecular mechanisms of human wound healing.

METHODS

This research was conducted through the Wound Etiology and Healing (WE-HEAL) Study as approved by the George Washington University Institutional Review Board (041408).

In vitro scratch assay was performed according to established methods. Human epidermal keratinocytes were cultured at $2x10^5$ cells/well of a 6 well plate. Cells were allowed to reach ~80% confluence. A scratch was made with sterile 1ml pipette tip. Individual wells were photographed at 0h 24h, 48h, 72h, 96h using an inverted phase contrast microscope (Leica). Wound closure was determined as the decrease in percentage in gap width over the initial gap width at respective time-points.

Cell Viability Imaging was done using ready probes (Life technologies). Live cells stained with Nuc-Blue reagent were detected by a standard DAPI filter. Nuc-Green reagent stained nuclei of cells with compromised plasma membrane integrity, detectable by a green FITC/GFP filter. Images were taken in a fluorescence microscope (Nikon Eclipse TE300) and then merged to get a composite image of the ratio of live/dead cells after 96 hours.

RESULTS

In the keratinocyte scratch assay percent closure was significantly less in cultured keratinocytes from chronic wound specimens than from normal keratinocytes at all time points measured. At 24 hr. the difference in % closure was 19.66±10.03 in normal compared to 8.83±5.04 in chronic wound specimens (p=0.0194). Similarly, differences at 48, 72 and 96 hr. were 35.97±11.16 vs. 19.86±8.43 (p=0.0063); 51.94±9.02 vs. 28.01±10.86 (p=0.0003); and 72.81±8.83 vs. 41.03±7.94 (p=0.0001), respectively. Significant difference was only seen between normal and hidradenitis keratinocytes at the 96 hour time point (72.81±8.83 vs.61.65±7.04; p=0.0143). Cell viability was significantly higher in keratinocytes from normal compared to chronic wound specimens at 96 hr. (% live cells: 86.15±4.13 vs. 59.94±11.68; p=0.002).

CONCLUSION

Using this keratinocyte scratch assay we were able to show that scratch closure in keratinocytes harvested from normal skin was faster than that seen in keratinocytes harvested from chronic wounds. This suggests that inherent biologic mechanisms at the level of the keratinocyte contribute to delayed wound healing in vivo.

STATUS

Undergraduate Student

AUTHORS

Alexandra Gross

Anirban Banerjee

Sean McNish

Victoria K. Shanmugam

RESEARCH MENTOR/ DEPARTMENT CHAIR

Victoria K. Shamnugam

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Methylglyoxal inhibits expression of the glucose transporter genes by inactivating *Rgt2/Snf3* glucose sensors

Methylglyoxal (MG) is a highly reactive, cytotoxic dicarbonyl compound, mainly formed as a by-product of glycolysis. It is one of the most potent glycating agents and readily reacts with proteins, lipids and nucleic acids to form advanced glycation end products (AGEs). However, the molecular targets of MG are largely unknown. Glucose is the preferred carbon source of yeast *Saccharomyces cerevisiae* and can sense and utilize it efficiently over a broad range of concentrations. It prefers to ferment rather than oxidize glucose, even when oxygen is abundant. The yeast cell-surface glucose sensors Rgt2 and Snf3 function as glucose receptors that sense extracellular glucose and generate a signal for induction of genes encoding glucose transporters (HXTs). Using molecular and cell biology approaches, including Western blotting, qRT-PCR analysis and fluorescence microscopy, we provide evidence that MG inhibits expression of the HXTs by inactivating the yeast glucose sensors Rgt2 and Snf3. MG inhibits the growth of glucose-fermenting yeast cells by inducing endocytosis and degradation of the glucose sensors. However, the glucose sensors with mutations at their putative ubiquitin-acceptor lysine residues are resistant to MG-induced degradation. Our results suggest that the glucose sensors are inactivated through ubiquitin-mediated endocytosis and degraded in the presence of MG. Under physiological conditions, MG is detoxified by the glyoxalase system into D-lactate, with glyoxalase 1 (Glo1) as the key enzyme in the anti-glycation defense. This study further indicates that the inhibitory effect of MG on the glucose sensors is greatly enhanced in the cells lacking Glo1. Thus, the stability of these glucose sensors seems to be critically regulated by intracellular MG levels. Taken together, these findings suggest that MG attenuates glycolysis by promoting degradation of the cell surface glucose sensors and thus identify MG as a potential glycolytic inhibitor.

STATUS

Graduate Student

AUTHORS

Salman Hashmi

Adhiraj Roy

Jeong-Ho Kim

RESEARCH MENTOR/ DEPARTMENT CHAIR

Jeong-Ho Kim

INSTITUTE OF BIOMEDICAL SCIENCES

Injury triggered mitochondrial ROS production facilitates repair of injured muscle cells

Skeletal muscle contraction produces the force needed for animal motility. This force generation requires energy produced by mitochondria, which facilitates actin-myosin movement required for muscle contraction. The resulting mechanical strain can damage the plasma membrane of individual skeletal myofibers. Unless rapidly repaired, these injuries can lead to death of the myofiber. We recently identified mitochondria in skeletal muscle as an integral requirement for the repair of plasma membrane damage; however, the mechanism by which mitochondria facilitate the repair of injured myofibers has not been resolved. Here, we used real-time imaging to monitor the spatial and temporal changes in muscle mitochondria and cytoskeleton after focal injury. Pharmacological inhibitors were used to investigate the role of mitochondrial activity and actin dynamics in the repair of injured plasma membrane. We find that calcium entering the muscle cell due to plasma membrane injury is taken up by mitochondria. Calcium increase causes increased oxidative phosphorylation and transient production of ROS by mitochondria. Blocking ROS, but not ATP production, compromises repair of injured cells. Mitochondrial calcium uptake is mediated by the mitochondrial calcium uniporter (MCU). Inhibition or genetic knockout of MCU compromises the ability of the cells to repair from focal injury. Calcium-triggered transient increase in mitochondrial ROS initiates signaling that promotes polymerization of F-actin at the site of injury. Blocking mitochondrial function, calcium uptake, and the ability of mitochondria to produce ROS all prevent plasma membrane repair by blocking actin polymerization. Similarly, a chronic increase in ROS also prevents actin polymerization and plasma membrane repair. These results identify a beneficial effect of mitochondrial ROS produced due to cell injury and demonstrate that mitochondria-mediated regulation of F-actin polymerization is the mechanism by which mitochondria facilitate repair of injured plasma membrane.

STATUS

Graduate Student

AUTHORS

Adam Horn

Aurelia Defour

SenChandra Sreetama

Aaron Reed

Luana Scheffer

Jesper Nylandsted

Jyoti K. Jaiswal

RESEARCH MENTOR/ DEPARTMENT CHAIR

Jyoti K. Jaiswal

INSTITUTE OF BIOMEDICAL SCIENCES

Discovery of Novel Drugs to Alleviate Muscle Weakness in Myositis

Idiopathic inflammatory myopathies (myositis) often exhibit refractory muscle weakness, which persists despite elimination of infiltrating inflammatory cells with immunosuppressive drugs. Myositis patients and our mouse model of myositis have been reported to acquire a deficiency of the metabolic enzyme AMP deaminase 1 (AMPD1), which catalyzes the rate-limiting step of the purine nucleotide cycle. In humans, a congenital AMPD1 deficiency due to a loss-of-function allele is associated with easy fatigability, weakness, and cramping. We hypothesize that an acquired AMPD1 deficiency contributes to muscle weakness in myositis, so we sought to find drugs that increased expression of AMPD1 to alleviate this refractory weakness. We created a coincidental reporter HEK293 cell line that used the AMPD1 promoter to drive the expression of a bicistronic transcript for the renilla and firefly luciferase genes intervened by a ribosomal skipping sequence, designed to reduce false positives by assessing the readout from two non-homologous reporters. The resulting cell line was utilized for quantitative high throughput screening (qHTS) of 3 libraries, totaling 4194 compounds at 7 to 11 dilutions each. Actives were then validated in cultured myotubes by RT-qPCR and an enzymatic activity assay of endogenous AMPD1. Regulation of the coincidental reporter in HEK293 cells was similar to that in muscle cells and the qHTS assay conditions were optimized for 1536 well-plates (Z'>0.5). The commercially available LOPAC1280 and FDA approved libraries identified microtubule polymerization inhibitors, such as podophyllotoxin and colchicine, as the most active compounds. Podophyllotoxin was verified to up-regulate endogenous AMPD1 mRNA and increase enzymatic activity in cultured myotubes. Additionally, qHTS of a 50 compound library of aza-podophyllotoxin analogues identified novel actives that are being pursued as lead compounds. Most of the active drugs identified by qHTS were microtubule polymerization inhibitors, suggesting a mechanistic link between microtubule polymerization and AMPD1 transcription. Active compounds identified by these assays will undergo preclinical testing in our mouse model of myositis for their ability to up-regulate AMPD1 and alleviate muscle weakness.

STATUS

Graduate Student

AUTHORS

Travis Kinder

Patricia Dranchak

James Inglese

Kanneboyina Nagaraju

RESEARCH MENTOR/ DEPARTMENT CHAIR

Kanneboyina Nagaraju

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Transplanting P21KO EPCs may improve vascularization in diabetes related PVD

BACKGROUND

One of the major secondary effects of diabetes is peripheral vascular disease (PVD). Unfortunately, 60% of non –traumatic lower limb amputation is related to PVD and is a consequence of diabetes. Therefore, it is important to treat PVD aggressively to prevent mobility handicap for subjects with diabetes. Studies indicate that delivery of endothelial progenitor cells (EPCs) improve vascularization in mouse model. However, major concern is to ensure survival of these cells in hyper glycemic condition. Previous study from our laboratory showed improved survival and better collateral vessel formation when p53KO EPCs were delivered post femoral artery occlusion in diabetic mouse models. In this study, we wanted to investigate whether transplantation of EPCs from P21 knock out (P21KO) mice at the site of femoral artery occlusion will improve regeneration and new collateral vessel formation. p21 is a downstream protein in the apoptosis cascade and therefore silencing of p21 rather than p53 may have less off-target effects. While investigating apoptosis resistant endothelial progenitor stem cells (EPCs) in diabetic mouse models we enquired into effect of hyperglycemia on mature human endothelial cells (HUVEC) in a time-course dependant manner.

METHOD

We exposed mature HUVEC (Human Umbilical Vein Endothelial Cell) and EPCs in normal (5.5mM) and high glucose (20mM) and carried out gene expression studies and assessed their respiration rate at different time points. We transplanted EPCs from p21KO mice in streptozotocin (STZ) induced diabetic mice (type 1 diabetes model) post occlusion of the right femoral artery. We measured blood flow at days 3, 7, 10, 14 and 21 after surgery and did gene expression study and stain quadriceps with CD31 antibody to determine vascularization.

RESULTS

We observed reduction in respiration rate of HUVEC only after 28 days of exposure to hyperglycemic condition which was associated with upregulation of P53, P21 and inflammatory markers after 28 days of exposer in hyperglycemic condition in HUVEC cells. Whereas, upregulation of P53 and P21 was noted within 48 hours of hyperglycemic condition exposure in EPCs.

For our in vivo studies using p21KO, wild type (WT) and saline in STZ induced diabetic mice, we observed enhanced vascularization on the hind limb after surgery and delivery of p21 KO EPCs, compared to WT and saline. Simultaneously, we also observed upregulation of endothelial markers like PECAM1, KDR, vWF and eNOS in hindlimb muscles that received p21 KO EPCs. Staining with CD31 is also showed improved vascularization in p21KO EPC injected mouse quadriceps.

CONCLUSION

These studies suggest that apoptosis of cells particularly stem cells plays a major role and prevention of cellular apoptosis may prove to be an important cell based therapy for diabetic PVD and limb salvage.

STATUS

Postdoctoral Student

AUTHORS

Nabanita Kundu

C.C. Domingues

Sabyasachi Sen

RESEARCH MENTOR/ DEPARTMENT CHAIR

Sabyasachi Sen

COLUMBIAN COLLEGE OF ARTS AND SCIENCES

The effect of Mitomycin C on adhesion and migration of Human Corneal Limbal Epithelial Cells

When a corneal wound heals, there is often a subsequent erosion of corneal epithelial cells. These are cells that have failed to adhere to the basement membrane. Using Human Corneal Limbal Epithelial (HCLE) cells in vitro, the question we ask is, can cell adhesion between the epithelial cells and the membrane be increased in order to prevent these erosions? The drug Mitomycin C (MMC) functions as DNA crosslinker to prevent cell proliferation. By adding MMC to HCLE cells, cell adhesion would be expected to increase. Cell adhesion assays were preformed on MMC treated and untreated HCLE cells. Time Lapse cell migration studies were carried out with different concentrations of MMC. Cells were incubated with MMC for 3 hours and tracked for 16hrs and 40 minutes at an interval of 10 minutes to obtain 100 frames. Visual Basic program was used to study the migration rates of treated and untreated cells and 0.0025% was found to be non-toxic to the cells. The migration rate was lower for treated cells compared to untreated (Control) cells.

Cell adhesion assays were also carried out on treated and untreated cells. The assay was done immediately after treatment or after 24hrs, to allow the cells to recover from any cytotoxic effects of MMC. Adhesion assay was performed immediately after treatment with a 90 and 30 minute time for adhesion. The first experiment showed increased adhesion of MMC treated cells to Fibronectin, CollagenIV and Collagen I. However the 30 minute adhesion time showed no difference between adhesion of treated and untreated cells. Further investigation will give conclusive results, this data will be important in understanding how to prevent corneal erosions during the wound healing process.

STATUS

Undergraduate Student

AUTHORS

V. Rose Lieberman

Sonali Pal-Ghosh

Kristy Ortega

Mary Ann Stepp

RESEARCH MENTOR/ DEPARTMENT CHAIR

Mary Ann Stepp

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Single Nucleotide Polymorphisms in *GCKR* and *DGKD* Affecting Serum Calcium Influence Other Musculoskeletal Traits

INTRODUCTION

The purpose of this study is to investigate whether rs780094 of the *GCKR* gene and rs1550532 of the *DGKD* gene are associated with serum calcium showed associations with phenotypic characteristics such as bone mineral density, bone mineral content, fat mass, percent lean mass, change in muscle volume after an exercise intervention, and physical activity level in pediatric African-American and young adult Caucasian populations.

METHODS

The Bone Health cohort consists of 150 African American children between the ages of 5-9. Each participant was administered a dual-energy x-ray absorptiometry (DXA) scan in order to obtain total body lean mass without head, total body fat mass without head, % body fat without head, total bone mineral density without head (BMD), lumbar BMD, total bone mineral content without head (BMC), and lumbar BMC. These BMD and BMC values were used in the Bone Mineral in Childhood Study z-score calculator to obtain z-scores, which adjust for ethnicity, sex, weight, and height. Each participant had a questionnaire filled out to assess total hours of sun exposure per week. Total sun exposure has been validated as an effective measure for physical activity level in pediatric populations. The Bone and Muscle cohort consisted of 160 college age males and females from the University of Massachusetts-Amherst population. Participants had to be 18-40 years of age, non-smokers, and classified as inactive to recreationally active as according to the International Physical Activity Questionnaire (IPAQ). Exclusion criteria included a calorie restrictive diet, increased physical activity from normal, and use of a weight gaining dietary supplement in the last six months. Anthropometric measurements of height, weight, biceps and arm circumference were taken for each participant. Bone mineral content (BMC), bone mineral density (BMD), fat mass, lean body mass, and percent body fat were obtained by performing a DXA scan. The FAMUSS cohort consists of 304 Caucasian males and 449 Caucasian females averaging 24.5 years old who participated in a 12-week resistance training program of their non-dominant arm. Participants were between the ages of 18-40. One repetition max bicep strength (pre-training, post-training, and % change), maximum voluntary contraction (pre-training, post-training, and % change), and whole muscle volume (pre-training, post-training, and % change) were the measurements obtained before and after the 12 week training program. Using TaqMan allelic discrimination assay both SNPs were genotyped in the Bone Health and Bone Muscle cohort, and only rs780094 was genotyped in FAMUSS cohort. Hardy-Weinberg equilibrium was validated and phenotypes were tested using ANOVA and ANCOVA with covariates of age and sex.

RESULTS

In the Bone Health cohort, rs1550532 was significantly associated with total sun exposure (p=0.006) and rs780094 was associated with lumbar BMD (without head) (p=0.05) and lumbar BMD (without head) (p=0.0349). In the Bone Muscle cohort, rs780094 was significantly associated with total body BMC in females (p=0.047) and total body % in males (p=0.029). In the FAMUSS cohort rs780094 was significantly associated with % change in whole muscle volume in females (p=0.0003).

continued on following page

STATUS

Medical Student

AUTHORS

Thomas Lynch

Courtney Sprouse

Cara Goerlich

Heather Gordish-Dressman

Christopher Payette

Heather Flynn

Leticia Ryan

Laura Tosi

RESEARCH MENTOR/ DEPARTMENT CHAIR

Laura Tosi

continued from previous page

DISCUSSION

There was a significant association between total sun exposure (hours/week) with rs1550532 in the Bone Health cohort, which consists of a pediatric African American population. Our results indicate that the C allele is strongly associated with total sun exposure and shows an increasing effect from the heterozygous to homozygous genotype. Total sun exposure has been validated as an effective measure for physical activity level in pediatric populations. Increased physical activity has been a major recommendation for prevention and improvement of Type 2 diabetes (T2D) (Steinberger 2003). Physical activity has been shown to increase insulin sensitivity in normal pediatric populations, and even improving metabolic markers of dysfunction in children who are already obese (Schmitz 2002). Additionally, the *DGKD* expression and activity level in skeletal muscle has been found to be reduced in T2D patients (Chibalin 2008). These results suggest that the rs1550532 alleles may play a role in understanding the relationship between physical activity, the development of T2D, and the role the *DGKD* gene plays. Further studies exploring *DGKD* expression and activity level associations with rs1550532 alleles and T2D incidence is necessary in adult African American populations. Our findings further suggest that the rs780094 genotype had sexually dimorphic results in regards to change in muscle volume in response to physical exercise. Female participants with the C allele experienced a significantly higher percent change in whole muscle over the 12 week study than males. Females homozygous for TT experienced just over one third the muscle volume growth with the same amount of strength training, while no significant difference was found amongst males. This finding may have implications in older female populations, particularly in regard to risk factors for sarcopenia or osteoporosis.

SIGNIFICANCE

This is the first study to associate rs1550532 with physical activity levels in an African American pediatric population, and further studies of rs1550532 alleles and *GCKR* expression in adult African American populations may provide valuable insight in identifying genetic risk factors for the development of T2D. This is the first study to associate rs780094 with muscle volume changes in response to physical exercise, which may warrant further investigation to understanding risk factors for developing sarcopenia and osteoporosis in older populations.

INSTITUTE OF BIOMEDICAL SCIENCES

Sequential trafficking and localization of HCMV anti-apoptotic protein vMIA alter mitochondrial calcium levels

Congenital infection with the human cytomegalovirus (HCMV) can cause deafness, blindness and microcephaly. During infection, HCMV inhibits host cell apoptosis increasing thereby the production of infectious progeny. One of its immediate early proteins, viral mitochondria-localized inhibitor of apoptosis (vMIA), is anti-apoptotic and essential for HCMV growth in humans. vMIA is synthesized in the endoplasmic reticulum (ER), traffics sequentially through ER-mitochondrial contacts (known as MAM), localizes to MAM lipid rafts, which contain the ER calcium channel, IP3R and chaperones, and to mitochondria. We previously found that HCMV infection significantly increases calcium handling proteins and channels in the MAM proteome, suggesting its regulation of calcium dynamics at the MAM. Consistent with this, vMIA increases ER calcium efflux. Since mitochondrial calcium ($[Ca^{2+}]_m$) uptake from the ER regulates cellular metabolism, analyzing whether vMIA trafficking through the MAM affects $[Ca^{2+}]_m$ levels may provide insight into its usurping of mitochondrial metabolic machineries. We examined the effects of vMIA trafficking and localization on $[Ca^{2+}]_m$ levels. To that end, we transfected HeLa cells with vectors encoding fluorescently tagged wild-type (WT) vMIA or vMIA mutant (cholesterol binding domain II, CBD-II, and high hydrophobicity B, HHB) proteins and observed their trafficking, localization, and effects on $[Ca^{2+}]_m$ levels using live-cell and confocal microscopy. Using pharmacological blocks, our lab had previously observed vMIA localization at mitochondria within 60 minutes. Here, we show that sequential trafficking and location of vMIA play a role in elevating the $[Ca^{2+}]_m$ levels by using vMIA mutants that either fail to localize to mitochondria or do not associate with MAM lipid rafts. Our studies show that vMIA increases $[Ca^{2+}]_m$ and that association with lipid rafts is not essential for this vMIA function. Thus, vMIA's trafficking and localization could play an important role in altering $[Ca^{2+}]_m$ dynamics at the MAM.

STATUS

Graduate Student

AUTHORS

Mansi Mehta

Shivaprasad Bhuvanendran

Jyoti Jaiswal

Anamaris Colberg-Poley

RESEARCH MENTOR/ DEPARTMENT CHAIR

Anamaris Colberg-Poley

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Longitudinal outcomes of Hidradenitis Suppurativa patients enrolled in the WE-HEAL Study

INTRODUCTION

Hidradenitis suppurativa (HS) is a chronic, debilitating inflammatory disease of apocrine sweat glands, characterized by recurrent abscessing inflammation. The prevalence is around 1-4% in young adults. Despite the prevalence of HS in the US, it is largely unstudied, and treatment is extrapolated from studies done in a northern European population.

Molecular drivers of HS are poorly understood, and traditional disease modifying anti-rheumatic (DMARD) therapies have been largely ineffective. However, targeted biologic therapies including TNF-α inhibitors have been used with some success. Adjuvant biologic therapy after radical resection has been shown to reduce risk of recurrence in HS.

The purpose of this study is to analyze the outcomes of patients with HS enrolled in the WE-HEAL Study and to assess how treatment with biologic agents affects disease activity scores including Hidradenitis Sartorius Score (HSS) and Hurley Stage in a US population.

METHODS

This research was conducted through the Wound Etiology and Healing Study (WE-HEAL Study), a biospecimen and data repository approved by The George Washington University IRB (041408). All subjects gave written informed consent for longitudinal collection of their data while they received treatment according to standard of care. Data from 561 patients enrolled in the WE-HEAL study was used for this analysis, 59 were HS patients and 502 were patients with chronic wounds used for demographic comparisons including age, sex, race, and smoking status. In the HS cohort, response of HSS and Hurley Stage were analyzed according to medication exposures.

RESULTS

In the WE-HEAL study, HS patients were significantly younger than patients with chronic wounds (40.1 ± 14.21 years compared to 62.3 ± 13.44, p=0.0001). Patients with HS were more likely to be female (66.1% compared to 48.9%, p=0.0086), African American (73% compared to 35%, p=0.0001), and active smokers (27.1% compared to 14.9%, p=0.005).

HSS score and Hurley Grade were higher in current and past smokers than in never smokers ($p<0.001$). There was no significant difference in HSS score or Hurley grade in the subjects treated with finasteride. However, in patients treated with TNF-α inhibitors there was a significant improvement in mean HSS score (34.92 to 18.76, $p<0.001$).

CONCLUSION

The cohort of HS patients followed in the WE-HEAL study is more representative of the population affected in the US with a higher prevalence of women and African Americans. Treatment with TNF-α inhibitors was associated with significant improvement in disease activity scores in this population.

STATUS

Medical Student

AUTHORS

Shaunak Mulani

Sean McNish

Sami Serafi

Sarah Harris

Victoria Shanmugam

RESEARCH MENTOR/ DEPARTMENT CHAIR

Victoria Shanmugam

INSTITUTE OF BIOMEDICAL SCIENCES

Third generation antisense improved FSHD myoblast differentiation

Facioscapulohumeral muscular dystrophy (FSHD) is caused by aberrant expression of double homeobox 4 (*DUX4*). Expression of DUX4 represses myogenic differentiation resulting in atrophic myotube phenotype. Knocking down DUX4 using an antisense approach compounds is a potential novel therapeutic approach. The Third Generation Antisense compounds (3GAs) consist of two identical segments linked together by their 5′ ends (J Med Chem. 2011 3027-36) and are designed to improve activity and reduce immunotoxicity. The purpose of this study is to determine if DUX4 targeted 3GAs can reduce DUX4 expression, improve the ability of FSHD myoblasts to differentiate, and improve myotube morphology. To determine the effects of 3GA treatments on FSHD myoblast differentiation, FSHD myoblasts were treated with 3GAs targeted to DUX4 and grown in differentiation media for seven days. Treated FSHD cells were compared to the untreated FHSD cells. Myoblasts from an unaffected sibling were used as baseline controls. Cells were stained with Giemsa staining and imaged to calculate the fusion index and evaluate cell morphology. Our results confirmed that FSHD myoblasts did not differentiate as well as the control myoblasts evident by showing lower fusion index and more atrophic myotubes. Treatment with selected 3GA targeted to DUX4 corrected the fusion index in FSHD myoblasts to control levels (107%; $p<0.05$). Treatment with 3GA significantly decreased the number of atrophic fibers in FSHD culture (88%; $p<0.05$). 3GAs against DUX4 effectively reduce the expression levels of DUX4 and partially corrected phenotypic abnormalities observed in FSHD myoblasts.

STATUS

Graduate Student

AUTHORS

Kelly Murphy

Sachchida Nand Pandey

Hunain Khawaja

Mallikarjuna Putta

Lakshmi Bhagat

Sudhir Agrawal

Yi-Wen Chen

RESEARCH MENTOR/ DEPARTMENT CHAIR

Yi-Wen Chen

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Impact of Mitomycin C on reinnervation of subbasal nerves in the mouse cornea

Debridement wounds to the mouse cornea heal initially but spontaneously develop recurrent erosions beginning 14 days after wounding. Erosions are characterized by a failure to completely reinnervate the cornea. Corneal epithelial cells at erosion sites cease to express ki67 7 days after wounding and by 14 days begin to express high levels of γH2AX. The surrounding cells fail to exclude Hoescht dye indicating cell death. Intense γH2AX expression shows the presence of double strand DNA breaks and indicates that cells are either undergoing apoptosis or are becoming senescent. Corneas with large erosions have numerous cells that express senescence associated β-galactosidase (SAβGal), a marker of senescence. Away from the erosion, the corneal epithelial cell proliferation is elevated relative to unwounded corneas and remains high for 28 days after wounding, as assessed by ki67. Treating mouse corneas with Mitomycin C (MMC) after reepithelialization is complete reduces erosion formation, restores proliferation rates and improves reinnervation of the subbasal nerves (SBNs) to levels similar to controls. To determine whether MMC improves reinnervation of SBNs when the corneal epithelium is left intact, a 1.5 mm trephine was used to crush the SBNs that innervate the center of the mouse cornea causing the corneal epithelial cells at the site to die. These corneas show a reduction of 50% in the density of their SBNs within 24 hours and without any treatment, axon density is restored to control levels by 7 days after wounding. Crush wounded corneas were treated with either vehicle or 0.02% MMC at the time of injury and 24 hours later. Subbasal axon density was assessed by Sholl analysis at 2, 3, 4, 7, 14, and 28 days after wounding. Reinnervation up to day 7 occurs at similar rates. However, by 14 days after wounding, the central cornea of vehicle treated corneas had higher axon densities than MMC treated corneas. When considered along with our data showing that MMC enhanced reinnervation after debridement wounds, these results suggest the possibility that MMC increases epithelial cell adhesion to subbasal nerves and/or with the basement membrane making it more difficult for reinnervating axons to extend between and under the corneal epithelial cells and their fully assembled hemidesmosomes.

STATUS

Staff

AUTHORS

Sonali Pal-Ghosh

Gauri Tadvalkar

Mary Ann Stepp

RESEARCH MENTOR/ DEPARTMENT CHAIR

Mary Ann Stepp

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Single Nucleotide Polymorphisms in CLDN14 and SMOC1 Affecting Bone Mineral Density Influence Other Musculoskeletal Traits

BACKGROUND

A recent genome-wide association study (GWAS) identified novel genes influencing bone mineral density (BMD). This three stage GWAS identified two novel loci: rs227425 in the SPARC-Related Modular Calcium Binding 1 gene (SMOC1) was significantly associated with BMD and rs170183 in the claudin 14 (CLDN14) gene was significantly associated with BMD in females.

OBJECTIVE

The purpose of this study was to determine if two novel single nucleotide polymorphisms (SNPs) known to affect BMD are associated with other musculoskeletal traits.

METHODS/DESIGN

The Bone Health Cohort consists of 150 African-American participants enrolled at Children's National Health System as part of a fracture analysis study. The FAMuSS study examined young adults who volunteered for 12-week unilateral resistance training of the non-dominant arm. SNPs were genotyped in both cohorts using a TaqMan allelic discrimination assay. Associations between SNPs and phenotypes were tested using ANCOVA using age and sex as covariates. Significant associations were then analyzed via t-test to identify significance between individual genotypes.

RESULTS/DISCUSSION

Our findings extend the influence of the CLDN14 gene beyond BMD and suggest its novel role in muscular responsivity to exercise among young adults and in fat mass among African American children. Our results also indicate sexual dimorphism in the effect of CLDN14 on muscle response to exercise. These findings could be used to identify individuals at risk for sarcopenia as well as proliferation of fat mass. Findings from the Bone Health Cohort implicate a novel role for the SMOC1 gene in fat mass among female and male African American children. No direct association between SMOC1 and fat mass has been identified prior to this study. In parallel with findings from the Bone Health Cohort in the CLDN14 gene, results regarding SMOCI in this cohort may promote identification of those at risk for fat mass accumulation in childhood, especially among a group at risk for obesity.

STATUS

Medical Student

AUTHORS

Christopher Payette

Courtney Sprouse

Cara Goerlich

Heather Gordish-Dressman

Thomas Lynch

Heather Flynn

Leticia M. Ryan

Eric Hoffman

Monica J. Hubal

Paul D. Thompson

Theodore J. Angelopoulos

Paul M. Gordon

Niall M. Moyna

Linda S. Pescatello

Paul S. Visich

Robert F. Zoeller

Laura L. Tosi

RESEARCH MENTOR/ DEPARTMENT CHAIR

Laura L. Tosi

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Nasopharyngeal microbiome diversity changes over time in children with asthma

BACKGROUND

The nasopharynx is a reservoir for pathogens associated with respiratory illnesses, such as asthma. Next-generation sequencing (NGS) has been used to characterize the nasopharyngeal microbiome in asthmatic infants and adults; less is known, however, about microbiome core composition and temporal dynamics in children and adolescents, which poses an obstacle to identifying microbial biomarkers of pediatric asthma (pulmotypes) and establishing associations between microbial succession and disease. Here we use NGS technology to characterize the nasopharyngeal microbiome of asthmatic children and determine its stability over time.

METHODS

Two nasopharyngeal washes collected ~6 months apart were taken from 40 asthmatic children living in the Washington D.C. area. Samples were sequenced for the 16S-V4 rRNA gene region (~250 bp) in a MiSeq platform. Raw data were processed in mothur (SILVA reference database) and Operational Taxonomic Units (OTU)-based alphaand beta-diversity metrics were estimated. Relatedness among samples was assessed using Procrustes, PCoA ordination and neighbor-joining clustering analyses. Differences in microbial diversity between patient time points and seasons were assessed in both rarefied and non-rarefied OTU datasets. Core microbiome analyses were also performed to identify potential biomarkers of asthma.

RESULTS AND DISCUSSION

A total of 2,096,584 clean 16S sequences corresponding to an average of 167 OTUs per sample were generated. Representatives of Moraxella*, Staphylococcus*, Dolosigranulum, Corynebacterium, Prevotella, Streptococcus*, Haemophilus*, Fusobacterium* and a Neisseriaceae genus accounted for 86% of the total reads. These nine genera have been previously found in the nasopharynxes of both asthmatic infants and adults, but in different proportions. Five OTUs (genus* above) defined the nasopharyngeal core microbiome at the 95% level. Microbial OTU abundance significantly varied between time points in 35 of the 40 patients analyzed, but no significant differences in diversity were observed seasonally. Future cross-sectional studies of the nasopharyngeal microbiome need to be aware of potential intra-patient longitudinal variation.

STATUS

Medical Student

AUTHORS

Marcos Perez-Losada

Lamia Alamri

Keith A. Crandall

Robert J. Freishtat

RESEARCH MENTOR/ DEPARTMENT CHAIR

Marcos-Perez Losada

INSTITUTE OF BIOMEDICAL SCIENCES

Dietary Spermidine protects against Ethanol and Lipopolysaccharide induced Hepatic Oxidative Stress and Fibrosis

Alcohol liver disease (ALD) is a leading cause of death worldwide. The well-accepted two-hit model of ethanol and endotoxin, lipopolysaccharide (LPS) for ALD mimics the human disease by combining ethanol mediated oxidative stress caused by the metabolites of ethanol or endotoxin mediated increase in cytokines resulting in a deleterious positive feedback loop that propagates inflammation and fibrosis. In the first hit, ethanol is oxidized to acetaldehyde by alcohol dehydrogenase and cytochrome P4502E1 in hepatocytes, generating reactive oxygen species (ROS) within the cells. The second hit perpetuates liver injury and fibrosis as a result of endotoxin-induced activation of Kupffer cells resulting in oxidative stress and the activation of hepatic stellate cells (HSC), causing the up regulation of fibrogenic markers, platelet derived growth factor β-receptor (PDGFβR), α-smooth muscle actin (αSMA), collagen I (Col1) and fibronectin; and epigenetic repressor gene, methyl-CpG binding protein 2 (MeCP2). In contrast, the adipogenic gene, peroxisome proliferator-activated receptor γ (PPARγ) is suppressed leading to the transdifferentiation of HSC from quiescent to activated myofibroblastic phenotype, resulting in fibrosis. Spermidine, a naturally occurring polyamine found in soybean, mushrooms and whole grains is known for anti-aging properties and resistance to stress. In this study, the role of dietary spermidine in ethanol-LPS induced hepatic oxidative stress and fibrosis was investigated. Ethanol-LPS mediated liver injury was induced in C57BL/6 mice using chronic 5% ethanol fed in a liquid diet for 4 weeks plus a single dose of ethanol (5g/kg body wt, gavage) and LPS (2mg/kg body wt, ip), 6h prior to the experiment. Spermidine (5mg/kg body wt) was added to the liquid diet for 4 weeks. Oxidative stress was determined using ROS and glutathione (GSH) fluorescent assays and expression of superoxide dismutase (SOD). The above mentioned genes and their products were measured using RT-PCR and Western blot, respectively. The extent of fibrosis was determined by measuring the hydroxyproline content for collagen and Sirius Red stain. Spermidine protected against ethanol-LPS induced oxidative stress by decreasing the levels of ROS and the expression of SOD, and increasing the levels of the GSH. It also prevented the activation of HSC by suppressing the up regulated MeCP2, that coordinately reversed the down regulated PPARγ and the up regulated fibrogenic genes (αSMA, PDGFβR, Col1 and fibronectin). Spermidine also prevented fibrosis by decreasing hydroxyproline content and collagen fibers. These data suggest that spermidine may have potential as an anti-oxidant and anti-fibrotic agent for the prevention/treatment of ALD.

STATUS

Graduate Student

AUTHORS

Ruchi Shah

Karina Reyes-Gordillo

Ravi Varatharajalu

Ying Cheng

Joseph Ibrahim

M. Raj Lakshman

RESEARCH MENTOR/ DEPARTMENT CHAIR

M. Raj Lakshman

INSTITUTE OF BIOMEDICAL SCIENCES

Characterization of microbial communities in schizophrenia and mood disorders

BACKGROUND

Mental and neurological disorders like mood disorders (MD) and schizophrenia constitute a worldwide health issue. Standard treatments often provide inadequate responses. Among factors involved in resistance to psychotropic drugs, microbiota has an underestimated influence on host behavior and in drug metabolism, as suggested by previous findings in humans, mainly based on inflammatory bowel disorders, which are associated with microbiota dysbiosis and are highly comorbid with psychiatric disorders. In this study we aim to characterize the gut microbiome of schizophrenia and MD patients.

METHODS

Gut microbiome from 30 individuals (8 controls, 7 MD patients, 15 schizophrenia patients) was surveyed with shotgun metagenomic sequencing. Exploratory and differential species abundance analyses were performed on read datasets.

RESULTS

Differential taxon abundance analysis revealed that samples did not differ at the phylum level; genera Lactobacillus (log2 fold change [LFC] = 8) and Peptoclostridium (LFC = 4) were more abundant in schizophrenia patients than in controls. In MD patients, genera Lactobacillus and Bifidobacterium were relatively more abundant (LFC > 2), while genera Streptococcus and Enterococcus showed a decreased abundance (LFC < -1). Differentially abundant taxa are involved in metabolism of key neurotransmitters (GABA, serotonin) and brain development at different levels.

Alpha-diversity measures showed a reduced species richness in schizophrenia and MD patients, further suggesting a link between the explored diseases and the microbial communities inhabiting the gut.

CONCLUSION

Our findings show that gut microbiota is different in schizophrenia and MD patients compared to controls, suggesting that microbiota profiling can constitute a valuable tool for the management and the treatment of psychiatric disorders. Further studies will focus on the metabolic features of microbial communities in different diagnoses.

STATUS

Postdoctoral Student

AUTHORS

Domenico Simone

Eduardo Castro-Nallar

Robert H. Yolken

Keith A. Crandall

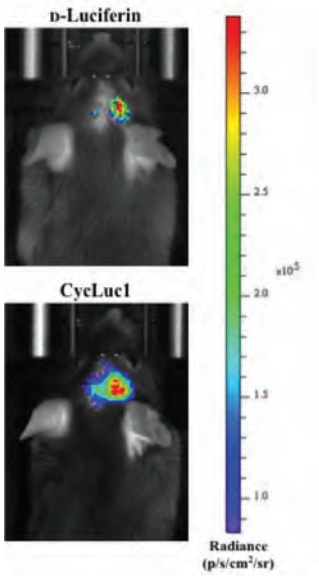
RESEARCH MENTOR/ DEPARTMENT CHAIR

Keith A. Crandall

SCHOOL OF MEDICINE AND HEALTH SCIENCES

A Synthetic Luciferin Improves In Vivo Bioluminescence Imaging of Gene Expression in Cardiovascular Brain Regions of Mice

Bioluminescence imaging is a powerful tool for in vivo investigation of biological processes. Incorporation of firefly luciferase into whole animals or organ specific areas, combined with exogenous administration of the substrate D-Luciferin, results in light production that can be captured with a charge-coupled device camera. We have demonstrated the utility of in vivo bioluminescence imaging to spatiotemporally monitor gene expression and transcription factor activation in individual cardiovascular brain nuclei during the development of cardiovascular disease. However, D-Luciferin uptake into the brain is low, which may limit the sensitivity of bioluminescence imaging, particularly when considering small changes in gene expression in single central nervous system areas. Therefore, approaches that improve the sensitivity of in vivo bioluminescence imaging are warranted. Here, we tested the hypothesis that a synthetic luciferase substrate, cyclic alkylaminoluciferin (CycLuc1), would be superior to D-Luciferin for in vivo monitoring of gene expression in cardiovascular brain regions. Male C57B1/6 mice (n=4) underwent targeted delivery of an adenovirus encoding the luciferase gene (*luc*) downstream of the CMV promoter to the subfornical organ, a circumventricular brain region that is critical in the control of the cardiovascular system. Following gene transfer and recovery, D-Luciferin or CycLuc1 were administered in a randomized fashion on 2 separate days and bioluminescence imaging was performed using an IVIS Lumina K system. The substrate dose (150 mg/kg) was similar between conditions and was chosen based on the typical use of this concentration for in vivo imaging with D-Luciferin. Administration of D-Luciferin revealed a bioluminescent signal from the subfornical organ of 3.2±1.2 x 10^5 photons/s at 10 minutes after substrate administration. In contrast, in the same animals at an equivalent concentration (figure), CycLuc1 injection was associated with a more intense light emission (7.7±2.6 x 10^5; p=0.06 vs. D-Luciferin) that was approximately 3-fold greater than that found with D-Luciferin (2.9±0.9 fold D-Luciferin). Similarly, at 20 minutes post substrate administration CycLuc1 provided a 3.3±1.1 fold higher bioluminescent signal than D-Luciferin (2.9±1.2 vs. 7.6±2.6 x 10^5 photons/s; D-Luciferin vs. CycLuc1; p=0.05). These preliminary findings demonstrate that replacing standard D-Luciferin with the synthetic luciferin CycLuc1 improves the sensitivity of bioluminescent detection from individual central nervous system cardiovascular control areas.



STATUS

Staff

AUTHORS

Hayk Simonyan

Chansol Hurr

Colin N. Young

RESEARCH MENTOR/ DEPARTMENT CHAIR

Colin N. Young

SCHOOL OF MEDICINE AND HEALTH SCIENCES

A Novel Method for Ellipsoid Zone Analysis with Hydroxychloroquine Use

PURPOSE

To develop a novel method for analyzing the Ellipsoid Zone (EZ) on Optical Coherence Tomography (OCT) for earlier detection of hydroxychloroquine toxicity to the retina.

METHODS

All patients screened for hydroxychloroquine toxicity at the George Washington University Department of Ophthalmology from January 1, 2012 to November 1, 2014 were identified. Inclusion criteria consisted of having a dilated fundus exam and at least one High Definition Spectralis OCT (HD-OCT, Heidelberg Engineering, Heidelberg, Germany). Exclusion criteria consisted of the presence of any plaquenil unrelated maculopathy or glaucoma. The EZ intensity was analyzed using the National Institutes of Health's Medical Imaging, Processing, Analysis, and Visualization (MIPAV) software. Five volumes of Interest (VOIs) were drawn over the EZ of both eyes 500 microns superior, inferior, nasal, and temporal to the fovea as well as directly subfoveal (*Figure 1*). Average voxel intensity was recorded. To account for variability in signal quality and intensity from scan to scan, additional VOIs were drawn on the RPE directly beneath each EZ VOI to serve as an internal control for each scan; the ratio of each respective Ellipsoid VOI to RPE VOI was used for calculations.

RESULTS

One hundred ninety-three patients were included in the study. One hundred seventy-three were female, and 20 were male. Average age and duration of hydroxychloroquine use was 61.8 years and 4.6 years, respectively. No patients developed clinical signs of toxicity from routine screening. EZ intensity was plotted for completed years of use as shown in *Figure 2*. EZ intensity for patients with more than ten years of hydroxychloroquine only decreased by 0.74% compared to those with less than 10 years of use (result not significant).

CONCLUSIONS

Routine use of hydroxychloroquine does not cause a detectable change in the ellipsoid zone, signifying no subtle damage to photoreceptors.

STATUS

Medical Student

AUTHORS

Rishi Singhal

Benjamin Reiss

Lindsay Smithen

Sam Mansour

Tony Chen

Aisha Mumtaz

RESEARCH MENTOR/ DEPARTMENT CHAIR

Sam Mansour

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Transplanted Chondrocytes Heal Mandibular Defects And Fracture Fixation Promotes Intramembranous Ossification

The mandible is one of the most common craniofacial fracture sites, sustaining 36-70% of all maxillofacial fractures. Although the mandible develops through intramembranous ossification, it heals by both intramembranous and endochondral ossification. To our knowledge, the role of fracture stability in mediating healing mechanisms has not been tested in the mandible, although it has already been applied clinically to determine the form of fixation used to treat mandible fractures. Vascularized bone grafting is considered the current gold standard for large mandibular defect reconstruction in cases of bone malunions and nonunions, infection, cancer, and aberrant craniofacial development. However there is still a significant unmet clinical need to develop improved strategies for promoting vascularized bone regeneration and reducing autograft failure. A recent study by Bahney et al. showed cartilage grafts are an effective alternative to bone autografts in healing tibial defects by stimulating both complete bone conversion and vascularization of the graft via direct transformation of transplanted chondrocytes into osteoblasts/cytes. In our study, we use murine models to determine how fracture stability directs the relative contribution of intramembranous and endochondral ossification during mandible healing, and characterize how cartilage grafts mediate healing of critical-sized mandibular defects. We found that stable trephine defects primarily healed through intramembranous ossification, whereas mandibles with unstable transverse fractures primarily healed through endochondral ossification. Our results demonstrate that cartilage engraftment promotes vascularization and produces complete bony-bridging of critical-sized mandibular defects. Interestingly, although engrafted chondrocytes are capable of transforming into osteoblasts in the tibia, this does not appear to be the primary mechanism of healing in the mandible. This work demonstrates the potential of cartilage grafts in healing mandible defects and poses a promising therapeutic alternative for mandible reconstructive therapy. Understanding the mechanisms by which fractures heal will lead to the development of improved strategies to prevent malunion.

STATUS

Medical Student

AUTHORS

Joshua Slocum

Sarah Anne Wong

Diane Hu

Chelsea Bahney

Ralph Marcucio

RESEARCH MENTOR/ DEPARTMENT CHAIR

Chelsea Bahney

INSTITUTE OF BIOMEDICAL SCIENCES

Defining novel spliced transcripts in muscle using long-read RNA-seq, and comparison of EDL, soleus and heart

Multiple proteins with diverse functions can be coded from a single gene through alternative splicing of RNA transcripts. Muscle is highly rich in alternative transcripts (isoforms) and expresses the largest genes in the mammalian genome. However, the complexity of splice events within these large genes have not been compared in muscles of different myofiber composition and metabolic traits. Most gene annotations are constructed from expressed sequence tags, therefore they are prone to artifacts and are composed of short read (<1kb) data. Assembling large transcripts from short reads is a challenge because the amount of contextual information available is not adequate to: 1) accurately determine if exons are missing from a transcript, 2) correctly map reads over repetitive sequences, and 3) overcome structural variation. Pacific Biosciences' Isoform Sequencing (IsoSeq) method has the potential to provide the necessary long reads (10+ kb) to overcome these challenges.

For the purpose of our studies, we wanted to capture the complexity of splicing events in large muscle transcripts and to provide novel insights into spliced transcripts differentially expressed between various muscle types. We applied the IsoSeq method to three metabolically distinct wild-type mouse muscles: soleus (oxidative myofibers), heart (cardiocytes) and extensor digitorum longus (glycolytic myofibers). Bioinformatics analysis was performed using the RS_IsoSeq software pipeline to classify raw reads into full-length and non-full length, to cluster full-length reads of the same spiced transcripts into consensus reads, to map the reads to the mouse genome and to compare our results to existing annotations using MatchAnnot software. We present data on the two longest transcripts in the genome: titin (101.6 kb), nebulin (22.4 kb), and other >10 kb muscle transcripts. Results of this study indicate that splice transcripts are differentially expressed in unique muscle-types and that the IsoSeq method can be used for discovery of complex transcripts.

STATUS

Graduate Student

AUTHORS

Prech Uapinyoying

Jeremy Goecks

Karuna Panchapakesan

Susan M. Knoblach

Eric P. Hoffman

RESEARCH MENTOR/ DEPARTMENT CHAIR

Eric P. Hoffman

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Attempts to develop a peptide based inhibitor to prevent HCMV growth

BACKGROUND/OBJECTIVE

Human cytomegalovirus (HCMV) is a beta-herpesvirus that causes asymptomatic infections in healthy adults, but severe illnesses in neonates, transplant patients, and immunodeficient individuals. HCMV encoded antiapoptotic protein, vMIA, prevents infected cells from undergoing mitochondria-mediated apoptosis, thus allowing productive viral replication. vMIA trafficking to the mitochondria is required for its antiapoptotic function. It has been proposed that vMIA interaction with the mitochondrial morphology regulating cellular protein mitofusin 2 (Mfn2) is required for vMIA to traffic to the mitochondria. In this study we aimed to develop an Mfn2 polypeptide - vMIA binding domain (VBD; $Mfn2_{aa262\text{-}390}$) as a tool to prevent vMIA localization and function at the mitochondria.

METHODS

Fluorescence microscopy was used to determine localization of Mfn2 and vMIA. Mouse embryonic fibroblasts expressing fluorophore tagged, mitochondrial outer mitochondrial membrane marker Tom20, as well as Mfn2, and vMIA were imaged by confocal microscopy. Images were analyzed and locations were quantified using MetaMorph. Statistical analyses were performed using SAS. Mfn2 VBD, was cloned, fluorophore tagged, and co-transfected with Tom20 to determine its localization.

RESULTS

Mfn2 was localized at the mitochondria in the presence or absence of vMIA. The presence of vMIA caused Mfn2 to redistribute similarly to vMIA - more evenly along the outer mitochondrial membrane. Mfn2 and vMIA colocalization suggests that vMIA interacts with Mfn2 and changes its distribution. The difference in Mfn2 distribution induced by vMIA was statistically significant. Mfn2 VBD did not localize to the mitochondria on its own or when vMIA was expressed in the cell indicating this Mfn2 polypeptide is unable to interact with vMIA.

CONCLUSION

vMIA interacts with and alters the distribution of Mfn2. However, vMIA trafficking to mitochondria is neither affected by the proposed vMIA binding domain of Mfn2 nor does this domain localize with vMIA. Thus, VBD may not be suited for inhibiting HCMV growth.

STATUS

Graduate Student

AUTHORS

Kassandra Wilson

Kyle Salka

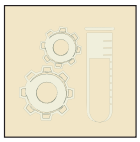
Jyoti K. Jaiswal

Anamaris M. Colberg-Poley

RESEARCH MENTOR/ DEPARTMENT CHAIR

Anamaris M. Colberg-Poley

BIOMEDICAL ENGINEERING



SCHOOL OF ENGINEERING AND APPLIED SCIENCE

Ultrasound-activated microbubbles for cartilage tissue engineering in 3D printed scaffolds

Gas-filled microbubbles encapsulated with lipids and other surfactants are highly responsive to ultrasound, which has led to their effective role as ultrasound contrast agents (UCA). In this study, for the first time, we used lipid-coated microbubbles (MB) prepared in-house in order to better harness the beneficial effects of ultrasound stimulation on proliferation and chondrogenic differentiation of human mesenchymal stem cells (MSCs) within a novel 3D printed poly (ethylene glycol) diacrylate (PEG-DA) hydrogel scaffolds. A significant increase in cell number ($p<0.001$) was observed with low intensity pulsed ultrasound (LIPUS) treatment in the presence of 0.5 % (v/v) MB after 1, 3 and 5 days of culture. MSC proliferation enhanced up to 40% after 5 days of culture in presence of MB and LIPUS while this value was only 18% when excited with LIPUS alone. We investigated the effects of acoustic parameters such as excitation intensity, frequency and pulse repetition period on MSC proliferation rate. Our 3-week chondrogenic differentiation results demonstrated that combining LIPUS with MB significantly enhanced both Glycosaminoglycan (GAG) and type II collagen production. Therefore, integrating LIPUS and MB appears to be a promising strategy for enhanced MSC growth and chondrogenic differentiation.

STATUS

Graduate Student

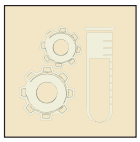
AUTHOR

Mitra Aliabouzar

RESEARCH MENTOR/ DEPARTMENT CHAIR

Kausik Sarkar

BIOMEDICAL ENGINEERING



SCHOOL OF ENGINEERING AND APPLIED SCIENCE

Amperometric Detection of Ultrasound-Induced Secretory Events in Potential Treatment of Type 2 Diabetes

OBJECTIVE

The objective of this study was to explore a potential new treatment method that utilizes a non-invasive application of ultrasound energy to induce exocytosis of insulin from pancreatic beta cells. Our amperometric measurements can not only provide confirmation of secretion, but also data that could lead to optimization in controlling the release via ultrasound application.

METHODS

Our experiments focused on detecting exocytotic secretions from pancreatic beta cells in response to ultrasound stimulation using carbon fiber amperometry. Exocytosis of insulin is measured via amperometric readings of the oxidation of dopamine. Dopamine that is loaded into cells is released via vesicles along with insulin. Results were obtained with commercially available electrodes as well as electrodes fabricated in-house. A sham group was included in which cells were loaded with dopamine but not stimulated for secretion.

RESULTS

To confirm the functionality of the in-house made electrodes, a triangular waveform was run through the electrode, and using an oscilloscope, the original signal was compared to the one from the electrode. Consequently, the amperometry experiments were run with both the in-house made electrodes and commercial electrodes. Similar results were obtained. Secretory amperometric readings were recorded after application of ultrasound at 800kHz and 1MHz with an intensity of 1W/ cm^2. The ultrasound pulse was applied for 5s, 10s and 15s at various time intervals. There is an immediate response of secretion after application of the 800kHz pulse for 5s at three intervals (t=180s, 360s and 540s). Similar results were obtained at 1KHz. With application of consequent 5s, 10s and 15s ultrasound pulses, a prolonged response was recorded for a prolonged stimulation. These results confirm that ultrasound stimulation induces secretory events in beta cells. Ongoing experiments focus on exploring the impact of varying parameters such as ultrasound intensity and pulse length on exocytotic events.

CONCLUSIONS

Our proposed technology would directly target beta cell dysfunction, one of the underlying causes of insulin deficiency in Type 2 Diabetes, and could result in the development of a new therapeutic approach for the treatment of Type 2 Diabetes.

STATUS

Undergraduate Student

AUTHORS

Bogdan Balteanu

Tania Singh

Ivan Suarez Castellanos

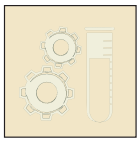
Aleksandar Jeremic

Vesna Zderic

RESEARCH MENTOR/ DEPARTMENT CHAIR

Vesna Zderic

BIOMEDICAL ENGINEERING



SCHOOL OF ENGINEERING AND APPLIED SCIENCE

Breast Cancer Thermography: A Literature Review

The current gold standard for breast cancer screening and detection is mammography. Approximately one-third of all biopsies ordered on the basis of mammography are negative and so women face unnecessary discomfort, anxiety, and occasional disfigurement. Breast thermography uses no radiation, does not require contact with the breast, and is more affordable. It has not yet, however, been shown to be a valid alternative or adjunct to mammography. This review provides a critical review of the work that has been done between 1979 and 2015 in the area of thermal imaging for breast cancer detection. Our intent is to guide and stimulate others interested in the field and to bring attention to the absence of standard scientific rigor in thermal imaging and its interpretation.

Forty papers were analyzed and categorized as segmentation (12), classification systems (4), system evaluation (12), data collection enhancement (4), or review (6). The review identifies the systems' performance (sensitivity, specificity), and researchers' analyses of results. This review highlights the deficiencies in the work done in the field and demonstrates that many research studies lack standardization. The review also describes the hardware used, images analyzed, and the results presented. It is clear that much of the research data and results are not reported comparably across studies. Sensitivity and specificity were presented in 16 of the 40 papers. Some papers were compared using their receiver operating characteristic curves. It plots true positive rate (sensitivity) against the false positive rate (1-sensitivity). Some performed only slightly better than chance (true positive rates and false positive rates are nearly equal). By reviewing these studies, others interested in the field of breast thermography will know what was done in the past, as well as what was and was not useful. Our lab is currently preparing to go into the clinic to take data for our own breast thermography project to test methods we have developed that will automate the detection process. A combination of high spatial and thermal resolution and the use of a subject as her own control may make it possible to perform accurate, objective, repeatable, and rapid thermal imaging as an adjunctive breast-imaging modality.

STATUS

Undergraduate Student

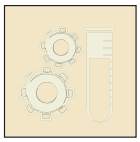
AUTHOR

Aleksandra Desansky

RESEARCH MENTOR/ DEPARTMENT CHAIR

Murray Loew

BIOMEDICAL ENGINEERING



SCHOOL OF ENGINEERING AND APPLIED SCIENCE

Vital Ring: a Wearable Wireless Multiple-Lead ECG Sensor Embedded in a Flexible Finger Ring

I. INTRODUCTION

Electrocardiogram (ECG) is an important tool widely used in the clinical diagnostic of heart diseases. It can be used to diagnose symptoms of myocardial infarction, pulmonary embolism, etc. [1] Among those symptoms, detection and early warning of the potential of heart attack such as myocardial infarction can be crucial in daily life for patients, especially those who live alone, because once happened, it need to be taken immediate care of. Unfortunately, the traditional equipment currently used in the hospital cannot fulfill this real-time on-demand monitoring requirement. To address this problem, the wearable ECG monitoring system comes into play.

Recently, wearable healthcare devices have attracted considerable interest both in the academic and industry. The important role ECG playing in the heart disease diagnostic and the convenient noninvasive way of measurement makes it an ideal candidate to be converted to wearable healthcare device, and have already draw many researchers' attention. Y. Chi and G. Cauwenberghs at UCSD have demonstrated a wireless ECG/EEG monitoring system using noncontact electrodes. [2] The gel free noncontact electrodes make the wearing of the device more comfortable and cleaner. However, their electrodes are rigid which makes it less compatible to soft human bodies. Moreover, it is uncomfortable to wear several hard electrodes of noticeable sizes. AliveCor® developed a single-lead ECG monitoring system in the smartphone case format, which can monitor the ECG at fingertip and displays on the smartphone screen. This system has gotten FDA approval, which confirms the possibility to achieve a wearable ECG system. Unfortunately, single-lead ECG measurements, which apply to all existing systems, cannot be used to diagnose myocardial infarction. The phone case format makes it convenient to carry around, but, on the other hand, limits it to single-lead measurement only. IMEC® developed a long term multiple-lead ECG monitoring patch, which can be attached to the upper body and last as long as one month. The only drawback is the usage of conduction gel, which is commonly used in the traditional ECG. The sticky gel is difficult to keep clean. Moreover, it can cause allergy to some patients [3]. The IMEC system uses Bluetooth Low Energy (BLE) to transfer data, which is suited for wearable healthcare equipment because of the low energy consumption and sufficient transfer rate. However, a dedicated BLE data transfer base device in their device is not necessary, because there are many BLE enabled devices available now, such as smartphones and laptops. Using a smartphone to communicate with these wearable devices is convenient, because people carry smartphone around and the smartphone has the ability to further analyze the data, to transfer the data to the physicians, and/or to upload the data to a database.

In this work, we propose and demonstrate a wearable ECG monitoring system capable of providing on-demand multiple-lead ECG signals in the format of a flexible finger ring. Such extreme form factor is enabled by a novel soft electronics/microfluidics co-packaging technique recently developed by us [4]. The flexibility is a key advantage to achieve a comfortable device, and also provides certain durability during impact. We will also use dry electrodes to eliminate the skin reaction issue and the clean issue mentioned before. We will use BLE to transfer the data to smartphone or laptop for further analysis of the data.

II. REFERENCES

[1] Drew, Barbara J., et al. "Practice Standards for Electrocardiographic Monitoring in Hospital Settings An American Heart Association Scientific Statement From the Councils on Cardiovascular Nursing, Clinical Cardiology, and Cardiovascular Disease in the Young: Endorsed by the International Society of Computerized Electrocardiology and the American Association of Critical-Care Nurses." Circulation 110.17 (2004): 2721-2746.

[2] Chi, Yu M., and Gert Cauwenberghs. "Wireless non-contact EEG/ECG electrodes for body sensor networks." Body Sensor Networks (BSN), 2010 International Conference on. IEEE, 2010.

[3] I D. Ruehlemann, K. Kuegler, B. Mydlach and P. J. Frosch. "Contact dermatitis to self-adhesive ECG electrodes," Contact Derm. 62(5), pp. 314-315. 2010.

[4] Zhang, Bowei et al. Flexible packaging of solid-state integrated circuit chips with elastomeric microfluidics. Scientific Reports, 3: 1098, 2013.

STATUS

Graduate Student

AUTHOR

Quan Dong

RESEARCH MENTOR/ DEPARTMENT CHAIR

Zhenyu Li

SCHOOL OF ENGINEERING AND APPLIED SCIENCE

Glibenclamide Prevents APD Shortening During Deoxygenation in Left Ventricular Working Hearts

INTRODUCTION

Sarcolemmal ATP-sensitive K+ channels (KATP) open in response to low [ATP]/[ADP] to link cardiac energetics and action potential duration (APD). The effect of workload and oxygenation on KATP activation in excised working hearts is important for arrhythmia mechanisms, yet is unknown. Using novel motion-corrected ratiometric optical mapping, we hypothesized that, due to KATP activation, APD shortening in LV working (LVW) hearts during hypoxia is more severe than in unloaded Langendorff perfused hearts (LANG).

METHODS

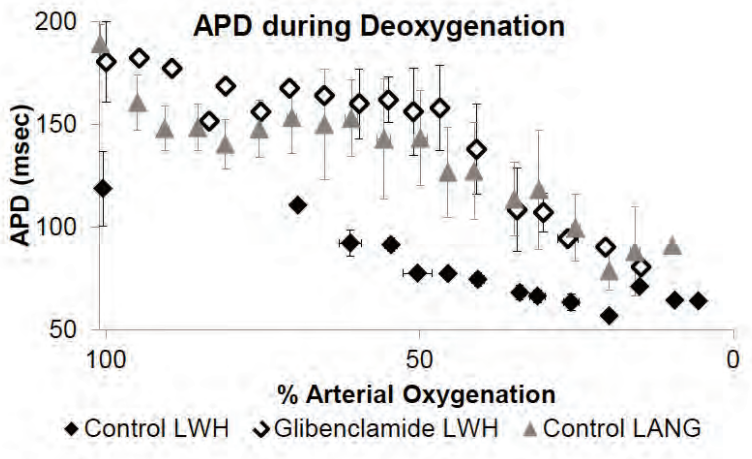
Epicardial APDs were measured from LVW and LANG rabbit hearts (n=11) using di-4-ANEPPS excitation ratiometry and a motion-tracking algorithm. Circulating perfusate was gradually deoxygenated by bubbling with N2 gas. Perfusate %O2 was measured. In a subset of studies, 10μM glibenclamide (GLIB) was added to identify the level of APD shortening attributed to KATP.

RESULTS

APD dropped more rapidly in LVW than LANG hearts during gradual deoxygenation (*Fig 1*). Between 75 to 50 %O2, LVW APD dropped at a rate of 1.33±0.84 $\%O_2$/msec while LANG APD was constant. LANG APD dropped most rapidly at 50 %O2. GLIB diminished APD shortening in LVW hearts to a rate of 0.61±0.11 $\%O_2$/msec until 45 %O2, when APD dropped rapidly (*Fig 1*). In LVW hearts with GLIB, the APD vs. $\%O_2$ curve closely mirrored the LANG curve.

CONCLUSION

APD shortens severely in LVW hearts during deoxygenation. High workload precipitates a mismatch of O2 supply:demand sooner, and to a greater extent, than in unloaded hearts. GLIB blocks KATP to decouple energetics and electrical activity to align the deoxygenation curves of loaded and unloaded hearts.



STATUS

Graduate Student

AUTHORS

Kara Garrott

Sarah Kuzmiak-Glancy

Anastasia Wengrowski

Hanyu Zhang

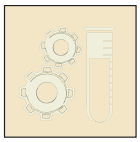
Jack Rogers

Matthew Kay

RESEARCH MENTOR/ DEPARTMENT CHAIR

Matthew Kay

BIOMEDICAL ENGINEERING



SCHOOL OF ENGINEERING AND APPLIED SCIENCE

A Contact-Lens-on-a-Chip Companion Diagnostic Tool for Personalized Ophthalmology

Maintaining contact lens cleanliness is critical to ocular health and safety. Due to prolonged contact with the eye over the course of the day and regular handling, lenses are quickly soiled with tear deposits and easily contaminated with bacteria and other microbes. As part of a contact lens care regimen, multipurpose solutions (MPS) are used to disinfect, clean, rinse, and store contact lenses between uses. However, MPS products do not take into account the fact that lens wearers have a wide range of individual tear chemistries that may affect cleaning and disinfection outcomes. In this work, we develop and demonstrate, to our knowledge, the first microfluidic system that integrates contact lens materials, MPS, and human tears at sub-μL scales in a single device to assess the efficiency of lens cleaning and disinfection for personalized contact lens care. This platform enabled the detection of significant differences in cleaning and disinfection outcomes between different individuals and between biofilm and planktonic bacteria.

STATUS

Graduate Student

AUTHORS

Allan Guan

Yi Wang

K. Scott Phillips

Zhenyu Li

RESEARCH MENTOR/ DEPARTMENT CHAIR

Zhenyu Li

SCHOOL OF ENGINEERING AND APPLIED SCIENCE

Characterization of Blood-Analog Fluids in a 180-degree Curved Artery Model

BACKGROUND

Spiral blood flow (or vortical) patterns occur in arteries with bends, curvatures and branches due to imbalances between pressure and centrifugal forces. The absence of these vortical patterns has been associated with various diseases like atherosclerosis, a leading cause of death in the U.S. [1]. Experimental investigation of such blood flow patterns requires blood-analog fluids that offer realistic response to physiological flow stimuli.

MOTIVATION AND OBJECTIVE

Spiral blood flow patterns have a role in the onset and detection of cardiovascular diseases like atherosclerosis, associated with plaque build-up in the near wall regions of curved arteries. The central objective of this study was to characterize blood-analog fluids matched for viscosity and refractive indices required for the experiments in a 180-degree curved artery model.

METHODS

The following 3-step method was used to characterize the two blood-analog fluids presented in Table 1:

1. Kinematic viscosity measurements were performed using an Ubbelohde viscometer and a rheometer (DHR-series).
2. Hydrodynamics data were acquired using two clinical pressure catheters (for pressure gradient) and one ultrasonic flow rate sensor.
3. Refractive indices were measured using a refractometer (Atago-PALRI) [2-3].

Table 1: Blood-analog fluids: Chemical compositions and summary of measurements

Chemical Components	Fluid 1 (% by volume)	Fluid 2 (% by weight)
Glycerol	20.0%	-
Saturated NaI	79.0%	-
KSCN	-	71.0%
DI Water	1.0%	29.0%
Kinematic Viscocity (Ubbelohde, v: mm^2/s)	3.59 (±0.0563%)	2.08 (±0.0142)
Kinematic Viscocity (Rheometer, v: mm^2/s)	3.27 (±0.0141%)	2.61 (±0.0004)
Density	1.75 (±0.0334%)	1.40 (±0.0031)
Refractive Index	1.4932	1.4865
Refractive index of acrylic test section: 1.481-1.503 [2]		

RESULTS

The rheological data exhibited Newtonian-fluid-like behavior and were in agreement with the Quemada (blood) model-based parameters of hematocrit and shear rate [4]. The hydrodynamic data exhibited phase-lags between the pressure gradient and the flow rate (Fig. 1) as analytically predicted by Womersley [5]. The refractive indices of the fluids are similar to acrylic test section, facilitating non-invasive laser based flow visualization.

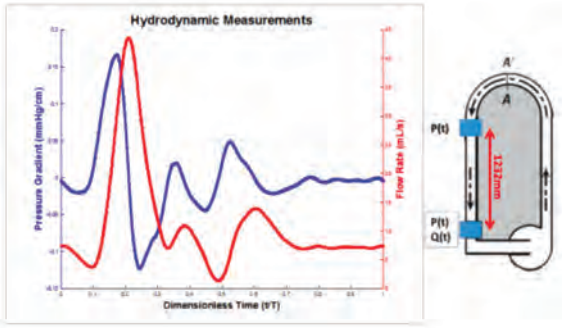


Fig. 1: Pressure and Flow Rate vs. Dimensionless Time: The carotid artery waveform showing pressure differential and flow rate for Fluid 2 (KSCN-based). To the right is a schematic drawing of the location where the pressure and flow rate measurements were recorded.

continued on following page

STATUS

Undergraduate Student

AUTHORS

Jessica Hinke

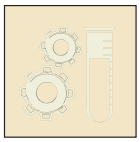
Mohammad R. Najjari

Kartik V. Bulusu

Michael W. Plesniak

RESEARCH MENTOR/ DEPARTMENT CHAIR

Michael W. Plesniak



continued from previous page

CONCLUSION

The hydrodynamic data generated in these experiments has the potential to impact hemodynamics of cardiovascular diseases under patient-specific conditions.

REFERENCES

1 Bulusu, K. V., Hussain, S. and Plesniak, M. W., Determination of secondary flow morphologies by wavelet analysis in a curved artery model with physiological inflow. *Exp Fluids*, 2014, 55:1832 DOI 10.1007/s00348-014-1832-3.

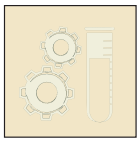
2 S.N. Kasarova et al. (2007) Analysis of the dispersion of optical plastic materials, Optical Materials 29, 1481-1490.

3 Gijsen, F.J.H., F.N. Van De Vosse, and J.D. Janssen. "The Influence of the Non-Newtonian Properties of Blood on the Flow in Large Arteries: Steady Flow in a Carotid Bifurcation Model." *Journal of Biomechanics* 32 (1999): 601-08.

4 Wyk, Stevin Van, Lisa Prahl Wittberg, Kartik V. Bulusu, Laszlo Fuchs, and Michael W. Plesniak. "Non-Newtonian Perspectives on Pulsatile Blood-analog Flows in a 180° Curved Artery Model." *Physics of Fluids Phys. Fluids* 27.7 (2015).

5 Womersley, J. R. "Method for the Calculation of Velocity, Rate of Flow and Viscous Drag in Arteries When the Pressure Gradient Is Known." *The Journal of Physiology* 127.3 (1955): 553-63.

BIOMEDICAL ENGINEERING



SCHOOL OF ENGINEERING AND APPLIED SCIENCE

Temporal salience measure for assessing image-based features

Medical imaging is a useful, minimally invasive medical procedure used in diagnostics. For example, mammograms are considered the gold standard in breast cancer diagnostics. However, like most imaging modalities, in order to obtain a diagnosis, the image must be analyzed by a trained professional, a radiologist. Since human interpretation is required, the process of diagnosis becomes subjective and can experience inaccuracies. This subjective evaluation of the quality of an image is based on whether it could present useful information for human. Thus, to quantitatively and objectively evaluate the quality of an image, in previous work, researchers measured the strength of scale-based contrast features based on human visual system (HVS), which is called the most salient features contained within a medical image, and use it to assess the task-based quality of medical image, like mammograms. Yet, the software implementation of this work had been lost for the most part. So firstly, our goal is to re-create the Perconti software, and validate it by using it with the old eye-track data to test the robust of our program. However, when people are doing the detection task, the duration of eye fixation is variant, which means the salience region will not be fixed all the time. To find out the connection of salience area with time variation, we propose to define temporal salience and compute it for a sequence of images using extensions of the original image-based salience measure. In our presentation, we intend on describing the individual components used in defining the salience measure and their respective purposes. We will discuss the process of how we go from the mammogram image to the final salience measure. The process includes the use of several image analysis techniques, from contrast masking, transformations and application of gabor filters. We will define these components and how they work.

STATUS

Graduate Student

AUTHORS

Zhen Hua

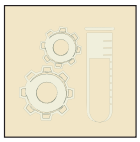
Alejandro Barrazavaldez

Shakti Gurikar

RESEARCH MENTOR/ DEPARTMENT CHAIR

Murry Loew

BIOMEDICAL ENGINEERING



SCHOOL OF ENGINEERING AND APPLIED SCIENCE

Self-Oscillating Vocal Fold Model Mechanics Associated with Aging

From infancy to old age, humans depend on their ability to voice speech in order to effectively communicate their needs. Voiced speech is produced when a critical lung pressure is achieved, forcing air through two bands of tissue stretched across the airway, known as the vocal folds (VFs). The aerodynamic forces then impart energy to the tissues of the VFs and induce self-sustained oscillations.

Growths on the VF surfaces, such as nodules and polyps, can result from the repeated and prolonged collision between the tissues of opposing VFs, and can be devastating to one's daily life. Approximately 30% of people will suffer from a voice disorder at some point in their lives with this probability doubling for those who rely heavily on their voice for work, such as teachers and singers. Further, by 2060, there is expected to be 92 million adults over the age of 64. As this large segment of the population grows, the incidence of voice disorders is expected to be between 12-35%.

The objective of this research is to study and improve synthetic VF models to replicate physiological VF motion and characteristic parameters of human speech and relate that to aging. This study includes clinical aerodynamic measures from healthy young men as well as healthy aged men to determine whether the various VF models may be differentially valuable for study of non-normative populations.

Synthetic, self-oscillating, and geometrically idealized multi-layer VF models are fabricated from Smooth-On EcoFlex silicone to exhibit material properties representative of the different layers of human VFs. Two-layer VF models are fabricated with cover layers of varying moduli of elasticities to mimic loss of muscle tone associated with aging. The VF models are evaluated experimentally in a vocal tract simulator to replicate physiological conditions.

The fabricated silicone synthetic VF models possessed modulus of elasticity values within the range of physiological values, and exhibited good repeatability in our experiments. Further, the two-layer pathological VF models exhibited mean speed quotient values within the range of healthy aged voice physiological values, indicating that silicone is an acceptable material for modeling aging VFs.

This study integrates speech science with engineering and flow physics and extends the use of synthetic VF models by assessing their ability to replicated behaviors observed in human subject data to advance a means of investigating voice production as well as the vocal changes associated with aging.

STATUS

Graduate Student

AUTHORS

Elizabeth Hubler

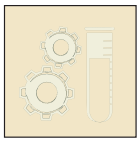
Adrienne B. Hancock

Michael W. Plesniak

RESEARCH MENTOR/ DEPARTMENT CHAIR

Michael W. Plesniak

BIOMEDICAL ENGINEERING



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Novel fabrication of Fluorescent Silk utilized in biotechnological and medical applications

Silk fibroin (SF) is a natural polymer widely used and studied for diverse applications in the biomedical field. Recently, genetically modified silks, particularly fluorescent SF fibers, were reported to have been produced from transgenic silkworms. However, they are currently limited to textile manufacturing. To expand the use of transgenic silkworms for biomedical applications, a solution form of fluorescent SF needed to be developed. Here, we describe a novel method of preparing a fluorescent SF solution and demonstrate long-term fluorescent function up to one year after subcutaneous insertion. We also show that fluorescent SF labeled p53 antibodies clearly identify HeLa cells, indicating the applicability of fluorescent SF to cancer detection and bio-imaging. Furthermore, we demonstrate the intraoperative use of fluorescent SF in an animal model to detect a small esophageal perforation (0.5 mm). This study suggests how fluorescent SF biomaterials can be applied in biotechnology and clinical medicine.

STATUS

Medical Student

AUTHORS

Dong Wook Kim

Ok Joo Lee

Seong-Wan Kim

Chang Seok Ki

Janet Ren Chao

Hyojong Yoo

Sung-il Yoon

Jeong Eun Lee

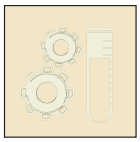
Ye Ri Park

Hae Yon

RESEARCH MENTOR/ DEPARTMENT CHAIR

Chan Hum Park

BIOMEDICAL ENGINEERING



SCHOOL OF ENGINEERING AND APPLIED SCIENCE

Ultrasound-enhanced Drug Delivery for Treatment of Onychomycosis

More than 32 million Americans are currently suffering from onychomycosis—an unattractive and potentially dangerous fungal nail disorder. There is currently no effective treatment for onychomycosis. The oral antifungal drugs take over 6 months to work and have overall failure rates of over 30% along with dangerous side effects including elevated liver function tests and hepatitis. The other current treatment option is the application of antifungal drugs to the top of the nail in a nail polish form. This treatment plan has been preferred by many patients as the drug has only non-serious, infrequently reported side-affects. However, the medicated nail polish also needs to be applied for 6 months and has a low cure rate of only up to 36%. **Our hypothesis is that ultrasound application can lead to the increased effectiveness of delivery of topically applied antifungal drugs and reduce the necessary time of application for successful treatment.** Our preliminary studies indicate that the use of ultrasound increases nail permeability by 50% for a drug mimicking compound. Additionally, we developed and tested a novel ultrasound device for treatment of onychomycosis that can be used to apply therapeutic ultrasound at different clinically-relevant parameters. Our ongoing research efforts focus on optimizing ultrasound parameters for nail drug delivery by utilizing a diffusion cell setup. People who would benefit the most from this treatment are those in their 60s or older, particularly those who suffer from diabetes, poor circulation, immunosuppressive diseases, or have cancer that is being treated with radiation.

STATUS

Undergraduate Student

AUTHORS

Alina Kline-Schoder

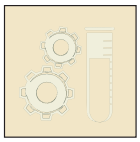
Zung Le

Vesna Zderic

RESEARCH MENTOR/ DEPARTMENT CHAIR

Vesna Zderic

BIOMEDICAL ENGINEERING



SCHOOL OF ENGINEERING AND APPLIED SCIENCE

Effects of acoustic parameters on nanodroplet vaporization

Gas-filled microbubbles encapsulated with lipids and other surfactants are highly responsive to ultrasound, which has led to their effective role as ultrasound contrast agents (UCA). However, due to their micron size distribution and short lifespan, they cannot be used for extravascular interrogations. To overcome these limitations, phase shift nanodroplets are introduced. Due to their small size and high stability, these nanodroplets have the potential to be used for tumor imaging and drug delivery. These nanodroplets undergo a phase transition from liquid to highly echogenic gaseous state when activated by sufficient acoustic energy through a process termed acoustic droplet vaporization (ADV). In this study, we synthesised lipid-coated perfluoropentane (PFP) filled nanodroplets and lipid coated perfluorobutane (PFB) filled microbubbles via sonication and mechanical agitation methods, respectively. We investigated the ADV threshold of these nanodroplets as a function of acoustic parameters such as excitation pressure, frequency, pulse length, and pulse repetition period (PRP). Since nanodroplets offer more advantages than ordinary microbubbles, we compared the acoustic reponses of vaporized nanodroplets with microbubbles at identical excitation parametrs. Our results indicate that ADV threshold varies significantly with acoustic parameters studied here such as frequency and pulse repetition periods. Furthermore, above ADV threshold, droplets showed similar responses to microbubbles.

STATUS

Graduate Student

AUTHORS

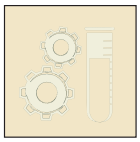
Krishna Kumar

Mitra Aliabouzar

RESEARCH MENTOR/ DEPARTMENT CHAIR

Kausik Sarkar

BIOMEDICAL ENGINEERING



SCHOOL OF ENGINEERING AND APPLIED SCIENCE

A 3D Method for Human Body Modeling and Composition Assessment

Excess body fat is a key underlying factor in the development of numerous chronic diseases, including type II diabetes, heart disease, stroke, and cancer. The primary objective of this project is to develop an accurate, reliable, convenient and cost-effective method of scanning body surface shapes and to use this technique to accurately assess the percent body fat (%BF). This technique will have the potential to be implemented in clinical or personal settings and utilized as a public health research tool. For this project, we are developing a highly innovative approach for non-rigid registration which will make it possible to capture human shapes using one commodity depth camera (Microsoft Kinect®). A supervised Machine Learning Algorithm is then used to map the resulted 3D body representation to accurate %BF. The use of Machine Learning techniques in calculating %BF is a significant innovation and will be a major improvement on the currently used methods such as Siri or Brozek equations that predict %BF based on density and cohort.

STATUS

Graduate Student

AUTHORS

Yao Lu

Samar Alsaleh

Shang Zhao

James K. Hahn

Geoffrey M. Hudson

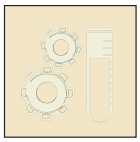
Jerome V. Danoff

Naji Younes

RESEARCH MENTOR/ DEPARTMENT CHAIR

James K. Hahn

BIOMEDICAL ENGINEERING



SCHOOL OF ENGINEERING AND APPLIED SCIENCE

NADH Fluorescence Recovery after Photobleaching (NADH-FRAP) for in-situ assessment of cardiac TCA cycle enzyme activity

Many elements can modify the proper performance of metabolic processes including during ATP production. The ability of mitochondria to produce energy is a function of both the capacity of electron harvesting in the TCA cycle and the ability to convert this into ATP. Current techniques such as standard molecular assays and fluorescence imaging do not isolate these components from each other, limiting not only the proper understanding of regional enzymatic activities but ultimately the progress of efficient therapies. The development of a technology based on the fluorescence recovery after photobleaching (FRAP) in a whole heart is proposed as a novel technique for measuring the replenishment of a fluorophore product of an enzymatic reaction after it has been photobleached with high intensity light under conditions that closely resemble *in-vivo* state. The assessment of the absolute rate of energy production through the visualization of the reduce form of nicotinamide adenine dinucleotide (NADH) is possible using NADH-FRAP. Hearts from adult rats were quickly excised and perfused. A low-power (1,5mW) and a high-power (500mW) UV light were used to monitor NADH-fluorescence and to photobleach the epicardium respectively; the signal was filtered (475±25nm) and captured using a CCD camera. Optimal parameters for imparting the photobleaching energy were determined and no tissue necrosis or unwanted phototoxicity was observed at the end of the studies, subjecting the non-destructive nature of NADH-FRAP. Likewise, three experiments were performed to study NADH-FRAP under different situations of energy demand. First, given the fact that temperature-dependency has been associated with enzymes dynamics, three temperatures ranging from hypothermia (22 and 30 °C) to normothermia (37 °C) were tested. Faster NADH production was observed during normothermia compared to hypothermia (8.05±1.02, 5.11±0.55 and 3.43±0.34 A.U./100msec, respectively). Second, considering that ATP is mostly used for contractions, the hearts were subjected to a contracting vs non-contracting situation. With a higher energy demand for contractions, NADH is produced faster than in an arrested heart (11.91±0.95 vs 8.91±0.53 A.U./100msec, respectively). Finally, the impaired ability of the TCA cycle to produce NADH after ischemia/reperfusion (IR) was measured using NADH-FRAP. NADH production is diminished after an episode of IR (8.17±1.82 vs 4.41±1.19 A.U./100msec, respectively). Accurate evaluation of TCA cycle activity in the heart is crucial for studying pathologies and therapies to enhance cardiac performance. NADH-FRAP could be used to study the pathology of a wide variety of metabolic diseases ranging from acute and chronic ischemic injury and infarction to heart failure and diabetes.

STATUS

Graduate Student

AUTHORS

Angel Moreno

Rafael Jaimes III

Sarah Glancy

Matthew Kay

RESEARCH MENTOR/ DEPARTMENT CHAIR

Matthew Kay

SCHOOL OF ENGINEERING AND APPLIED SCIENCE

Music-Based Emotion and Social Interaction Therapy for Children with Autism Using Interactive Robots

I. INTRODUCTION

The purpose of this research is to develop and evaluate a multisensory robotic therapy system to stimulate the emotional and social interactivity of children with autism. Past studies have shown that robots excel in singling out and "articulating" emotions to autistic children when compared to humans. Conversely, humans can sometimes display multiple emotions at once, as well as body movements that contradict their facial cues. This can make it difficult for an autistic child to distinguish the intended emotion, and can result in a wave of sensory overload. Moreover, as studies have shown a strong connectivity within the neural domains for emotion, music and motor skills, this research aims to integrate music into the learning environment, in hopes of observing if and how it could help children in relating body movements and gestures to specific emotions.

II. METHODOLOGY

Our interactive robotic framework involves two robots: Darwin Mini, a humanoid robot that displays dynamically varied body movements and gestures and Romo, an iPhone-rover type robot that displays facial cues corresponding to specific emotions. The testing method will begin with sitting the child down with each robot separately as each displays emotional cues corresponding to specific emotions while music is simultaneously played in the background to help the children retain the correlations. The child will then watch as each robot is guided through through a maze with specific sections that would normally invoke a sensory overload during hearing, smell, taste, sight, and balance scenarios. The child can then see which emotions each robot uses to react to these scenarios, and hopefully mimic what the robots do in a real life scenario. In order to assess the effectiveness of the robotics' interaction with the children, the emotional state of the child will be monitored throughout the time the child is interacting with the robot using a Kinect-based motion detection system and a speech analysis system, as shown in Figure 1. These systems will be able to analyze speech patterns and motion sequences to determine the level of engagement the child has with the system, as well as the emotional state of the child. Knowing the engagement and emotional state will also help the system modify the emotions being displayed if the child is determined as being in distress to help alleviate the child's emotional state.

III. DISCUSSION AND FUTURE WORK

The analysis components are still in the development stages. Looking forward, the system will be fully autonomous and sent to clinics to start trials with autistic children.

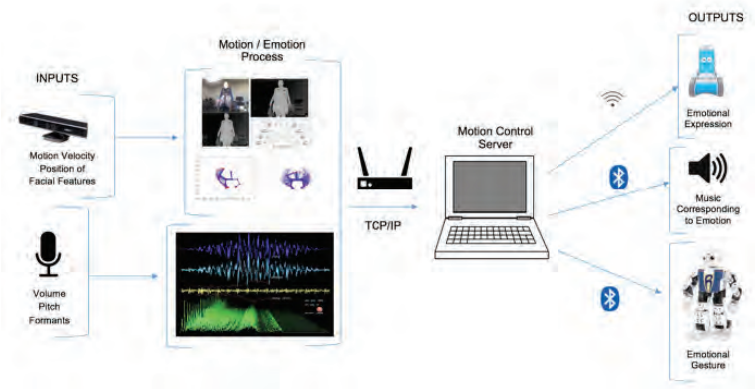


Figure 1: Block Diagram Showing Evaluation System Inputs and Responses for Live-Feedback

STATUS

Undergraduate Student

AUTHORS

Srineil Nizambad

Paul Azzi

Conor Sheridan

Matt Spadafora

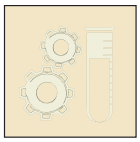
Rachael Bevill

Chung-Hyuk Park

RESEARCH MENTOR/ DEPARTMENT CHAIR

Chung-Hyuk Park

BIOMEDICAL ENGINEERING



SCHOOL OF ENGINEERING AND APPLIED SCIENCE

The application of Hierarchical Temporal Memory in Anomaly Detection

Detecting anomalous in medical field has always been an important issue, for correctly recognizing anomalous from the data such as echocardiogram images and ECG signals can help the doctor take the right action when time is limited. However , conventional methods show limited ability in both detecting anomalous accurately and in real time .This paper use a new data mining technique—Hierarchical Temporal Memory. Aiming to model the learning process of Neocortex ,HTM learns both the spatial and temporal pattern of the data , thus can analysis and detect anomalous in real time and adaptively as the data changes . Secondly , HTM uses a hierarchical learning structure , which is able to capture the spatial and temporal pattern of the data in a large scale with practical amount of memory . This research apply HTM to the medical data of echocardiogram images and ECG signals , the result proves that HTM is more powerful than prvious methods in detecting and even predicting the data pattern in real time.

STATUS

Graduate Student

AUTHORS

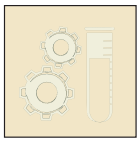
Jianghao Shen

Murray Loew

RESEARCH MENTOR/ DEPARTMENT CHAIR

Murray Loew

BIOMEDICAL ENGINEERING



SCHOOL OF ENGINEERING AND APPLIED SCIENCE

Ultrasound stimulation of insulin release from pancreatic beta cells

OBJECTIVE

Type 2 diabetes mellitus is a complex metabolic disease that has reached epidemic proportions. Controlling type 2 diabetes is often difficult as pharmacological management routinely requires complex therapy with multiple medications, and loses its effectiveness over time. Thus, new modes of therapy are needed that will directly target the underlying causes of impaired glucose homeostasis. The objective of this study is to explore a novel, non-pharmacological approach that utilizes the application of ultrasound energy to augment insulin release from pancreatic beta cells.

METHODS

Our experiments focus on determination of effectiveness and safety of ultrasound application in stimulation of insulin release from pancreatic beta cells. ELISA insulin release assay was used to determine and quantify the effects of ultrasound on insulin release in cultured INS-1 beta cells. Effects of ultrasound on cell viability were assessed by trypan blue exclusion method. Planar ultrasound transducers with center frequencies of 400 kHz,600 kHz, 800 kHz and 1 MHz were used to expose cells for a duration of 5 minutes at an intensity of 1 W/cm^2. Insulin release and cell viability results were studied as a function of temperature increase and non-thermal activity as measured experimentally and simulated using PZFlex modeling software.

RESULTS

Our results indicated that cell viability was not significantly affected during and for up to 30 minutes after treatment when cells were exposed to ultrasound frequencies of 800 kHz and 1 MHz. However, cell viability was highly reduced (by around 80-90%) when the cells were exposed to ultrasound frequencies of 400 kHz and 600 kHz($p < 0.001$). ELISA results showed that significant amounts of insulin were released from beta cells exposed to 400kHz and 600 kHz ultrasound at the cost of cell viability ($p < 0.05$). Cell exposure to ultrasound at frequency of 800 kHz resulted in approximately 4-fold increase in insulin release ($p < 0.005$). Cell exposure to ultrasound at frequency of 1MHz also showed increased insulin release (around 50%) though no statistical significance was achieved when compared to sham treatment.

CONCLUSIONS

If shown successful our approach may eventually lead to new methods in the treatment of diabetes and other secretory diseases. Our future studies will focus on application of ultrasound to human pancreatic islets to determine whether it would be possible to stimulate beta cells without stimulating other endocrine and exocrine cells of the pancreas.

STATUS

Graduate Student

AUTHORS

Ivan Suarez Castellanos

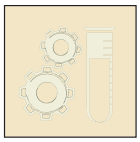
Aleksandar Jeremic

Vesna Zderic

RESEARCH MENTOR/ DEPARTMENT CHAIR

Vesna Zderic

BIOMEDICAL ENGINEERING



SCHOOL OF ENGINEERING AND APPLIED SCIENCE

Development of a Breast Thermogram Analysis Tool

Although the gold standard for breast cancer screening and evaluation is mammography, we continue to seek complementary modalities that may reduce or eliminate its requirements for radiation and physical compression. Tumor growth causes angiogenesis, which is the growth of new blood vessels to supply the tumor. The consequent increased blood flow causes the temperature to increase around the tumor and on the surface of the breast. Passive, non-contact infrared measurement of the temperature (thermography) would seem, therefore, to be a good candidate as a complementary modality for screening and/or diagnosis. Previous theoretical and simulation studies in our lab have shown that certain relationships exist between the presences of a tumor and increased localized surface temperature [1]. We are now developing a system for automated abnormality detection and analysis using thermal images of breasts. An automatic segmentation method is used to extract the breast regions from the acquired images; this limits the area to be searched for locally-warm regions. A mapping program then is used to find the region on the contralateral breast that corresponds to the ipsilateral high-temperature region. By comparing these two corresponding regions, we can decide whether the candidate abnormal region has a locally or global higher temperature. The segmentation and mapping tools have been validated with real and simulated data. A pilot study is still under review by the IRB committee, but the development of this system will benefit and speed up both the collection and analysis of the thermal images soon to be acquired.

REFERENCES

1 Jiang, Li, Wang Zhan, and Murray H. Loew. "Modeling static and dynamic thermography of the human breast under elastic deformation." *Physics in Medicine and Biology* 56.1 (2011): 187.

STATUS

Undergraduate Student

AUTHORS

Sragvi Tirumala

Shijian Fan

Abia Khan

Murray H. Loew

RESEARCH MENTOR/ DEPARTMENT CHAIR

Murray H. Loew

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Metastatic Breast Cancer and Granulomatosis with Polyangiitis

INTRODUCTION

Anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis, which includes granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA), are life-threatening vasculitis. Several studies reported that up to 8% of patients with a malignant disease had ANCA-associated vasculitis. Sixty three percent of malignancies associated with vasculitides, were hematologic in origin. In this report, we describe a rare case of a recurrent breast cancer and GPA in the same lung lesion.

CASE REPORT

A 66-year-old woman with a past medical history of scleroderma, inflammatory lung disease, and remote bilateral breast cancer status post bilateral mastectomy and chemotherapy was admitted for lung biopsy. The patient developed flu-like symptoms and was started on oral antibiotics after she was seen in an urgent care clinic. Despite this, she developed worsening dyspnea and hemoptysis. Her outpatient CT chest showed multiple lung cavities with bilateral fibrotic changes. Her initial blood test was positive for anti-neutrophil cytoplasmic antibodies (ANCA), anti-cyclic citrullinated peptide antibodies (CCP), and rheumatoid factor (RF). Because of this, she was admitted for a lung biopsy as a workup for vasculitis disease. Initially, the patient was isolated in a room with negative pressure to rule out tuberculosis (TB). Her QuantiFERON TB test and acid fast bacilli smears were negative. Later, a thoracic surgery team was consulted to perform lung biopsy through video-assisted thoracoscopic surgery (VATS). Her lung biopsy revealed metastatic breast cancer that was positive for estrogen receptor, and a necrotizing granulomatous inflammation that was consistent with granulomatosis with polyangiitis (GPA) formerly known as Wegener ‘s disease. The oncology team recommended to start her on anastrozole as a treatment for breast cancer. The rheumatology team recommended a loading dose of intravascular methylprednisone and then a maintenance dose of oral prednisone. A permacath was placed in order to start outpatient rituximab infusion as a treatment for vasculitis. In addition, she was started on trimethoprim-sulfamethoxazole for pneumocystis pneumonia prophylaxis and advised to continued her home dose of mycophenolate mofetile for treatment of scleroderma.

DISCUSSION

There are two forms of vasculitis: primary and secondary. Secondary vasculitis has been linked to several processes, such as medications side effect, allergic reaction, rheumatologic and neoplastic disease. A close relationship between the diagnosis of malignancy and onset of vasculitis has been reported in a number of patients. Most vasculitides were cutaneous leukocytoclastic (45%) and polyarteritis nodosa (36%). The exact pathogenesis of malignancy-associated vasculitis is unclear. However, we hypothesize that the inflammatory responses provoked by the underlying neoplasm might contribute to the pathogenesis. To the best of our knowledge, this is the first case report of recurrent breast cancer and development of GPA that may be representative of an association between the two condition. Clinicians must be aware of associations between various medical conditions as it most certainly changes the management. While we do not dispute that, our case may be just a co incidence of two medical conditions at once, we believe a very low incidence of GPA deserve a second look in finding an association with other medical conditions should one be present.

STATUS

Medical Resident

AUTHORS

Abeer Alfaraj

Talal Alzahrani

Aneesha Hossain

Jalil Ahari

RESEARCH MENTOR/ DEPARTMENT CHAIR

Jalil Ahari

CANCER/ONCOLOGY

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Histone demethylase KDM2B regulates lineage commitment in normal and malignant hematopoiesis

The development of the hematopoietic system is a dynamic process that is controlled by the interplay between transcriptional and epigenetic networks to determine cellular identity. These networks are critical for lineage specification and are frequently dysregulated in leukemias. Here, we identified histone demethylase KDM2B as a critical regulator of definitive hematopoiesis and lineage commitment of murine hematopoietic stem and progenitor cells (HSPCs). RNA sequencing of *Kdm2b*-null HSPCs and genome-wide ChIP studies in human leukemias revealed that KDM2B cooperates with polycomb and trithorax complexes to regulate differentiation, lineage choice, cytokine signaling, and cell cycle. Furthermore, we demonstrated that KDM2B exhibits a dichotomous role in hematopoietic malignancies. Specifically, we determined that KDM2B maintains lymphoid leukemias, but restrains RAS-driven myeloid transformation. Our study reveals that KDM2B is an important mediator of hematopoietic cell development and has opposing roles in tumor progression that are dependent on cellular context.

STATUS

Graduate Student

AUTHORS

Jaclyn Andricovich

Yan Kai

Weiqun Peng

Adlen Foudi

Alexandros Tzatsos

RESEARCH MENTOR/ DEPARTMENT CHAIR

Alexandros Tzatsos

INSTITUTE OF BIOMEDICAL SCIENCES

Pan-Cancer Analysis of RNA Editing

Analysis of the human exome and transcriptome by next-generation sequencing has improved the state of cancer research, because it allows for the detection of variant alleles that may drive tumorigenesis. The consequence of variants introduced post-transcriptionally in the transcriptome through RNA editing is that function and regulation of mRNA and miRNA can be affected, resulting in nonfunctional proteins or proteins with different functions than those intended in the genome sequence. Despite the extensive studies, many functional variants introduced through RNA editing are likely to have been missed because they occur at a low frequency, or in a tissue- or tumor-specific manner.

My research is focused on the application of RNA2DNAlign, a new sequence alignment program developed by the Horvath lab, to detect or identify novel variants through the comparison of the normal and tumor exome and transcriptome sequences from the same individual. We downloaded human genome and transcriptome datasets from individuals affected by several different cancer types: breast invasive carcinoma, liver hepatocellular carcinoma, and kidney renal clear cell carcinoma. We analyzed RNA-editing patterns within and across cancer types. Our analysis identified RNA-editing events that have not been reported before and are specific to the cancer type.

The larger implication of my research is that it may be possible to identify novel variants that drive or contribute to tumorigenesis. These variants can potentially be used to develop improved diagnostic and therapeutic molecular tools.

STATUS

Graduate Student

AUTHORS

Sonali Bahl

Anelia Horvath

RESEARCH MENTOR/ DEPARTMENT CHAIR

Anelia Horvath

COLUMBIAN COLLEGE OF ARTS AND SCIENCES

miR-141 Regulates CDC25a in Breast Cancer

BACKGROUND

The most aggressive strains of breast cancer cells are found to be ER-/PR-/HER2-. miR-141, a member of the miR-200 family of miRNAs, has been identified for its role in breast cancer progression and has demonstrated differential expression in breast cancer cell lines. Moreover, our bioinformatics analysis suggests that miR-141 targets CDC25A, a known protein phosphotase that regulates the transition of cells from G1 to S phase. We therefore hypothesize that miR-141 binds to and regulates CDC25A gene, acting as a tumor suppressor miRNA.

METHODS

qRT-PCR analysis was used to determine the expression of miR-141 in five breast cell lines, including MCF-7, T47D, MCF-10A, MDA-MB-231 and HS578T. After microdissection from breast cancer FFPE samples, we analyzed the expression of miR-141 during the progression of breast cancer, from normal, ADH, DCIS to IDC. Based on our target scan analysis, we selected ten probable targets for miR-141, including CDC25A. CDC25A expression was analyzed in two representative cell lines by qRT-PCR and Western blot, MCF-7 and MDA-MB-231 when transfected with control miR, miR-141 mimic, miR-141 inhibitor and inhibitor-mock. MTT assays were also used to explore cell viability following transfection of control miR and mimic in these same cell lines. A luciferase assay is underway to determine the binding specificity of miR-141 to CDC25A.

RESULTS

Expression of miR-141 was found to be hardly detectable in MDA-MB-231 and HS578T relative to the other three cell lines. In patient samples, miR-141 expression was downregulated in IDC compared to early stage in 40% of the cases, and upregulated in 47%, with no clear change observed in 13% (n = 15). qRT-PCR detection for CDC25A expression was decreased in MCF-7 and MDA-MB-231 cells when miR-141 was overexpressed. Western Blot analysis exhibited lower expression of CDC25A in MDA-MB-231 cells transfected with miR-141 mimic compared to those transfected with mock or inhibitor. The MTT assay revealed decreased cell proliferation in both MCF-7 and MDA-MB-231 when transfected by miR-141 mimic.

CONCLUSIONS

Overall, these data suggest that miR-141 targets CDC25A, regulating its expression. Therefore, miR-141 may provide a novel approach for decreasing cell proliferation and halting tumor growth in breast cancer.

STATUS

Undergraduate Student

AUTHORS

Dara Baker

Danielle Soberman

Tao Chen

Xiaohui Tan

Sidney W. Fu

RESEARCH MENTOR/ DEPARTMENT CHAIR

Sidney W. Fu

SCHOOL OF MEDICINE AND HEALTH SCIENCES

The Natural Surgical History of Patients with Germline Von-Hippel Lindau Gene Mutations

INTRODUCTION

Germline mutations of the Von Hippel Lindau (VHL) gene cause multiple pathologic manifestations including renal and adrenal tumors, hemangioblastomas of the brain and spinal cord, pancreatic neuroendocrine tumors, and cystadenomas of the epididymis and broad ligament. As a result, affected patients undergo numerous surgical interventions over the course of their lives. The purpose of this retrospective review is to better characterize the natural surgical history of this condition in the modern management era.

MATERIALS AND METHODS

We queried the National Institute of Health (NIH) database for all deceased patients with a history of VHL. These charts were reviewed and detailed surgical history for treatment of VHL-related manifestations was collected. Surgical procedures performed both at outside institutions and at NIH were included.

RESULTS

123 patients were identified of which 4 did not require any surgical procedures. Mean patient age at the time of first surgical procedure was 33 years (range 6-67) and mean age at death 51.5 years (18-95). The mean time that each patient was followed from first procedure to death was 18 years (0-51). The population of patients studied underwent procedures dating from 1970 to 2014. The mean number of kidney related procedures per patient who required at least one kidney procedure were 2.69. Patients underwent a mean of 5.7 (0-31) surgical procedures for treatment of VHL manifestations during their lifetime. Figure 1 presents number of procedures by organ system in our population. 72 out of 123 (58.5%) patients had at least one renal surgery for treatment of a renal tumor and 40 (32.5%) had an adrenal surgery. Only 10% (12/123) ultimately required bilateral nephrectomy and subsequent dialysis.

CONCLUSIONS

Patients with germline VHL mutations require many surgical interventions throughout a lifetime. Only a small minority of patients will eventually require bilateral nephrectomy and transplant. Brain and spinal cord tumors are the most common cause for surgical intervention followed by genitourinary tumors. These data may be useful in counseling newly diagnosed patients.

STATUS

Medical Student

AUTHORS

Shawna Boyle

David Kim

Alice Semerjian

James Peterson

W. Marston Linehan

Adam R. Metwalli

RESEARCH MENTOR/ DEPARTMENT CHAIR

Shawna Boyle

SCHOOL OF NURSING

Program Development of an End-of-Life Care Clinical Simulation Teaching Module

BACKGROUND

The need for palliative and end-of-life care (EOLC) is rising sharply globally and in the US. Although death and dying theory is taught in pre-licensure nursing programs, quality clinical opportunities for hands-on experience caring for dying patients are rare. Studies demonstrate that a controlled, emotionally safe clinical simulation experience optimizes student learning about EOLC.

OBJECTIVES

This clinical simulation-based EOLC program development and evaluation provided students a hands-on simulation-based experience in care of the dying patient. Pre-and post-surveys measured whether change occurred in learner knowledge and attitudes toward this care using an instrument with established validity and reliability.

METHODS

Participants (n=35) experienced a four-part clinical scenario alternating between intervention and guided reflection via debriefing. Change in learner knowledge and attitudes toward EOLC was measured anonymously using the *Frommelt Attitudes toward Care of the Dying Scale* (FATCOD) instrument before, immediately following and three weeks after the simulation experience.

RESULTS

Study results indicate that the experiential learning of the EOLC simulation intervention increased student's knowledge of and positive attitudes toward care of the dying, and answered the research questions posed in this study. In 12 out of 30 questions there was a statistically significant change in positivity in post-tests versus the pre-test. Areas showing positive knowledge improvement include the use of opioid medication for symptom management, comfort with the amount of time required in care of the dying as well as dynamics concerning family teaching and their involvement in the care of their dying member. Increased attitude positivity was shown concerning personal discomfort when communicating about death with dying patients, being present at the time of a patient's death and fear of establishing close relationships with dying patients.

CONCLUSIONS

With EOLC-related content being added to the 2016 *NCLEX-RN* exam the demand for EOLC training in pre-licensure programs is growing, as are nursing school enrollments nationwide. Simulation-based EOLC training is effective, but not efficient, and in some cases, not feasible. The use of state-of-the-art online instructional technologies to create structured ELNEC-based EOLC simulation experiences targeted specifically to pre-licensure nursing students will provide a consistent and efficient means to deliver sensitive content to a greater number of students while conserving key faculty resources and managing curricular imperatives, especially in accelerated BSN programs. One key barrier to training students in EOLC is lack of faculty training in this area which is being addressed by ELNEC and AACN.

STATUS

Faculty/Doctoral Student

AUTHOR

JoAnn Conroy

RESEARCH MENTOR/ DEPARTMENT CHAIR

Deborah Chapa

INSTITUTE OF BIOMEDICAL SCIENCES

Rnaseh2c is a candidate metastasis susceptibility gene in breast cancer

While 5-year survival for localized breast cancer is around 98%, survival for patients with metastatic disease plummets to 26%. This statistic indicates that the majority of mortality associated with breast cancer is due to metastatic disease, for which no targeted treatments are available. One of factors that affects whether a patient will develop metastases is genetics. We have previously shown using mouse models that the genetic background on which a tumor arises significantly influences its metastatic capacity. Furthermore, we have used a haplotype mapping approach to identify candidate genes whose expression in tumors correlates with metastasis. One of these candidates, *Rnaseh2c*, had expression positively correlated with metastasis. Interestingly, *Rnaseh2c* has not been previously linked to cancer or metastasis prior to our analysis. This gene encodes a scaffolding subunit of the Ribonuclease H2 enzyme which removes ribonucleotides that have been misincorporated into the DNA. Mutations in this gene are known to cause the neurological autoinflammatory disorder Aicardi-Goutieres Syndrome (AGS). This disease overlaps clinically with congenital viral infections and the autoimmune disease System Lupus Erythematosus. Given this information, we hypothesized that altering the expression of *Rnaseh2c* in breast cancer cells affects metastasis by engaging the immune system. Modulating the expression of RNASEH2C using shRNAs and exogenous expression vectors in a murine mammary cancer cell line resulted in significant changes in pulmonary metastasis, confirming this gene as a metastasis modifier. In order to investigate immune system involvement, we analyzed metastasis in immunocompromised mice. T cell deficiency ablated the effect of reduced RNASEH2C expression on metastasis, supporting our hypothesis that the immune system is involved in mediating the metastatic effect. We also performed mRNA-sequencing to achieve an unbiased survey of gene expression changes in response to altering RNASEH2C expression. Gene ontology pathway analysis revealed that 20% of the genes exhibiting altered expression between tumors with RNASEH2C knockdown versus overexpression are involved in immune system-related pathways including T cell signaling and antigen presentation. In addition, some of the genes with significant changes were Type I interferons, T cell surface markers, and immune response regulators. Together these results confirm *Rnaseh2c* as a novel metastasis modifier gene and support our hypothesis that its effect on metastasis is mediated by the immune system. This mechanism may highlight a new target for immune modulatory therapies to combat the devastating outcome of metastatic breast cancer.

STATUS

Graduate Student

AUTHORS

Sarah Deasy

Kent Hunter

RESEARCH MENTOR/ DEPARTMENT CHAIR

Kent Hunter

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Regulation of oncogenic phenotype by a miR-200c/141-BMI1 autoregulatory loop

The polycomb group protein BMI1 is an important regulator of breast cancer stem cell (BCSC) phenotype and is often overexpressed in breast cancer cells. Its overexpression leads to increase in BCSC fraction and therapy resistance. BMI1 functions via polycomb repressive complex 1 (PRC1) -mediated gene silencing and also via PRC1-independent transcriptional activities. BMI1 itself is posttranscriptionally regulated by several microRNAs including miR-200 family members. Here we studied cross-regulation of the *miR-200c/141* cluster by BMI1 and its relevance to oncogenic function of BMI1. We show that BMI1 functions as a transcriptional repressor of the *miR-200c/141* cluster and that BMI1 inhibitors upregulate expression of miR-200c and miR-141. Our results suggest that BMI1 directly binds to the *miR-200c/141* promoter and regulates it through transcription factor binding motifs E-box2 and Z-box1 to repress expression of the *miR-200c/141* cluster. We also show that PTC-209, a small molecule inhibitor of BMI1 strongly induces cellular senescence and transcriptionally upregulates expression of *miR-200c/141* cluster in breast cancer cells. Furthermore, inhibition of expression of miR-200c or miR-141 overcomes tumor suppressive effects of PTC-209 on oncogenic phenotype such as inhibition of migration and invasion and downregulation of BCSC phenotype.

STATUS

Faculty

AUTHORS

Manjari Dimri

Mingu Kang

Goberdhan P. Dimri

RESEARCH MENTOR/ DEPARTMENT CHAIR

William B. Weglicki

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Transoral supraglottic resection and neck dissection in definitive management of supraglottic squamous cell carcinoma

INTRODUCTION

Major advances have come about in the treatment of laryngeal carcinoma with the utilization of transoral approaches. These approaches include transoral laser microsurgery (TLM) and transoral robotic surgery (TORS). These methods are less invasive than the traditional open neck surgical approach. The aim of this retrospective study was to determine the efficacy of TLM and TORS in the treatment of supraglottic squamous cell carcinoma.

METHODS

This is a retrospective study of 19 patients with supraglottic squamous cell carcinoma managed with transoral surgery and neck dissection. The study patients were classified as follows: 1 (5.3%) stage I, 1 (5.3%) stage II, 11 (57.9%), stage III, and 6 (31.6%) stage IV. Neck dissection was done on 16 out of the 19 patients. Three patients did not undergo neck dissection, 2 for early stage (T1N0, T2N0), and the third, (T4Nx), for multiple comorbidities precluding neck dissection with prolonged general anesthesia. Three patients (15.8%) received adjuvant radiation. Adjuvant radiotherapy was given in 2 cases for advanced neck disease with multiple metastatic nodes (T3N2b and T2N2c), and in 1 for advanced T stage and management of the neck (T4Nx) because neck dissection was not done.

RESULTS

The 3-year overall survival rate for all patients included in the study was 77.4%. The 3-year disease specific survival rate was 94.7%. The 3-year distant metastasis-free survival was 70.4%.

CONCLUSION

The results of this study show that transoral partial or complete supraglottic laryngectomy and neck dissection with adjuvant radiotherapy in select cases is an effective means of treating supraglottic squamous cell carcinoma. These outcomes are comparable to historically reported survival outcomes assessing the efficacy of transoral surgical approaches for supraglottic carcinoma and are also comparable and better than historically reported survival outcomes for non-surgical management of supraglottic cancer with radiation therapy.

STATUS

Medical Student

AUTHORS

Jonathan Friedman

Nader Sadeghi

RESEARCH MENTOR/ DEPARTMENT CHAIR

Nader Sadeghi

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Inhibition of the JAK/STAT and Bcl-2 pathways enhances anti-tumor effects in an in vitro model of T cell Acute Lymphoblastic Leukemia (T-ALL)

T cell Acute Lymphoblastic Leukemia (T-ALL) is an aggressive hematologic malignancy comprising 15% of pediatric and 25% of adult cases of ALL. With current treatment options, T-ALL survival rates have reached 50-60% in adults and 85% in children. Despite great strides in the treatment, T-ALL still shows resistance to first-line therapies in over 50% of adults and 25% of children, and relapse is often chemorefractory. Mutations in the Janus Activating Kinase / Signal Transducer and Activator of Transcription (JAK/STAT) pathways and overexpression of the B cell lymphoma-2 (Bcl-2) protein are highly linked to the progression of T-ALL, and to the resistance of a number of available treatments for lymphoid malignancies. JAK/STAT is one of the main signaling pathways involved in hematopoietic cell growth. Indeed, the JAK/STAT pathway is often constitutively activated by T-ALL. The Bcl-2 pathway also plays an important role in cell survival. Overexpression of Bcl-2, an anti-apoptotic member of the Bcl-2 family, promotes cell survival by binding and neutralizing pro-apoptotic members. Inhibition of key proteins in both of these pathways has been greatly explored individually, but little is known about their combined effects on T-ALL. It is hypothesized that T-ALL manipulates both of these pathways as a means of escaping individual inhibition of either JAK/STAT or Bcl-2. Our hypothesis is that inhibiting both the JAK/STAT and Bcl-2 pathways with two small molecule inhibitors; Ruxolitinib (JAK 1/2 inhibitor) and Venetoclax (BH3 mimetic targeting Bcl-2), will inhibit T-ALL growth and survival. Proliferation of T-ALL was assessed by MTT assay and viability was measured by trypan blue and flow cytometry at 24, 48 and 72-hour time points post-treatment. Single-drug dose responses were conducted for both inhibitors. Six doses of both Ruxolitinib and Venetoclax were tested from a range of 0.156uM – 5uM for Ruxolitinib and 1.56nM- 50nM of Venetoclax. A response was seen for the three highest doses of both inhibitors (1.25uM, 2.5uM, and 5uM for Ruxolitinib and 12.5nM, 25nM, 50nM for Venetoclax). However, a synergistic effect was only achieved when combining 1.25uM Ruxolitinib with 25nM Venetoclax or 2.5uM Ruxolitinib with 12.5nM or 25nM Venetoclax. The combination dose of 1.25uM Ruxolitinib and 25nM Venetoclax demonstrated the greatest combined synergistic effect (CI<1) for all three assays at both 48 hours and 72 hours post-treatment. This optimal *in vitro* dose of 1.25uM Ruxolitinib and 25nM Venetoclax significantly lowered proliferation and viability of jurkat cells compared to no treatment ($P<0.0001$), vehicle control ($P<0.0001$) and the single-drug dose control groups ($P<0.0001$). Targeting both the JAK/STAT and Bcl-2 pathway with orally available FDA approved small molecule inhibitors could provide a novel alternative treatment for patients who relapse, fail or are resistant to first-line chemotherapeutic regiments.

STATUS

Medical Student

AUTHORS

Tara Gavcovich

Kirsti L. Walker

Myriam N. Bouchlaka

Christian M. Capitini

RESEARCH MENTOR/ DEPARTMENT CHAIR

Christian M. Capitini

CANCER/ONCOLOGY

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Incidence and characterization of pure non-urothelial cancers: A 10-year review

BACKGROUND

Bladder cancer is the sixth most common malignancy in the United States. Urothelial carcinoma makes up 90% of bladder cancer histology, which may be pure or mixed. It includes adenocarcinoma (Ad), squamous (SqC), glandular, sarcomatoid (St), micropapillary, small cell (SC) and plasmacytoid variants. Pure non-urothelial cancers have a worse overall survival when compared to urothelial cancer with mixed histologic features. However, little research has been done to characterize pure non-urothelial histologies, and there are no randomized clinical trials evaluating treatment modalities for non-urothelial cancers. This retrospective study characterizes pure non-urothelial cancers and their treatments.

METHODS

A retrospective chart review of the last 10 years was performed using data from the George Washington University Cancer Center Tumor Registry Data. Statistical analysis was performed using the Fisher's test and Kaplan-Meier survival curves.

RESULTS

Out of 449 consecutive patients with bladder cancers, 19 patients had pure non-urothelial carcinoma (4.2%): 7 SqC, 6 Ad, 3 SC, 2 lymphoma (Ly), and 1 St. SqC and Ad were more likely than SC to be diagnosed at an advanced stage (*p=0.04*), with median age of diagnosis at 53.5 years for Ad, 68 years for SC and 69 years for Sq. None of the SC metastasized. Primary treatment for 94% of patients was a surgical intervention (9 TURBT, 2 partial cystectomy, 2 radical cystectomy, and 2 nephroureterectomy); 1 received neoadjuvant therapy. 11 patients received adjuvant chemotherapy – 7 with gemcitabine-based regimens and 10 with platinumbased regimens. While not statistically significant, median overall survival varied – 404 days for Ad, 213 days for SqC, and 1567 days for SC.

CONCLUSIONS

SC was a more favorable histology when compared to SqC or Ad, presenting at an earlier stage with lower incidence of metastasis that perhaps reflected the improved overall survival. Identifying patients with more aggressive disease earlier allows for the potential role for more aggressive therapies that may result in improved outcomes. While the sample size is small, it identifies characteristics and potential differences between bladder cancer with rare histologies.

STATUS

Staff

AUTHORS

Kanika Gupta

Ehab El-Bahesh

Antoine Finianos

Brandon Clark

Samuel Simmens

Jeanny B. Aragon-Ching

RESEARCH MENTOR/ DEPARTMENT CHAIR

Jeanny B. Aragon-Ching

INSTITUTE OF BIOMEDICAL SCIENCES

Development and Optimization of a Recombinant Attenuated Salmonella Cancer Vaccine

BACKGROUND

Treatment options for high risk neuroblastoma are desperately needed since surgical options for neuroblastoma are often limited, and chemotherapy has dose-limiting side effects. Immunotherapy in the form of vaccines are attractive alternatives as they will be more precise than current therapies and can potentially confer lifelong protection against relapse.

However, despite the promise of cancer vaccines, further improvements must be made. Circulating survivin-specific cytotoxic T lymphocytes (CTLs) are detectable at low levels in high-risk neuroblastoma patients at diagnosis and it is possible to expand surviving-specific CTLs ex vivo from healthy donors and cancer patients. These CTLs show in vitro cytotoxicity towards HLA matched survivin expressing tumors.

One promising FDA-approved vaccine strategy involves the use of attenuated Salmonella strains. Due to their adjuvant-like properties they can overcome the immuno-suppressive effects of the tumor microenvironment known to be a major cause of vaccine failure.

OBJECTIVE

Our goal is to utilize attenuated Salmonella vaccine strains as a method of achieving in vivo priming of APC and expansion of survivin specific CTLs as a vaccine for the treatment of high-risk neuroblastoma.

METHODS

An array of attenuated Salmonella strains expressing different phenotypes were manufactured and tailored to serve as vaccines to elicit survivin responses. A/J mice were immunized with RASVs, serum from treated animals were assayed for the presence of survivin antibodies and splenocytes were harvested to detect survivin-specific T cells.

RESULTS AND FUTURE PLANS

Human and mouse survivin has been cloned and sequenced into 12 different candidate RASVs, and their expression verified. Animals injected with survivin protein were shown to express anti-survivin antibodies 28 days after treatment 100 fold higher than baseline levels. Current efforts are aimed at further screening of the RASVs. Candidate RASVs that produce significant cytokine and antibody responses will be tested in an immunocompetent mouse model of neuroblastoma using the cell line neuro-2a. Immune responses will be compared to mice given empty RASV and mice subcutaneously injected with a survivin protein/adjuvant emulsion.

CONCLUSION

If this approach is successful it will produce candidate RASVs that may improve the survival rates of children with neuroblastoma.

STATUS

Graduate Student

AUTHORS

Nicholas Hand

Steven Zeichner

Russell Cruz

Catherine Bollard

Roy Curtiss III

RESEARCH MENTOR/ DEPARTMENT CHAIR

David Leitenberg

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Quantitative MRI Criteria for Optic Pathway Enlargement in Children with Neurofibromatosis Type 1

Neurofibromatosis type 1 (NF1) is a common genetic disorder with an incidence of 1:3000 births.[1] About 20 percent of children with NF1 develop an optic pathway glioma (OPG), a low-grade neoplasm of the anterior visual pathway (AVP).[1] Half of children with OPGs experience visual acuity loss ranging from mild deterioration to blindness.[2] Ophthalmologic examination and magnetic resonance imaging (MRI) are currently used to determine if NF1 patients have developed secondary OPGs and need tumor treatment.[1] These methods are not free of error and can be problematic though.

Children with NF1 frequently have development delay and attention deficit disorder and cannot cooperate for ophthalmologic examination.[3] Additionally, radiologic assessment of optic nerve enlargement is often done in a subjective and qualitative manner making it difficult to establish standardized criteria to determine temporal changes in OPG size. Therefore, currently no risk stratification method using a quantitative marker or robust criteria to define presence or absence of an OPG exists which has resulted in delayed or unnecessary treatment in some patients. This study sought to assess quantitative differences in AVP structures in healthy patients, NF1 patients, and NF1 patients with OPGs in order to establish size thresholds for defining abnormally large AVP measures.

Manual MRI segmentation is a method used to delineate the boundaries of the anterior visual pathway and was used to obtain three-dimensional measurements such as optic nerve diameter and volume, optic chiasm volume, and total brain volume.[4] High-resolution T1-weighted cube MRI sequences (resolution ~0.4 x 0.4 x 0.6 mm^3) from one hundred and eighty-six children (82 control, 54 with NF1, and 50 with NF1 and OPGs) ranging from 0.3 to 18.6 years of age were obtained using a retrospective convenience sample from Children's National Medical Center and were manually segmented.

Our criteria set values above the 95th percentile from control subjects as the threshold for defining an abnormally enlarged AVP measure. Using this criteria, NF1 patients (with and without OPGs) demonstrated greater maximum values than controls for all comparisons ($P<0.05$). Patients with NF1 and OPGs had larger optic nerve diameters and volumes, optic tract volumes, and maximum optic tract diameters when compared to controls with sensitivities ranging from 68 to 80 percent. We hope these results can improve the specificity of diagnosis and care for patients with OPGs secondary to NF1.

REFERENCES

1 Avery RA, Fisher MJ, Liu, GT. Optic pathway gliomas. *J Neuro-Ophthalmol* 2011;31:269-278.

2 Avery RA, Hardy KK. Vision specific quality of life in children with optic pathway gliomas. *J Neurooncol* 2014;116:341-347.

3 Avery RA, Bouffet E, Packer RJ, Reginald A. Feasibility and comparison of visual acuity testing methods in children with neurofibromatosis type 1 and/or optic pathway gliomas. *IOVS* 2013;54:1034-1040.

4 Despotovic I, Goossens B, Philips W. MRI segmentation of the human brain: challenges, methods, and applications. *Computational and Mathematical Methods in Medicine* 2015; 1-23.

STATUS

Medical Student

AUTHORS

Rabia Idrees

Awais Mansoor

Elijah Biggs

Mohammad Alsharid

Roger J. Packer

Marius George Linguraru

Robert A. Avery

RESEARCH MENTOR/ DEPARTMENT CHAIR

Robert A. Avery

CANCER/ONCOLOGY

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Diffuse Large B-cell Lymphoma: An Unusual Presentation

Diffuse large B-cell lymphoma (DLBCL) is the most common type of mature B-cell neoplasm accounting for 28% of this group of malignancy. African-American males ages 25 to 54 years have the highest incidence of DLBCL in comparison to other groups. Patients with DLBCL usually present with pain that is secondary to rapid growth and infiltration of this tumor in relation to the surrounding organs. These patients can also manifest with B symptoms that include fever, night sweats, and weight loss. The diagnostic test for these patients is an excisional lymph node biopsy. In this report, we discuss our experience of diagnosing a patient with DLBCL who presented with an atypical picture leading to prior months of undiagnosed symptomatic disease. We discuss our approach to this patient in order to share our own challenges and the challenging diagnostic course that the patient went through. This case was an instrumental learning experience for us, and we hope that this case will shed some insight into the broad differential when faced with a patient that comes in for vague abdominal pain.

STATUS

Medical Student

AUTHORS

Mohib Khan

Talal Alzahrani

James Gehring

RESEARCH MENTOR/ DEPARTMENT CHAIR

Talal Alzahrani

SCHOOL OF MEDICINE AND HEALTH SCIENCES

The Impact of Obesity on Patient Reported Outcomes following Stereotactic Body Radiation Therapy for Prostate Cancer

PURPOSE/OBJECTIVE(S)

The relationship between obesity (Body Mass Index > 30 kg/m^2) and quality of life (QoL) following prostate cancer (PCa) radiation therapy (RT) is unknown. Stereotactic body radiotherapy (SBRT) is able to track moving targets and deliver highly conformal radiation therapy with high accuracy in a non-coplanar manner. Excess abdominal fat may compromise the precise delivery of such beams, putting surrounding organs at risk for greater radiation exposure. This study compares QoL in obese and non-obese PCa patients after SBRT.

MATERIALS/METHODS

Between February 2008 and April 2012, 88 obese and 178 non-obese patients with PCa where treated with SBRT at Georgetown University Hospital. Quality of life was assessed via the Expanded Prostate Cancer Index Composite (EPIC)-26 at baseline, 6, 12, 18, and 24 months after 5-fraction delivery of 35-36.25 Gy with the CyberKnife. Patients who received androgen deprivation therapy (ADT) where excluded from this analysis.

RESULTS

Pre-treatment characteristics of obese and non-obese patient groups were similar. Urinary and bowel function and bother scores between BMI groups were comparable at baseline and subsequent follow-ups. Sexual function was also similar at all time points between both groups. At 24 months, obese men experienced borderline clinically significant decrease in sexual function and greater sexual bother compared to non-obese patients. Fatigue and self-perceived weight change scores were significantly lower in obese patients compared to in non-obese patients at 18 months.

CONCLUSION

Obese men undergoing SBRT for prostate cancer report comparable quality of life to that reported by non-obese men after PCa-SBRT, within 24 months of treatment. Longer follow-up is required to determine the impact of obesity on cancer control.

STATUS

Medical Student

AUTHORS

Harsha Koneru

Robyn Cyr

Thomas Yung

Siyuan Lei

Brian T. Collins

Leorey Saligan

Deepak Kumar

Simeng Suy

Anatoly Dritschilo

Sean P. Collins

RESEARCH MENTOR/ DEPARTMENT CHAIR

Sean P. Collins

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Circulating miRNA Biomarkers in Early Breast Cancer Detection following Mammography

The currently accepted stepwise model of breast tumorigenesis assumes a gradual transition from normal breast epithelial cells to atypical ductal hyperplasia (ADH), to ductal carcinoma in situ (DCIS) and then to invasive ductal carcinoma (IDC). Percutaneous core needle biopsy (CNB) is the standard technique following an abnormal mammographic finding. However, CNB is less reliable in differentiating simple ADH (sADH) from ADH component coexisted with advanced lesions such as DCIS and/or IDC (cADH). Therefore, to identify and validate novel reliable molecular biomarkers is essential in order to improve the efficiency of therapeutic recommendations, as well as to minimize anxiety and unnecessary procedures. miRNAs function as tumor suppressors or oncogenes and play a critical role in cancer initiation and progression by regulating their target genes. Unlike messenger RNAs (mRNAs), which could be easily degraded, miRNAs are found to be stable not only in body fluid, but also in Formalin-Fixed, Paraffin-Embedded (FFPE) tissues. The stability of miRNAs in FFPE and blood samples suggests that they may be the ideal biomarkers for the early diagnosis and prognosis of cancer, including breast cancer. The goal of this research is to use FFPE and blood samples from the two different groups of patients, analyze the candidate miRNAs to differentiating simple sADH from cADH. In our published studies, we identified a series of miRNAs that are differentially expressed during stepwise transition of breast carcinogenesis, including miR-671-5p. In this study, we showed that the expression of miR-671-5p and miR-638 decreases in ADH, DCIS, and IDC compared with the matched adjacent normal tissues. In addition, we examined the candidate miRNA expression in two groups of ADH blood samples: 28 sADHs and 32 cADHs by qRT-PCR. We found that miR-671-5p expression was decreased in cADHs, but not in sADHs, compared with their matched normal controls. Our recent publication demonstrated that miR-671-5p functions as a tumor suppressor miRNA during breast cancer progression by regulating FOXM1 expression. Using NanoString technology, we found another miRNA, miR-545-3p to be significantly overexpressed in cADHs compared with sADH. miR-545-3p is related to Snai2, which is a member of Snail family transcription factor, encoding a transcription repressor involving in epithelial-mesenchymal transitions (EMT). Our data suggest that miRNAs, such as miR-671-5p and miR-545-3p may be potential circulating biomarkers for early breast cancer detection following mammography and CNB.

STATUS

Medical Student

AUTHORS

Alexa Lean

Jialu Lucy Yang

Xiaohui Tan

Christine B. Teal

Rachel F. Brem

Sidney W. Fu

RESEARCH MENTOR/ DEPARTMENT CHAIR

Sidney W. Fu

CHILDREN'S NATIONAL MEDICAL CENTER

Topographic histological and molecular studies of diffuse intrinsic pontine glioma treated with convection enhanced delivery

BACKGROUND

Diffuse intrinsic pontine glioma (DIPG) is a pediatric brain tumor with grim prognosis. Treatment is hindered by the impermeable blood brain barrier (BBB). To combat this, convection-enhanced delivery (CED) has been employed to deliver drugs directly into the tumor. CED's ability to bypass the BBB, has made it a promising delivery method for treatment of primary brain tumors including DIPG. OBJECTIVE: To perform analyses of sections across a CED received DIPG brain obtained at autopsy to determine cellular and molecular effect of CED. DESIGN/METHODS: Whole brain was obtained postmortem from a DIPG patient who received CED treatment (124I-8H9) six months before death. Sagittal sections representing cortex, brainstem and cerebellum were generated. Sub-blocks were produced and used for histological staining including hematoxylin and eosin (H&E), and cellular proliferation marker Ki67. Procedural MR scans were used to discriminate CED treated area versus non-CED regions. RESULTS/DISCUSSION: CED treated tumor regions were compared to untreated tumor regions. Non-CED treated tumor regions show an increased hypercellularity compared to CED-treated regions. To assess CED-induced DNA damage, histological assays were done using phopho-Histone H2A.X (phospho-H2A.X), which indicate double stranded DNA break. Our study indicated that the 124I-8H9 CED treated brain regions exhibited localized necrosis, decreased cellularity, and enhanced DNA damage. Our preliminary data is the first study to show the effect of CED in DIPG using rapid autopsy tissue. Further studies are required to investigate the molecular effects of CED treatment on tumor cell DNA.

STATUS

Graduate Student

AUTHORS

Michael Lin

E. Panditharatna

M. Kambhampati

C. Ho

S.N. Magge

R. Keating

R.J. Packer

M.M. Souweidane

J. Nazarian

RESEARCH MENTOR/ DEPARTMENT CHAIR

Javad Nazarian

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Using the ALBI Grade as a Prognostic Marker for Radioembolization of Hepatocellular Carcinoma

PURPOSE/OBJECTIVE(S)

The Childs-Pugh class (C-P) is a commonly used scoring system to measure liver function in patients with hepatocellular carcinoma (HCC). While originally developed for patients undergoing esophageal resection for varices in the setting of cirrhosis and portal hypertension, it is now a widely accepted measure of liver function. The Albumin-Bilirubin (ALBI) grading system is a model developed in 2015 to assess liver function that has eliminated the subjective measures present in C-P. We correlate the ALBI grading system and C-P classes to overall survival in our HCC patients receiving radioembolization.

MATERIALS/METHODS

With IRB approval, we retrospectively evaluated patients who received radioembolization for HCC between 2009-2014. We evaluated the albumin and bilirubin levels in our patients prior to receiving their first radioembolization (n = 121). The ALBI grades were calculated from these data with the formula (log10 bilirubin x 0.66) + (albumin x -0.085) and separated into grades based on the thresholds set in the original manuscript. These grades were then correlated to outcomes using Mantel-Cox Log analysis. The statistical comparisons were duplicated with C-P classes.

RESULTS

Median survival for C-P class A and B were 13.1 and 8.4 months ($p < 0.0005$), respectively while median survival for ALBI grades 1 and 2 were 20.9 and 11.0 months ($p < 0.0005$), respectively. Our C-P class A patient group was re-stratified using the ALBI formula and found to have two cohorts of patients with statistically significant differences in survival. The median survival between ALBI grades 1 and 2 within this patient group was 20.9 and 11.0 months ($p = 0.002$), respectively. Too few C-P class C or ALBI grade 3 patients were within our dataset for statistically significant results.

CONCLUSION

We demonstrated that the ALBI grading system is a more sensitive marker of liver function than the C-P classes in the setting of mild to moderate dysfunction. Using the ALBI grade, we identified a subset of patients that have significantly better outcomes from radioembolization for HCC within C-P class A.

STATUS

Medical Student

AUTHORS

Homan Mohammadi

Y. Abuodeh

W. Jin

J.M. Frakes

M. Friedman

B. Biebel

J. Choi

G. El-Haddad

B. Kis

J. Sweeney

R.D. Kim

S.E. Hoffe

RESEARCH MENTOR/ DEPARTMENT CHAIR

Sarah E. Hoffe

INSTITUTE OF BIOMEDICAL SCIENCES

Alternative splicing of *FGFR3* as a mechanism for prostate cancer health disparities

BACKGROUND

Prostate cancer (PCa) is the most diagnosed cancer in men and the second leading cause of male-cancer related deaths in the U.S. Dramatic ethnic disparities have been observed in PCa patients, as African-American (AA) men are 60% more likely to be diagnosed with PCa and have a 2.4 fold higher mortality rate compared to European American (EA) men. Increasing evidence suggests that, after accounting for epidemiological factors, a remaining component of this disparity is due to intrinsic genetic and biological factors. Interestingly, recent exon array data from our lab suggest that differential expression of splicing factors (SFs) and differential alternative splicing may be occurring in AA PCa. We hypothesize that differential alternative splicing involving exon 14 of the *FGFR3* gene is generating a shorter, more oncogenic variant in AA PCa. Differential splicing of *FGFR3* and increased expression of SFs in AA patients may be mechanisms contributing to AA PCa health disparities.

PURPOSE

In this study, we investigate the role of differential expression of splicing factors and exon skipping in the receptor tyrosine kinase family on prostate cancer health disparities.

RESULTS

Exon array data suggested *FGFR3* as a candidate for differential alternative splicing. Exon profiling and RT-PCR validated differential expression (exon skipping) of exon 14 of *FGFR3* in AA patient samples and cell lines. Cloning confirmed the presence of the *FGFR3-L* variant (containing exon 14) and the *FGFR3-S* variant (without exon 14) from an EA and AA PCa cell line, respectively. Enrichment of *FGFR3-S* resulted in increased cell proliferation in an AA cell line. Additionally, our exon array data predicted increased expression of seven SFs in AA patients. RT-PCR and IHC analysis validated increased expression in AA specimens. Knockdown of a subset of these SFs resulted in decreased invasion and *FGFR3* splice switching in an AA cell line.

CONCLUSIONS

We have identified an oncogene of interest, *FGFR3*, which undergoes exon skipping that is specific to AA PCa. In cell lines, this shorter isoform of *FGFR3* leads to an increased oncogenic phenotype based on proliferation assays. We have shown that AA PCa patient specimens have increased expression of specific SFs compared to EA specimens and knockdown of a subset of SFs reduces AA PCa cell invasion and causes splice switching of *FGFR3*. Thus, differential expression of SFs and exon skipping in *FGFR3* may be one mechanism contributing to the increased aggressiveness of PCa in AA patients.

STATUS

Graduate Student

AUTHORS

Jacqueline Olender

Bi-Dar Wang

Patricia Latham

Norman H. Lee

RESEARCH MENTOR/ DEPARTMENT CHAIR

Norman H. Lee

INSTITUTE OF BIOMEDICAL SCIENCES

Identification of Driver Mutations in Diffuse Intrinsic Pontine Glioma Using Comprehensive Spatial & Temporal Molecular Studies

Diffuse intrinsic pontine glioma (DIPG) is a pediatric brainstem tumor with almost 100% rate of mortality. One of the major factors contributing to the poor prognosis is our limited understanding of DIPG biology, and thus the lack of effective therapy. Up to 80% of DIPG patients harbor a de novo mutation in genes (*H3F3A*, HIST13B/C) encoding histone variants (H3.1/3 K27M). However, the identity of potential partner mutations and the hetero/homogeneity of such mutations across tumor/brain are not known. To address tumor spatial heterogeneity, we obtained nine DIPG whole brains at autopsy. A total of 158 samples from formalin fixed and frozen tissue were produced for in depth analyses. Immunohistochemical staining was generated for all tumor and normal locations within each DIPG whole brain specimen (n=64) representing 11 neuroanatomical locations. Comprehensive molecular characterization (whole exome sequencing, MiSeq deep amplicon, RNA sequencing, digital droplet PCR, and methylation profiling) of 134 samples across nine whole brains were generated to assess tumor signature and hetero/homogeneity status. Histological and molecular data were merged and subjected to detailed bioinformatics screening to identify: i) novel driver and partner mutations, ii) accessory mutations, iii) spatial distribution of these mutations, iv) fidelity of mutation clusters in extended/metastatic tumor mass, and v) identification of clonal and subclonal tumor populations in primary and extended tumors. Our study identified H3K27M associated partner mutations, which include alterations in cell-cycle (*TP53/PPM1D*) or specific growth factor pathways (*ACVR1/PIK3R1*). Mutation based-evolutionary reconstruction indicated H3K27M mutations potentially arise first and are associated with obligate partner mutations throughout the tumor and its spread, from diagnosis to end-stage disease. This data supports the necessity of partner mutations for development of DIPG. Later oncogenic alterations arise in sub-clones and often affect the PI3K pathway. Our findings are consistent with early tumor spread outside the brainstem. Importantly, we show that needle biopsies are representative of the major H3K27M associated partner mutations in primary and extended tumors in DIPGs. Our identification of spatial and temporal homogeneity of driver mutations indicates that efforts to cure DIPG should be directed at specifically targeting obligate oncohistone partnerships.

STATUS

Graduate Student

AUTHORS

Eshini Panditharatna

H. Nikbakht

L. Mikael

C-Y. Ho

M. Kambhampati

E. Hwang

T. Gayden

R. Packer

N. Jabado

J. Majewski

J. Nazarian

RESEARCH MENTOR/ DEPARTMENT CHAIR

Javad Nazarian

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Going skin deep: a case of nodulo-pustular lesions in acute myeloid leukemia

CASE DESCRIPTION

A 59 year old female with acute myeloid leukemia M7 variant presented with one week of progressive facial, head, and neck lesions preceded by a small right thigh macular lesion that had developed into a larger papulo-pustular lesion. Subsequently, a number of similar papular lesions erupted across her forehead and grew into painful nodulo-pustular lesions. Associated right sided periorbital edema prompted her hospitalization.

She has a history of recurrent upper respiratory infections, pulmonary aspergillosis, staphylococcus epidermidis vertebral osteomyelitis, diabetes mellitus, and genital herpes. For AML, she had received two remission induction cycles of idarubicin/cytarabine, then high dose ara-C five months prior to admission. For persistent neutropenia, she required daily granulocyte-colony stimulating factor. Other medications included carvedilol, lisinopril, gabapentin, lorazepam, oxycodone, and valacyclovir.

Admission vital signs were unremarkable. Examination revealed cervical lymphadenopathy and multiple nodulo-pustular lesions scattered across the forehead and neck, with a similar lesion on her right thigh. Lesions ranged from papules with surrounding erythema to 2 cm indurated erythematous nodules with central ulcerations and drainage. Right sided periorbital edema was present without visual field deficits, conjunctival injection, or extraocular movement pain. Labs included: WBC 3,720 with ANC of 2,976, hemoglobin 9.4 g/dL, platelets of 80,000, HCO_3 21 mEQ/L without anion gap, glucose 115 mg/dL, and lactate 1.5 mEq/L. A skin biopsy was obtained, and IV vancomycin, acyclovir and voriconazole were initiated due to concern for superinfection. Lesions continued to progress to pustules that eventually crusted. Biopsy revealed acute neutrophilic dermatitis. Antibiotics were discontinued and prednisone was initiated with further improvement. Two months later, she was rehospitalized for bilateral pneumonia with skin lesion recurrence, now on her chest and left wrist. Skin biopsy again confirmed acute neutrophilic dermatitis.

DISCUSSION

Sweet Syndrome is associated with acute myeloid leukemia. Though typically presenting as well-demarcated papules and plaques with surrounding erythematous base, this presentation was atypical, as lesions were predominantly nodulo-pustular. She had multiple risk factors for Sweet Syndrome that may have contributed including chronic intermittent upper respiratory infections. Even after she steroid treatment at initial presentation, she had recurrence in the setting of pneumonia, suggesting an infectious precipitant. She also received daily tbo-filgrastim, a growth factor associated with Sweet Syndrome when neutrophils rapidly increase. The patient's M7 variant of AML also provides a unique aberration that may have made her more susceptible. In patients with a combination of risk factors including URIs, AML, and G-CSF use, Sweet Syndrome may present atypically. Skin biopsy should be considered in such patients to confirm diagnosis and initiate appropriate treatment with corticosteroids.

STATUS

Resident

AUTHORS

Adrienne Poon

Minh-Hai Ngo

William B. Ershler

Jennifer Primeggia

RESEARCH MENTOR/ DEPARTMENT CHAIR

Jillian Catalanotti

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Is the force awakened? Publication trends in Oncology Big Data as phase II CancerLinQ is launched

BACKGROUND

The American Society of Clinical Oncology launched CancerLinQ project in 2010 to provide real-time data collection, mining and visualization, clinical decision support, and quality feedback. Creation of a big data software platform is currently underway to power the CancerLinQ in the phase II of the project. This would allow for evidence driven practice and rapid learning for cancer care providers. Additionally, adequate knowledge about the utility of Big Data to encourage provider utilization in high Impact Factor (IF) journals is needed. We aimed to assess trends and quality of Big Data published in Oncology.

METHODS

Peer-reviewed English papers published between 2011 and 2015 reporting on cancer and Big Data were identified using PubMed. Manual review was conducted. Cohort construction and statistical analyses were performed utilizing SPSS v 21.0 Results: We identified 325 publications, 135 met inclusion criteria in 105 journals, of which 36% (n=38) are considered specialized hematology and/or oncology journals. Specialized journals published 29.62% (40/135). Equal distribution of publications was found in clinical and basic science journals; 54 (37%) and 50 (40%) respectively. There was a trend of increased publications in clinical journals from 2012 to 2015 (16.7% to 42.9%, P = 0.39). Of the available Impact factors (IF) – the median is 3.234 (range 0.00-41.456) with 25/125 (20.0%) of available IF being > 5.00 and 12/125 (9.6%) being > 10.00 with no difference in the proportion of IF > 5.00 in clinical versus basic science journals; 11/51 (21%) versus 11/47 (23) % p = 1.00, respectively.

CONCLUSIONS

The need for further publication of studies addressing Big Data use in furthering oncology research is being met by the research community in response to the CancerLinQ as demonstrated by the rapid increase in publications. We hypothesize that this will increase the likelihood of cancer providers using CancerLinQ in the future, although an increase in publication in specialized journals and in those with high impact factors is still necessary. Currently, despite the increased trend of publications addressing Big Data in oncology, less than one-third of these publications are in specialized journals.

STATUS

Staff

AUTHORS

Hind Rafei

Benjamin Viernes

Angelike Liappis

Dalia A. Mobarek

RESEARCH MENTOR/ DEPARTMENT CHAIR

Dalia A. Mobarek

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Cracking the Case

Chest pain is one of the most common chief complaints encountered by internists. It is important to recognize less common etiologies in a young healthy patient without cardiac risk factors or associated gastrointestinal or pulmonary symptoms. This case presented a 37-year-old female without any past medical history who presented with five days of constant, progressive, central pleuritic chest pain despite non-steroidal anti-inflammatory use. She had an associated non-productive cough with exquisite tenderness to palpation from the mid sternum to the xiphisternal junction with an otherwise normal cardiopulmonary exam. Imaging revealed a widened mediastinum. Although conventionally taught to immediately associate a widened mediastinum on chest x-ray with an ascending aortic dissection, in this patient who had no alarming symptoms to suggest this diagnosis, it was important to develop a broad differential for her widened mediastinum as treatment and outcomes vary drastically. The differential can be categorized into one of the following: traumatic, infectious, inflammatory/autoimmune, neoplastic, anatomic and vascular. In this patient who denied trauma and was afebrile without a leukocytosis but had significant lymphadenopathy, the differential narrowed fairly quickly. It was further narrowed when a sternal fracture with an anterior mediastinal mass was found. A mediastinal biopsy revealed classic bi-nucleated Reed-Sternberg cells, confirming Hodgkin's Lymphoma. This case highlights the importance of creating a broad differential diagnosis for chest pain including anterior mediastinal mass in the appropriate setting. While sternal fracture without trauma is a rare cause of chest pain, clinicians should consider it especially in the presence of an anterior mediastinal mass. Sternal fractures are most commonly due to trauma. Less commonly such fractures can be due to secondary malignancy, myeloma and rarely osteoporosis, frequently in the setting of glucocorticoid use. In this patient's case, it was caused by contiguous spread of Hodgkin's disease. Osseous involvement occurs in 5-20% of patients with Hodgkin's disease, but is only observed in 1-4% of cases at initial presentation. When present at diagnosis, the sternum is the most common site affected.

STATUS

Medical Student

AUTHORS

Kendall Stone

Joseph Delio

Anne Lesburg

RESEARCH MENTOR/ DEPARTMENT CHAIR

Alan Wasserman

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Factors Contributing to the Utilization of High-Risk Clinics for Genetic Counseling and Testing Services

BACKGROUND

Lifetime risk of developing cancer is significantly increased in those with identified hereditary mutations, and panels of more than 60 genes associated with cancer susceptibility are now available. The Health Information National Trends Survey (HINTS), conducted by the National Cancer Institute, regularly surveys Americans on their knowledge of cancer-related information. Studies analyzing this survey data indicate that population awareness of cancer genetic testing services is increasing, which has largely been attributed to marketing campaigns and the media. However, few studies analyze factors that contribute to the actual utilization of these services in high-risk clinics.

HYPOTHESIS AND AIMS

We hypothesize that marketing campaigns and news media have contributed to increased awareness of genetic testing services, but the majority of patients who utilize cancer genetic services are referred by healthcare providers. Understanding the factors that promote or discourage patient utilization of these services will help us better target high-risk populations for engagement in cancer genetic services.

METHODS

To investigate the utilization of genetic services, a research survey was adapted from Cycle 3 of the 2014 HINTS and distributed to patients who attend the Ruth Paul Cancer Prevention Clinic at the GW MFA. This clinic performs hereditary cancer risk assessment, genetic counseling and testing, and provides health management recommendations based on guidelines outlined by the National Comprehensive Cancer Network. All patients attending the clinic, including those with and without cancer diagnoses, are invited to complete the survey. The 37-question survey contains four domains: (1) how the patient usually seeks health information, (2) how the patient has used media and the internet to understand cancer genetics, (3) how often the patient visits health professionals, and (4) why the patient pursued testing at the high-risk clinic.

RESULTS

Survey distribution and data collection is ongoing.

CONCLUSIONS AND FUTURE RESEARCH

Once complete, data from the survey will be compared to information collected by HINTS from the general population, and will ultimately improve population awareness of cancer genetic counseling and testing by building on strategies that promote utilization.

STATUS

Medical Student

AUTHOR

Sarit Toltzis

RESEARCH MENTOR/ DEPARTMENT CHAIR

Rebecca Kaltman

SCHOOL OF MEDICINE AND HEALTH SCIENCES

The Impact of ATR Mutations in Melanoma on Genomic Stability, Tumor Invasion Potential, and Metastasis

Throughout the day, the skin is constantly exposed to harmful UV rays. The body has various defense mechanisms to protect the skin from detrimental DNA damage, such as melanin production by melanocytes in the epidermis, as well as intracellular DNA damage repair proteins. When these defense mechanism fail, cells can accumulate multiple DNA breaks which in turn leads to genomic instability and the potential for cancer development.

This summer, I studied the impact of ATR, a kinase involved in the UV-induced ssDNA damage response, on melanoma development and progression. We propose that defects in the DNA damage response mechanism involving ATR leads to the ability to accumulate multiple mutations and speeds up melanoma progression. Dr. Ganesan's lab has already discovered that loss of ATR activity increases melanoma tumor volume, number of tumors, and number of metastases. For my project, I sought to further validate this hypothesis by studying the downstream effects of loss of ATR activity. We used RT-PCR to confirm a mouse model with the kinase domain of ATR floxed out. Additionally, using western blot analysis, we studied the level of CHK1 phosphorylation, a downstream target of the ATR DNA damage response mechanism, in ATR mutant versus ATR wild-type human melanoma cultures. Lastly, we genotyped 100 mice using PCR to collect at least 5 mice each with a ATR wt/wt, ATR fl/wt, or ATR fl/fl genotype for use in future experiments on immune cell infiltration into the tumor microenvironment. A preliminary study of T cell, B cell, and macrophage infiltration into the tumors was performed using flow cytometry.

While we were able to confirm that the ATR kinase domain had successfully by floxed out of the mouse models, we were unable to come to any further conclusions during my summer experience. More protocol troubleshooting was needed for the western blot analysis of CHK1 phosphorylation, as well as for the flow cytometry analysis of the immune cell infiltration. We successfully collected at least 5 mice in each ATR genotype category for later use in immune cell infiltration studies with flow cytometry, as well as gene expression investigation using a Nanostring immune profiling panel. While I was unable to complete the experiments for this project, positive results would suggest that ATR mutation plays a vital role in the progression of melanoma, and could be a potential therapeutic target to slow expansion of disease.

STATUS

Medical Student

AUTHORS

Katerina Yale

Chi-Fen Chen

Anand Ganesan

RESEARCH MENTOR/ DEPARTMENT CHAIR

Anand Ganesan

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Spectral Changes Caused by Radiofrequency Ablation of Cardiac Tissue

New diagnostic catheters can be developed by delivering and acquiring light through a small fiberoptic bundle. This can provide a useful real time feedback guidance to observe tissue damage caused by thermal injury used to treat cardiac arrhythmias. Yet, little is known about the exact spectral changes caused by radiofrequency ablation (RFA) in different types of cardiac tissue. We hypothesized that the most sensitive optical ranges for characterizing thermal injury can be revealed by comparing spectral information from different areas of the heart before and after RF ablation. Freshly excised porcine hearts were used to acquire and analyze excitation emission matrices (EEMs, 300-600nm with 10 nm spectral step) from ventricular muscle, left atrial endocardium, and aorta. Each type of tissue exhibited distinct EEMs that underwent reproducible changes in fluorescence and reflectance upon RF ablation. Specifically, RFA resulted in a reduction of the NADH fluorescence peak in ventricular and atrial muscle EEMs (360/460nm excitation/emission maxima). It also led to a broadening of collagen fluorescence peak in the aorta and in left atrial tissue. RFA caused an increase in diffuse reflectance (seen as widening of the EEM diagonal line) in all three tissue types. Thermal coagulation of heme-containing proteins, including different forms of myoglobin, led to a weaker absorption in the Soret band range (410-430nm). The latter was particularly noticeable in ventricular tissue but was also significant in the left atrial tissue. We conclude that EEMs provide a wealth of quantitative information that can guide the development of new optical probes to monitor tissue injury and the degree of thermal damage caused by RF ablation of different parts of the heart. *Supported by the NIH R41 HL120511 and the LuxCath-GWU Research Agreement.*

STATUS

Research Intern

AUTHORS

Mohammed AlJishi

Huda Asfour

Luther Swift

Narine Muselimyan

Marco Mercader

Narine Sarvazyan

RESEARCH MENTOR/ DEPARTMENT CHAIR

Narine Sarvazyan

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Rheumatological Disease from Cardiac Point of View: A Systematic Review

OBJECTIVES

Rheumatic diseases are associated with an increased risks of premature cardiovascular mortality. The aim of our study was to conduct a systematic review of the literature regarding the cardiovascular involvement in various rheumatic diseases. Commonly used treatments for rheumatic disease and their cardiovascular side effects were studied as well.

METHODS

Online databases (Pubmed and Medline) were searched from inception to January 2016. Search terms included: "systemic lupus erythematosus", "rheumatoid arthritis", "cardiovascular diseases", "cardiovascular mortality", "sudden cardiac death", and "atherosclerosis". Studies meeting the following criteria were included: (a) Articles are written in English language, (b) Reference to the cardiac involvement in rheumatic diseases, and (c) Articles where full text available.

RESULTS

We identified 12,336 citations. After screening retrieved citations, 160 articles were included based on the predetermined criteria. Overall, pericarditis was considered the most common finding in rheumatic disease (50%). In addition, myocarditis was more prevalent in Churg-Strauss syndrome (30%), Takayasu's disease (45%), and systemic sclerosis (25%), and coronary angiitis was more common in polyarteritis nodosa (40%), Takayasu's disease (40%), and Behcet disease (17%). Accelerated atherosclerosis has been increasingly reported especially due to chronic systemic inflammation associated with rheumatic disease. As expected, the cardiac side effects of systemic glucocorticoids are well documented and frequently seen in the management of rheumatic diseases (12%). Followed by epoprostenole (11%) and rituximab (11%).

CONCLUSIONS

Cardiovascular diseases are commonly encountered in rheumatic disease. The current systematic review was useful in describing the prevalence of cardiovascular involvement in each of the rheumatic disease. Close collaboration is needed between cardiologists and rheumatologists in managing this group of patients for overlapping conditions. Further research is needed to understand the impact of cardiovascular diseases on morbidity and mortality in rheumatic diseases.

STATUS

Research Fellow

AUTHORS

Mossab Aljuaid

Gurusher Panjrath

RESEARCH MENTOR/ DEPARTMENT CHAIR

Gurusher Panjrath

CARDIOLOGY/CARDIOVASCULAR RESEARCH

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Intranasal oxytocin administration in patients suffering from Obstructive Sleep Apnea

Obstructive sleep apnea is a condition that affects millions of people yet very few treatment options exist. People with OSA cease breathing multiple times during the night. If left untreated, besides poor sleep quality and excessive daytime fatigue, OSA can lead to more serious conditions such as hypertension, arrhythmias and other cardiovascular consequences. The current recommended treatment is continuous positive airway pressure with which many patients are poorly compliant. Previous work in the Mendelowitz lab has demonstrated a cardioprotective role of oxytocin in a rodent model of OSA. We therefore hypothesized intranasal administration of oxytocin to patients suffering from OSA can have similar benefits on autonomic function. Patients suffering from OSA underwent sleep studies on two consecutive nights. Night one served as a control while intranasal oxytocin was administered on the second night at the start of the sleep study. The recorded sleep studies were then analyzed examining differences in heart rate, oxygen saturation and air flow during apneic events between the two nights.

STATUS

Medical Student

AUTHORS

Ryan Bateman

Vivek Jain

Matthew Kay

David Mendelowitz

RESEARCH MENTOR/ DEPARTMENT CHAIR

David Mendelowitz

SCHOOL OF NURSING

Behavioral modifications in hypertension patients living in rural communities

BACKGROUND

70 million American adults are living with high blood pressure, yet only 52% have adequate control. Lifestyle modifications are effective in preventing and managing high blood pressure, but whether people with high blood pressure who live in rural areas change their lifestyles are not well understood.

OBJECTIVES

The goal for this study was to determine the current amount of exercise routinely performed by people with hypertension in rural communities. Barriers to exercise were also examined in addition to determining if there is a correlation between lack of resources in a rural setting and amount of exercise being performed. Dietary recommendations were evaluated to determine the correlation between meeting dietary recommendations and exercise.

METHODS

A descriptive design was used to recruit a convenient sample of 142 participants with a diagnosis of hypertension who live in rural areas. Participants completed a paper-pencil survey that assessed their current amount of exercise routinely performed and analyzed their dietary intake. Factors associated with exercise and dietary intake were also analyzed.

RESULTS

Among the participants, 10.8% had a normal weight, while 28.5% were overweight and 60.6% were obese. Participants who did not meet neither the moderate physical activity nor vigorous activity recommendations reported significantly higher barriers than people who met either recommendations (2.37 vs 1.91, $t=2.41$, $p<0.05$). There was no significant difference in perceived barriers between participants who did or did not do any exercise in the past month. Moreover, no significance was noted in barrier perceptions between participants who met vigorous activity recommendations or not. There were no significant associations between physical activity and consuming five or more fruits and vegetables daily, except for muscle-strengthening activities. People who met each physical activity recommendation have a tendency to be more likely to also meet dietary recommendations. Of the 142 participants, 21.8% met the recommendations of 5 or more services of fruit or vegetables per day. A large portion of participants (66.9%) noted reduction of sodium intake and most (53.5%) had been advised by a healthcare professional to do so.

CONCLUSIONS

Very few studies have examined behavioral modifications in the rural setting. The need for lifestyle recommendations to occur is prevalent. This research will provide valuable information for further research regarding behavioral modifications in those living in rural settings with chronic diseases such as hypertension. This study in particular demonstrates a correlation with those performing exercise per recommendations and not encountering barriers. It is imperative to first understand behaviors and associated factors before designing effective interventions to improve patients' blood pressure control in rural settings. This study specifically focused on one patient population thus limitations exist. More research is needed to analyze why patients do not follow dietary and exercise recommendations.

STATUS

Graduate Student

AUTHOR

Tara Brandner

RESEARCH MENTOR/ DEPARTMENT CHAIR

Debbie Chappa

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Dietary Sodium Intake: Perceptions of an Urban Heart Failure Population

BACKGROUND

Dietary sodium restriction is a mainstay of disease management and self-care in heart failure (HF). Heart failure education programs that include recommendations on limiting sodium intake are fairly variable across centers and populations. A clear assessment is lacking on efficacy of such programs in enhancing levels of patient understanding regarding recommendations on sodium intake and knowledge of sodium content in commonly consumed food items. This pilot study was designed to assess the knowledge pertaining to sodium-restricted diets in underserved, at-risk patients with chronic, stable HF at an urban, academic center.

METHODS

Adult English-speaking patients with either stable, chronic HF reduced ejection fraction (HFREF) or HF preserved ejection fraction (HFPEF) were included. Baseline characteristics such as demographics, knowledge of HF self-care including understanding of sodium intake and related health implications were collected. Subsequently, a pictorial survey was administered that asked participants to categorize food items into high-, medium- or low-sodium based on the FDA-recommended daily sodium intake of 2.4g. Unordered Pearson chi-square tests were performed for differences between each group.

RESULTS

A total of 24 participants (mean age 57.3, 58.3% male, 75% HFREF) participated in the survey. Seventy-five percent of participants had a high-school or equivalent level education and 25% had an advanced degree. Participants were able to accurately categorize foods into high-, moderate-, or low-sodium categories 74%, 36% and 63% of the time, respectively (respective 95% confidence intervals 0.69-0.79, 0.29-0.43, 0.56-0.63). These percentages differed significantly from each other ($p<0.0001$ high vs moderate, $p<0.004$ high vs low, $p<0.001$ moderate vs low).

CONCLUSIONS

Understanding of dietary sodium intake varies significantly among HF patients. Despite intensive HF education, patients were not able to accurately identify sodium content in appropriate categories. Further research is needed on barriers to understanding of dietary education and its effect on outcomes.

STATUS

Medical Student

AUTHORS

Puja Chabra

Michael Frangieh

Alexander Sullivan

Mortada Shams

Qusai Al Saleh

Freba Farhat

Gurusher Panjrath

RESEARCH MENTOR/ DEPARTMENT CHAIR

Gurusher Panjrath

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Fat Mass Is a Better Predictor of Cardiovascular Disease Risk than Biochemical Parameters in a Type 2 Diabetes Population

Endothelial dysfunction, leading to vascular complication, is a major concern in a type 2 diabetes (T2DM) and obese population. Arterial stiffness is an established predictor of endothelial health and cardiovascular disease (CVD) risk. Arterial stiffness is commonly measured by two tonometry based tests: pulse wave velocity (PWV) and pulse wave analysis (PWA), which provide the values of Augmentation index-75 (AI-75) and Augmentation Pressure (AP). Serum biochemistries are also used to monitor disease progression. In this cross-sectional study, we wanted to determine which biochemical or biophysical measure is the best overall predictor of arterial stiffness. The measures investigated were: C-Reactive Protein (CRP), IL-6, TNF-alpha, Leptin, Adiponectin, Insulin, Glucose, LDL, Non-HDL Cholesterol, BMI, Total Fat Mass, Fat Free Mass, % fat, % body water, waist circumference, hip circumference, and waist/hip ratio with PWV, AI-75, and AP.

Data from 16 subjects with Diabetes Mellitus ≤ 8 years, age 40-70 years, with HbA1c 6.0 – 9.0, and a BMI of 25 – 39.9 were analyzed.

Looking at the Pearson correlation between individual biochemical and biophysical measures, and the individual measures of Arterial Stiffness (PWV, AI-75, AP), the results show that CRP is very strongly correlated to PWV (p=0.6), and moderately correlated to AP and AI-75 (p=0.44, 0.30). Leptin is found to be relatively equally well correlated to PWV, AI-75, and AP (p=0.30, 0.34, 0.30). However, when looking at a composite AS score (from standardized versions of PWV, AI-75, and AP) versus the biophysical and biochemical measures, the only measures of significance were CRP, Fat Mass, and Hip measurements. When these values were placed in a multivariate model, the only independent predictors of AS were Fat Mass (p=.018), and Hip measurements (p=0.016). When taking the numerous measures of AS into account, it is found that Fat Mass and Hip measurements were the single best predictors of arterial stiffness, even better than any of the serum biochemistry parameters. In conclusion, if we want to determine a single factor which has a the most bearing on a type 2 diabetes subjects arterial stiffness, then degree of fat mass seems to be the best predictor even better than any of the biochemical parameters. Therefore, in our study, fat mass appears to be an important indicator of CVD risk.

STATUS

Staff

AUTHORS

Fiona Dore

Aytan Mammadova

Richard Amdur

Sabyasachi Sen

RESEARCH MENTOR/ DEPARTMENT CHAIR

Sabyasachi Sen

SCHOOL OF MEDICINE AND HEALTH SCIENCES

ACC/AHA Guideline Authors Self-Disclosed Relationships Compared to the Open Payments Database: Do Discrepancies Represent Undisclosed Conflicts of Interest?

BACKGROUND

In order to identify true conflicts of interest, accurate physician disclosures in clinical guidelines and research are necessary to characterize relationships with industry (RWI). The Patient Protection and Affordable Care Act's "Sunshine Act" requires the Center for Medicare and Medicaid Services to display payment information made by pharmaceutical manufacturers and group purchasing organizations to physicians and teaching hospitals. We tested the hypothesis that there would be discrepancies between industry-reported payments and author disclosures.

METHODS

Authors of the fifteen ACC and AHA guidelines published in 2013 and 2014 were matched to payments made during the same time period in the government database, Open Payments. Duplicate authors across guidelines were assessed independently. In the guidelines, a significant payment is ≥$10,000 within 12 months; a modest payment is <$10,000. Percent agreement was calculated; a chi square test was used to detect statistical significance.

RESULTS

Of the 203 guideline authors, 159 authors had relationships with industry. 65.4% of these relationships were disclosed representing a total of 575 disclosures. Of those disclosed relationships: 45.2% were for consulting, 39.7% were for related to research, and 5.2% were for speaking services. Industry reported 1,016 payments to these authors: 60.3% in the Other category (travel, meals, gifts, royalties), 20.5% for consulting, and 13.0% for research. These authors received a total of $16,540,202 in payments with research having the highest mean payment (Research $97,019 ± 297,923) and other having the lowest mean payment (Other $1,777 ± 9,720). Overall, mean payments were $78,888 ± 66,416 in cases of agreement and $10,775 ± 17,193 in cases of author error ($P<0.0001$). In a multivariate regression, agreement was more likely if the payment was significant or in consulting and research categories. Disagreement was higher than agreement in every category ($P<0.0001$).

CONCLUSIONS

Our analysis shows extensive industry relationships among ACC and AHA guideline authors. There is significant disagreement in every category between author disclosures and company payments, regardless of category. The two parties are more likely to agree if the payment is significant or made for research or consulting. Although RWIs are rampant, it is impossible to discern true conflicts of interest, given the difficulty in discerning the exact nature of a relationship in the current reporting system. As such, caution is advised in interpreting RWIs as COIs.

STATUS

Medical Student

AUTHORS

Ramzi Dudum

Omar Harfouch

Heather A. Young

Brian G. Choi

RESEARCH MENTOR/ DEPARTMENT CHAIR

Brian G. Choi

SCHOOL OF MEDICINE AND HEALTH SCIENCES

The Quality and Content of Health Information in Internet Websites for Patients on Chest Pain Symptoms

OBJECTIVE

Chest pain is a common symptom where causes range from benign to serious. We assess quality and content of websites for patients about chest pain that describe causes and when to seek care.

METHODS

We used five search engines (Google, Bing, Yahoo, Ask, AOL) and searched for "chest pain". For included websites, we assessed specific content potentially useful to patients with chest pain, information quality using DISCERN, HONcode and JAMA benchmark criteria, readability using four validated scores, and LIDA for accessibility, usability and reliability.

RESULTS

In 27 included websites, 96% and 81% mentioned cardiac and non-cardiac causes of chest pain, respectively, while 85% described when to seek emergency care. Only 51% of websites mentioned potential tests used to diagnose symptoms, 22% described potential treatments, and 11% mentioned consequences if treatment is delayed or avoided. Average DISCERN ratings were 20 ± 7 / 45 points (low to medium quality). 44% of websites had HONcode certification, and 11% fulfilled all JAMA benchmark criteria. Average Flesch-Kincaid Reading Ease score was 59, which is (fairly difficult to read). With LIDA, the average scores were "medium" for accessibility 83% and usability 59%, and "low" for reliability 43%.

CONCLUSION

Internet websites intended to help patients understand and triage symptoms of chest pain contain highly variable information content, and are on average of low to medium quality and difficult to read. This is concerning given that the Internet is a primary source of health information and that chest pain is a common, potentially life-threatening symptom.

STATUS

Research Fellow

AUTHORS

Abdulaziz Joury

Mashhoor Alshathr

Mohammad Alkhunaizi

Najlaa Jaleesah

Jesse M. Pines

RESEARCH MENTOR/ DEPARTMENT CHAIR

Jesse M. Pines

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Enhanced Systemic Oxidative/Nitrosative Stress and Cardiac Dysfunction in HIV-1 Transgenic Rats Receiving Combination Anti-retroviral Drug Therapy (cART)

INTRODUCTION

We determine if clinically used cART treatment promoted systemic oxidative/nitrosative stress and cardiac toxicity in HIV-1 transgenic rats (Tg).

METHODS

A protease inhibitor-based cART (atazanavir-ritonavir plus Truvada) was given orally to control (Fischer-344) and HIV-1-Tg rats at doses similar to human equivalent for 18 weeks. Plasma samples were obtained from tail-bleeding every 6 weeks; cardiac function was obtained by echocardiography.

RESULTS

cART treatment for 6 weeks led to a 40% increase in plasma 8-isoprostane (in vivo lipid peroxidation indicator) level in controls, but to a 2.6-fold elevation in HIV-1-Tg rats. Correspondently, RBC-GSSG level of cART-Tg-rats was increased 2.5-fold vs 1.4-fold for cART-controls. HIV-1-Tg rats displayed significantly higher (25-35%) levels of total plasma triglyceride and cholesterol; after 12 weeks, both lipid levels were further elevated (40-60%) in the cART-Tg-group but not in the control rats. At 18 weeks, cART treatment induced a 17.5% ($P<0.01$) lower plasma Mg in HIV-1-Tg rats, but only a 6% (NS) decrease in control rats. Concomitantly, isolated blood neutrophils from cART-Tg rats displayed significantly higher (>3-fold) basal superoxide anion activity compared to the other groups. In association, significantly higher levels (>3-fold vs. other groups) of plasma nitrotyrosine were found in the cART-Tg group. At the cardiac level, intensive staining for nitrotyrosine was seen in peri-vascular connective tissue of ventricles from cART-Tg rats consistent with increased nitrosative stress. Echocardiography detected small ($p<0.05$) decreases in systolic function (decreased left ventricular ejection fraction [LVEF] and % fractional shortening [%FS]) at 12 weeks in cART-Tg-rats; but at 18 weeks, more pronounced and significant decreases in LVEF (up to 9%) and %FS (up to 17%) were revealed. Interestingly, significant and progressive decreases in mitral valve E/A ratio were observed from 6-18 week for both Tg and cART-Tg rats indicative of early signs of LV diastolic dysfunction. A pilot effort to assess genomic changes using NGS indicated that Nrf2 (nuclear factor-erythroid-2-related factor-2) mRNA expression was reduced 50% ($p<0.05$) in cART-Tg rat livers, but HO-1 (heme oxygenase-1) expression was up-regulated. Moreover, iNOS mRNA expression was increased 2X ($p<0.01$) in the cART-Tg blood leukocytes.

CONCLUSION

HIV-1 expression conferred higher degrees of susceptibility to cART-induced oxidative/nitrosative stress and cardiac dysfunction, in part due to impaired Nrf2-mediated antioxidant response; increased HO-1 and iNOS expressions were due to excessive inflammatory/oxidative stress and might also contribute to elevated peroxynitrite formation in the cART-Tg rats (Supported by NIH-R21-HL-125038, and McCormick Center Genomic Supplemental Fund).

STATUS

Faculty

AUTHORS

I. Tong Mak

J.H. Kramer

J.J. Chmielinska

A. Horvath

C.F. Spurney

W.B. Weglicki

RESEARCH MENTOR/ DEPARTMENT CHAIR

William B. Weglicki

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Organ Turn Down at a Single Center: Donor Heart Organ Turn Down, Is It Rational?

PURPOSE OF STUDY

Donor heart selection for heart transplantation is not standardized. Donor hearts are declined for reasons including function, size mismatch, hypertrophy, and recipient factors such as mechanical circulatory support (MCS) dependence, ventilator dependence, diabetes, renal insufficiency, donor cold ischemic time (CIT), etc. It has not been substantiated as to what factors are most prevalent in donor heart turn-down for specific recipients.

METHODS USED

Between 2010 and 2015, we assessed 784 donor heart offers. We found 270 declined heart donors with a total of 307 reasons for organ decline. Poor quality was characterized by older donor age, presence of hypertension and diabetes, cardiac arrest, evidence of infection, high dosage of vasopressors/medication, etiology of death, other medical history. Duplicate offer was defined by the potential recipient being transplanted or having another donor heart offer. Human leukocyte antigen (HLA) factors were defined by unacceptable D/R HLA antigens, D/R positive crossmatches, or unavailability of serum for crossmatching. Recipient factors included the recipient refusing transplant, not being located, or too sick at time of offer. Combination transplant was defined for need of multiple organ transplants or an organ of different laterality.

SUMMARY OF RESULTS

The most common cause for donor heart turn-down was size mismatch between donor/recipient (D/R) followed by poor quality, duplicate offer, social history/CDC risk, recipient factors, HLA factors, and combination transplant. See table.

CONCLUSIONS

A majority of donor hearts are turned down for size mismatch and not quality. These hearts are most likely used by other programs where D/R size matching is appropriate. Further investigation into donors with poor quality should be pursued as some may be viewed acceptable by other programs. A donor/recipient scoring system may be helpful to minimize turned down donor hearts.

Endpoints	Reasons for Refusal (n=347)
Size Mismatch between Donor/Recipient	36.9% (128/347)
Poor Quality	25.6% (89/347)
Duplicate Offer	11.2% (39/347)
Social History/CDC High Risk	2.9% (10/347)
Recipient Factors	2.3% (8/347)
HLA Factors	7.5% (26/347)
Combination Transplant	2.0% (7/347)

STATUS

Medical Student

AUTHORS

Evan Norris

Tamar Aintablian

Michele Hamilton

Jon Kobashigawa

RESEARCH MENTOR/ DEPARTMENT CHAIR

Jon Kobashigawa

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Acute Pacing-Induced Cardiomyopathy

The first pacemaker devices became available in the late 1960s and have since become the mainstay of therapy for patients with complete heart block (1). Since that time, pacemaker implantation has risen dramatically because of both the increase in clinical indications for pacemaker use and the aging of the population. This increased use has lowered the mortality rate and improved quality of life among patients with cardiac arrhythmia (2). Artificial pacing has been associated with detrimental effects on left ventricular function in patients who require right ventricular pacing such as patients with complete heart block (3). Several animal studies have shown that right ventricular pacing reduces tissue perfusion and increases norepinephrine release in myocardial muscles (4). This results in histological changes that include myofibrillar cellular disarray and dystrophic calcifications (5). After heart block was induced by ablation and pacemakers were subsequently implanted, such histological changes in animals' hearts develop within 3–4 months. Therefore, this adverse clinical outcome has led to a phenomenon called pacing-induced cardiomyopathy (PICM). PICM is defined as a 10% reduction in the left ventricular ejection fraction (EF) over one year after pacemaker implantation, resulting in an EF of less than 50%. Other causes of cardiomyopathy should be excluded to diagnose patients with this condition (6). PICM has been reported in up to 9% of patients who have right ventricular pacing and 1% who have biventricular pacing (7). Patients with this condition usually present with symptoms of congestive systolic heart failure such as exertional dyspnea, orthopnea, paroxysmal nocturnal dyspnea, and lower extremity edema (8). A recent study revealed several factors that raise the risk of PICM such as male gender, a low EF, and a wide QRS (6). Our report describes a patient with a severe acute form of PICM and discusses the prevention and therapy of this condition.

REFERENCES

1 Nathan DA, Center S, Wu CY, Keller W. An implantable synchronous pacemaker for the long term correction of complete heart block. Am J Cardiol. 1963;11:362-367.

2 Kurtz SM, Ochoa JA, Lau E, et al. Implantation trends and patient profiles for pacemakers and implantable cardioverter defibrillators in the united states: 1993-2006. Pacing Clin Electrophysiol. 2010;33(6):705-711. doi: 10.1111/j.1540-8159.2009.02670.x [doi].

3 Thambo JB, Bordachar P, Garrigue S, et al. Detrimental ventricular remodeling in patients with congenital complete heart block and chronic right ventricular apical pacing. Circulation. 2004;110(25):3766-3772. doi: 01.CIR.0000150336.86033.8D [pii].

4 Lee MA, Dae MW, Langberg JJ, et al. Effects of long-term right ventricular apical pacing on left ventricular perfusion, innervation, function and histology. J Am Coll Cardiol. 1994;24(1):225-232. doi: 0735-1097(94)90567-3 [pii].

5 Karpawich PP, Justice CD, Cavitt DL, Chang CH. Developmental sequelae of fixed-rate ventricular pacing in the immature canine heart: An electrophysiologic, hemodynamic, and histopathologic evaluation. Am Heart J. 1990;119(5):1077-1083.

6 Khurshid S, Epstein AE, Verdino RJ, et al. Incidence and predictors of right ventricular pacing-induced cardiomyopathy. Heart Rhythm. 2014;11(9):1619-1625. doi: 10.1016/j.hrthm.2014.05.040 [doi].

7 Yu CM, Chan JY, Zhang Q, et al. Biventricular pacing in patients with bradycardia and normal ejection fraction. N Engl J Med. 2009;361(22):2123-2134. doi: 10.1056/NEJMoa0907555 [doi].

8 Nielsen JC, Andersen HR, Thomsen PE, et al. Heart failure and echocardiographic changes during long-term follow-up of patients with sick sinus syndrome randomized to single-chamber atrial or ventricular pacing. Circulation. 1998;97(10):987-995.

9 Lieberman R, Padeletti L, Schreuder J, et al. Ventricular pacing lead location alters systemic hemodynamics and left ventricular function in patients with and without reduced ejection fraction. J Am Coll Cardiol. 2006;48(8):1634-1641. doi: S0735-1097(06)01920-6 [pii].

10 Kindermann M, Hennen B, Jung J, Geisel J, Bohm M, Frohlig G. Biventricular versus conventional right ventricular stimulation for patients with standard pacing indication and left ventricular dysfunction: The homburg biventricular pacing evaluation (HOBIPACE). J Am Coll Cardiol. 2006;47(10):1927-1937. doi: S0735-1097(06)00473-6 [pii].

STATUS

Staff

AUTHORS

Sripooja Satya

Talal Alzahrani

RESEARCH MENTOR/ DEPARTMENT CHAIR

Marco Mercader

SCHOOL OF MEDICINE AND HEALTH SCIENCES

An Atypical Presentation of Takotsubo Cardiomyopathy

INTRODUCTION

Takotsubo cardiomyopathy is a condition characterized by a reversible left ventricular dysfunction that affects mostly postmenopausal women over the age of 60. The risk factors for this disease include mental or emotional stress, physical stress, winter weather, and viral infections. Therefore, this condition is linked to an up-regulation of the sympathetic nervous system.

CASE PRESENTATION

An 86-year-old woman with a history of hypertension, hyperlipidemia, and diabetes who initially presented with a one-day history of nausea, vomiting, diarrhea and abdominal pain. She was diagnosed with cholecystitis with corresponding common bile duct stone and pancreatic, hepatic duct dilation on CT. She was started on IV fluid, but developed pulmonary edema after approximately 700 mL, evidenced by an acute onset of shortness of breath. She subsequently was placed on BiPAP as well as IV Lasix. Phenylephrine was also started to maintain blood pressure. Subsequent chest x-ray showed resolving pulmonary edema. EKG showed atrial sensed ventricular paced rhythm. Troponins were <0.02, B-natriuretic peptide was elevated at 510 pg/mL. She was started on ertapenem and transitioned to ceftriaxone after sensitivities of blood cultures returned. She had an ERCP to remove the stone and further lab studies showed down trending AST, ALT, and total bilirubin.

She had a cardiac CT for further evaluation of the pulmonary edema that had occurred after receiving fluid bolus. The CT showed non-flow-limiting coronary disease, with a left ventricular ejection fraction of 35%, elevated left ventricular diastolic pressure. The CT also showed left ventricular segmental wall motion abnormality including extensive akinesia of the septum, apex, anterolateral and anterior wall, as well as hyperdynamic basal free wall and akinesia of the apical right ventricular wall. Due to the distribution of the akinesis and free wall motion abnormalities, it was concluded that this patient has biventricular Takotsubo cardiomyopathy.

This patient had Takotsubo cardiomyopathy likely as a result of a fluid bolus in the setting of acute cholecystitis. This patient improved after the ERCP and was able to be discharged home in a stable condition, with a scheduled outpatient cholecystectomy at a future date. She was also discharged on 25 mg metoprolol succinate per cardiology recommendations, with appropriate follow-up in place.

CONCLUSION

In this report, we discussed an atypical presentation of Takotsubo cardiomyopathy that was associated with biventricular akinesis.

STATUS

Medical Student

AUTHORS

Shivani Shah

Talal Alzahrani

Brian Choi

RESEARCH MENTOR/ DEPARTMENT CHAIR

Andrew Choi

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Exposure to di-2-ethylhexylphthalate affects blood pressure and electrocardiograms in mice

Di(2-ethylhexyl) phthalate (DEHP) is a plasticizer that is used in the manufacturing of FDA approved medical devices and consumer products that employ polyvinyl chloride (PVC) (1). DEHP can comprise up to 40% of the total weight of intravenous bags, and up to 80% of medical tubing. DEHP concentrations can reach 200-300 µg/mL in blood storage bags. Previous studies have identified a link between DEHP exposure and alterations in cardiomyocyte function in vitro; this study aimed to determine the adverse effects of DEHP in an in vivo model using a clinically relevant exposure. Radiotelemetry transmitters (DSI) were surgically implanted into male C57/BL/6 mice (n=8) to record blood pressure and electrocardiograms in freely moving animals. Briefly, the transmitter catheter was placed in the carotid artery to measure blood pressure and biopotential leads were routed subcutaneously to collect an ECG signal. After post-surgical recovery, animals were placed on a control diet or exposed to 200 mg/kg/day DEHP for 4-8 weeks via drinking water. Blood pressure and ECG signals were collected continuously via receivers positioned underneath the animal cages. Data was collected via DSI Dataquest A.R.T., and ECG parameters were analyzed via Ponemah software. Data analysis was performed using Graphpad (Student's t-test) with significance determined at $p<0.05$. No significant changes were noted in animal weight, heart weight, water consumption or behavior. A significant increase in systolic blood pressure was observed in the DEHP-treated animals (145± 3 mmHg) compared to the control animals (136 ± 1 mmHg). In the DEHP-treated animals there were notable increases in diastolic pressure (119 ± 5 mmHg) and mean arterial pressure (132 ± 3 mmHg). The control animals had diastolic and mean arterial pressures of 107 ± 2 and 121 ± 2mmHg respectively. We also observed significant slowing in electrical conduction between the atria and ventricle, as determined by ECG PR interval time, in DEHP-treated animals. PR interval time was 42.6 ± 0.4 ms in DEHP-treated animals versus 39.3 ± 1.1 ms in controls. However, no significant changes to QRS complex were observed. Previous reports have demonstrated that DEHP has a diminishing affect on cardiac contractility, suggesting these changes in blood pressure are possibly caused by alterations in sympathetic tone and/or increased vascular resistance. Results of comprehensive in vivo studies are necessary to guide the regulation and utilization of DEHP in medical devices.

ACKNOWLEDGEMENTS

The authors gratefully acknowledge Dr. Narine Sarvazyan for helpful discussions. This project was funded by NIH K99 ES023477 to NGP and NIH UL1TR000075 and KL2TR000076.

REFERENCES

1 Posnack, NG. 2014. The Adverse Cardiac Effects of Di(2-thylhexyl) phthalate and Bisphenol A. Cardiovasc Toxicol (2014). 14:339-357.

STATUS

Lab Intern

AUTHORS

Meredith Sherman

A. Swiercz

N. Muselimyan

L. Swift

P. Marvar

N.G. Posnack

RESEARCH MENTOR/ DEPARTMENT CHAIR

Nikki G. Posnack

INSTITUTE OF BIOMEDICAL SCIENCES

Impaired Autonomic Regulation in Posttraumatic Stress Disorder

Post-traumatic stress disorder (PTSD) is associated with a significantly increased risk of cardiovascular disease (CVD) and accumulating clinical evidence suggests that autonomic dysregulation due to sympathetic overactivity and/or parasympathetic insufficiency may contribute to progression of CVD in PTSD. Therefore, utilizing a translational approach, we sought to examine autonomic function in both a clinical PTSD population as well as in an animal model of PTSD. In experimental studies, mice were instrumented with radiotelemetry probes to evaluate autonomic indices following Pavlovian fear conditioning. Fear conditioning involves the pairing of a conditioned stimulus (e.g. tone) paired with an aversive uconditioned stimulus (e.g. foot shock) that evokes a conditioned response (e.g. freezing). Twenty-four hours following fear conditioning, spectral analysis of heart rate was performed and the low-to high-frequency ratio (LF:HF) was used as an index of sympathovagal balance. Fear conditioned animals displayed a significant increase in the LF:HF ratio relative to baseline (1.21 ± 0.46; $p<0.05$) indicating a shift in sympathovagal balance. Two weeks following fear conditioning, we assessed the contribution of sympathetic activity to the maintenance of blood pressure using the ganglionic blocker chlorisondamine (12ug/g i.p.). In response to sympathetic nervous system blockade, fear conditioned animals had a greater fall in blood pressure compared to control (Δ Systolic -71.7± 1.9 vs -39.8 ± 5.8 mmHg; $p<0.05$). Collectively, these results suggest impairments in autonomic control in an animal model of PTSD prior to the onset of CVD. Finally, these findings will be compared to an ongoing clinical study using a population of combat-related PTSD (n=13) versus age-matched controls without PTSD (n=9). Continuous elecrocardiography, beat-to-beat arterial blood pressure (BP) measurements, and 24-hour ambulatory BP measurements have been collected at rest, during, and following mental stress. In an effort to translate our pre-clinical results, these data will be analyzed for spectral analysis of heart rate variability, BP variability, and 24-hour ambulatory BP patterns.

SUPPORT OR FUNDING INFORMATION

NIH R00 HL107675-03 American Heart Association - 15CSA24340001

STATUS

Graduate Student

AUTHORS

Adam Swiercz

Jeanie Park

Lauren Hopkins

Cassandra Moshfegh

Jan Wiaderkiewicz

Colin N. Young

Paul J. Marvar

RESEARCH MENTOR/ DEPARTMENT CHAIR

Paul J. Marvar

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Dopamine D2 Receptors Regulate Wnt3 Signaling and Apoptosis in Human Renal Proximal Tubule Cells

Lack or downregulation of the dopamine D2 receptor (D2R) increases renal reactive oxygen species (ROS) production and vulnerability to renal inflammation in human renal proximal tubule cells (hRPTCs). Common single nucleotide polymorphisms (SNPs) rs6276, 6277, and 1800497 in the D2R gene (*DRD2*) are associated with decreased D2R expression and function. In hRPTCs carrying these *DRD2* SNPs, there is increased expression of profibrotic factors, production of extracellular matrix (ECM), and apoptosis. We hypothesized that the D2R plays a pivotal role in protecting hRPTCs from apoptosis and fibrosis by regulating Wnt3 signaling. hRPTC-*DRD2* SNPs cause activation of Wnt3/β-catenin pathway, proved by decreased β-catenin phosphorylation and increased expression of downstream pro-apoptotic factors Bax and FasL. Silencing D2R by *DRD2* siRNA activated β-catenin by decreasing its phosphorylation in hRPTC-D2R wild-type (WT), resulting in increased Bax and FasL expressions. These findings were reversed, including the decreased Wnt3 mRNA and protein expression in hRPTC-*DRD2* SNPs transfected with WT *DRD2* plasmid. Compared with those observed with transfection of *DRD2* plasmid, stimulation with the selective D2R agonist quinpirole produced the same effects. We also found that hRPTC-*DRD2* SNPs treated with Wnt3 siRNA prevented the increase in Bax and FasL but increased the protein expression of anti-apoptotic factors cFlar and Birc5, and decreased the number of apoptotic cells. These data show that apoptosis is increased and the Wnt3/β-catenin signals are activated in hRPTC-*DRD2* SNPs.

STATUS

Faculty

AUTHORS

Xiaoxu Zheng

Fei Han

Gaosi Xu

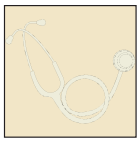
Prasad Konkalmatt

Pedro A. Jose

Ines Armando

RESEARCH MENTOR/ DEPARTMENT CHAIR

Alan G. Wasserman



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Insurance Coverage of Biologics for Moderate-to-Severe Psoriasis: A Database Review

BACKGROUND

With the variability in health insurance coverage for psoriasis systemic therapies, recent shifts in coverage for biological therapies have yet to be evaluated.

PURPOSE

To determine changes in insurance coverage of biologics for moderate to severe psoriasis between 2009 and 2014, with a focus on insurance policies as stated in prior authorization (PA) forms, coverage denials, and time course of approval process.

METHODS

A retrospective chart review was performed on patients with a diagnosis of psoriasis (ICD-9 696) seen at the George Washington University Medical Faculty Associates Department of Dermatology between January 1st 2009 and December 31st 2014. Exclusion criteria included <9% Body Surface Area (BSA), loss to follow-up, lack of biologic treatment, biologic treatment via clinical trial, and lack of health insurance. For all other patients, metrics collected included age, gender, BSA, health insurance plan, prior therapies, prescribed biologic, PA necessity, time in days between PA submission and coverage decision, and provided denial justifications.

RESULTS

864 patients with a diagnosis of psoriasis within the time period were identified, 114 of who met the inclusion criteria. PA requirement increased from 15.6% of patients prescribed a biologic in 2009 to 75.0% patients prescribed a biologic in 2014. The mean duration in days between PA submission and coverage decision from the insurance company increased from 4.0 days in 2009 to 6.7 days in 2014. PA denial rates increased from 0% in 2009 to 20.8% in 2014. The most common reason for coverage denial was failure to attempt alternative therapies prior to requesting biologics. Other denial reasons included prescribed dosage discrepancies and inability to determine benefit. Upon analysis of PA forms of 4 insurance companies, the number of coverage requirements increased from 2009 to 2014.

CONCLUSION

Insurance coverage of biologics for moderate-to-severe plaque psoriasis has become increasingly regulated between the years of 2009 and 2014. Given both the cost burden and potential benefits of these therapies, further examination of healthcare coverage and treatment accessibility is warranted for optimal patient outcomes.

STATUS

Medical Student

AUTHORS

Mai Abdelnabi

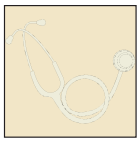
Aakash Patel

Monica Rengifo-Pardo

Alison Ehrlich

RESEARCH MENTOR/ DEPARTMENT CHAIR

Alison Ehrlich



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Thrombotic Thrombocytopenia Purpura Complicated with ANCA Induced Vasculitis

CASE PRESENTATION

A 68-year-old woman with a past medical history of hypertension and relapsing thrombotic thrombocytopenic purpura (TTP) presented with acute kidney injury. The patient had been diagnosed with TTP 9 years previously and had three subsequent relapses. The last episode was seven years prior to the biopsy. During this period, she had received treatment with steroids, Rituximab, and plasmapheresis. Non-steroidal anti-inflammatory drugs had been taken for hip pain during the previous six months but had been discontinued approximately one month before presentation due to a slight increase in serum creatinine (Cr) from a baseline of 1.0 to 1.3. Despite this measure, renal function continued to deteriorate with Cr reaching 2.3. The patient reported no fevers, chills, sinus, or respiratory symptoms. There was no skin rash. A renal ultrasound showed no evidence of hydronephrosis. Urinalysis revealed nephrotic-range proteinuria and microscopic hematuria with no dysmorphic forms. Hematologic testing revealed normocytic anemia with a hemoglobin level of 9.2. Serology revealed positive perinuclear anti-neutrophil cytoplasmic antibody (P-ANCA) at 1:320, as well as positive antinuclear antigen (ANA), anti-Smith, Sjögren syndrome-related antigen A (SSA), ribonucleoprotein (RNP), and anti-chromatin B antibodies. Anti-ds DNA antibody, cytoplasmic ANCA, and anti-glomerular basement membrane antibodies were all negative. A kidney biopsy demonstrated necrotizing glomerulonephritis with scant immune complex formation, consistent with ANCA-associated glomerulonephritis. No evidence of TTP was found on the biopsy. The patient was admitted for emergent immunosuppression, including intravenous steroids and Rituximab, resulting in improved kidney function.

DISCUSSION

TTP is characterized by microangiopathy that leads to thrombocytopenia and hemolytic anemia. Clinical manifestations include fever, severe renal disease, and neurological symptoms such as headaches, confusion, and even transient ischemic attacks. Autoantibodies against disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13 (ADAMTS 13) proteases are thought to be the most common cause of TTP. Several studies have shown an association between TTP and vasculitic disorders, including thromboangiitis obliterans, Behçet's disease, and ANCA-associated vasculitis. ANCA-associated vasculitis divided into three main disorders. These disorders are granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and eosinophilic granulomatosis with polyangiitis. Renal-Limited Vasculitis (RLV) is pauci-immune necrotizing glomerulonephritis that is considered as part of GPA and MPA. Patients with RLV may subsequently develop extrarenal manifestations of GPA or MPA. We hypothesize that patients with TTP due to autoimmune antibodies are at risk for autoimmune vasculitis. These disorders are treated successfully with rituximab and steroids.

STATUS

Staff

AUTHORS

Talal Alzahrani

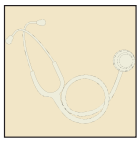
Najet Naser

Raeva Malik

Helen P. Cathro

RESEARCH MENTOR/ DEPARTMENT CHAIR

Helen P. Cathro



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Perioperative aspirin recommendations in children with fenestrated fontan undergoing adenotonsillectomy

OBJECTIVE

Pediatric patients who have undergone the Fontan procedure are often on a long term aspirin regimen which can complicate perioperative management. In high risk procedures such as adenotonsillectomy, hemorrhage can be a significant complication and aspirin use may increase the risk. There is a need for evidence-based protocol on how to manage aspirin intake in the perioperative period for Fontan patients. We report the case of a patient with Fontan palliation who underwent adenotonsillectomy and presented with postoperative hemorrhage.

METHODS

PubMed was searched for guidelines, case reports, and reviews on pediatric Fontan patients, adenotonsillectomy, and perioperative aspirin cessation.

RESULTS

Current literature lacks a consensus on perioperative management of aspirin for patients on a long term aspirin regimen. Pediatric patients who have undergone the Fontan procedure are at an increased risk of thrombosis which suggests that aspirin should be continued perioperatively, except during high risk procedures where there is increased risk of hemorrhage. Hemorrhage is a significant but uncommon complication of adenotonsillectomy and does not appear to be increased in high-risk patients with comorbid conditions. However, there is need for more updated evidence-based literature on aspirin and bleeding complications following adenotonsillectomy.

CONCLUSION

The current literature does not offer guidance regarding the ideal perioperative management of aspirin for patients with aspirin dependent cardiac conditions, such as those status post Fontan repair. Retrospective evaluation of current management and prospective protocols should be studied to aid in the management of this growing population.

STATUS

Medical Student

AUTHORS

Mariam Ashraf

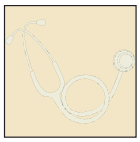
Pamela Mudd

Jamie Schwartz

Karen Thompson

RESEARCH MENTOR/ DEPARTMENT CHAIR

Pamela Mudd



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Health Communication Experiences of Youth with Type 1 Diabetes

BACKGROUND

Effective communication between adolescents/young adults (AYAs) with type 1 diabetes (T1D) and healthcare providers (HCPs) is essential to optimize health outcomes. Understanding AYA preferences for healthcare interactions can help HCPs more effectively engage AYA patients.

OBJECTIVE

To gain insight into AYA-HCP communication and identify factors that AYAs with T1D value when working with HCPs.

METHODS

As part of a longitudinal study, 20 AYAs (M age=18.8±1.5 yrs; 70% female; 65% Caucasian) with T1D receiving care in a pediatric diabetes clinic (n=5 HCPs) participated in a qualitative interview and completed the Patient Assessment of Chronic Illness Care (PACIC). Interviews (M length=13.9±5.1 min) were recorded, transcribed, and coded by two independent coders to identify themes. Hemoglobin A1c (M=8.5±1.7%) was taken from medical records.

RESULTS

Themes emerged related to HCP interaction style, support for autonomy, comfort with disclosure, and difficulties when glycemic control was poor. AYAs valued a straightforward approach to T1D care, with HCPs who encouraged shared decision-making and were directed towards AYAs instead of parents. AYAs perceived higher quality communication when HCPs took interest in their lives beyond T1D. Most AYAs were comfortable disclosing risky behavior (e.g. sexual activity, alcohol use) but preferred HCPs to initiate these conversations. Most participants had not discussed transition to adult care with their HCP but reported general confidence in planning for transition. AYAs with A1c >8.5% endorsed external stressors affecting T1D management and some felt HCPs were less supportive when glycemic control was poor. On the PACIC, participant satisfaction with T1D care was generally high (M PACIC score=3.57±.57). Higher A1c was associated with lower decision support by HCPs (r=-.49, p<.05). Participants who changed HCPs during the study (n=4) also reported lower decision support (p<.05) and were more likely to describe their HCP as impersonal or punitive.

CONCLUSIONS

Results suggest AYAs desire collaborative, consistent HCP relationships, but need HCPs to initiate discussions about risky behavior and healthcare transition. Given low decision support among AYAs with higher A1cs or HCP inconsistency, HCPs working with these patients should encourage self-efficacy and promote organization of care. Results should be replicated in a more diverse sample of AYAs with T1D to further inform key themes related to HCP relationships in youth.

STATUS

Medical Student

AUTHORS

Katherine Baumann

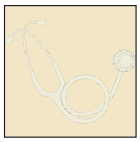
MaryJane Simms

Fran R. Cogen

Maureen Monaghan

RESEARCH MENTOR/ DEPARTMENT CHAIR

Maureen Monaghan



SCHOOL OF MEDICINE AND HEALTH SCIENCES

The Optimal Neurosurgical Management of Unstable High Thoracic Spine Fractures

Fractures of the upper thoracic spine, T1-T5, provide a challenging surgical environment, even for the most skilled spinal surgeons. These fractures are difficult to access because of the surrounding structures unique to this location such as the heart, the great vessels, and the apices of the lungs. Currently, these high thoracic fractures can be approached in a variety of ways—anterior thoracotomy, lateral extracavitary, posterolateral, or a combination of each of these. Through this study, the authors intend to present an algorithm for the challenging surgical management of T1-T5 pathology resulting in instability or spinal cord injury.

Herein, the authors present a series of 9 patients who presented with T1-T5 pathology resulting in spinal cord compression or unstable fractures that were managed surgically through these various approaches. This analysis compares fusion rates and the perioperative complication rates associated with each of these surgical techniques. This investigation will also analyze and compare pre- and postoperative neurological examinations, as well as functional ability.

From this study, the authors demonstrate: improvement in overall functional ability, successful fusion rates for all approaches, and no major complications with any case in this series. Additionally, based on our series it was determined that T1-T2 pathology was best managed with the lateral extracavitary approach, whereas T3-T5 pathology was best managed with an anterior thoractomy. However, in the setting of either solely posterior or solely posterolateral pathology with an intact spinal column, a simple posterior decompression with instrumentation was sufficient for stabilization and fusion.

STATUS

Medical Student

AUTHORS

James Boddu

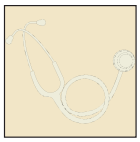
John F. Hamilton

Aaron Danison

Joy Rostron

RESEARCH MENTOR/ DEPARTMENT CHAIR

John F. Hamilton



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Patients with High Educational Attainment Are More Likely to Have Screening for Hepatitis C Virus

INTRODUCTION

Approximately 3 million people in the United States are afflicted with chronic Hepatitis C virus (HCV) infection. Infection is most prevalent in patients born between 1945-1965, and the African American community is disproportionately affected. A screening test is available and recommended, but many patients with HCV infection are unaware that they are infected. There are many obstacles to obtaining preventative care, and a lower level of education has been associated with decreased access. This study evaluated the impact of education level on access to HCV screening in a historically underserved community.

METHODS

Individuals attending a health exposition in August 2015 sponsored by the Rodham Institute completed an anonymous survey. The exposition was hosted in an urban setting with a predominantly African-American population. The survey included questions regarding demographics, access to care, insurance status, and HCV screening and awareness. Responses were excluded if education level was not specified or any questions went unanswered. Statistical analysis was performed using Fisher's exact test, with significance set at $p < 0.05$.

RESULTS

There were 102 respondents. Ninety-two (90.2%) completed the HCV screening and education questions and were included in the study. Thirty (32.6%) had a college degree; 19 (63.3%) of them had discussed HCV screening with their primary care providers. Sixty-two (68.8%) had high school education or less and 24 (38.7%) discussed HCV screening with their doctor ($p<0.0440$). There were 27 respondents born between 1945 and 1965. Twelve (44.4%) had a college education and 15 (55.6%) had less. Within this cohort, 10 (83.3%) college-educated respondents and five (33.3%) of the others had discussed HCV screening with the primary doctor ($p<0.0185$).

DISCUSSION

The African-American population is disproportionately affected by HCV, and many of these patients are unaware of their infection status. Our study found that in this underserved community, those with higher education were more likely to discuss HCV screening with their primary care provider than those without. Interestingly, this trend was more pronounced among the 1945-1965 birth cohort, in whom universal screening is recommended. Although our study may be limited by a small sample size, it highlights that access to higher education may be associated with increased knowledge of HCV and availability of screening. It is imperative that physicians continue to discuss HCV screening with all at-risk patients in order to spread awareness and reduce morbidity. The study demonstrates that education is an important social determinant of health.

STATUS

Medical Student

AUTHORS

Shreya Chablaney

Matthew Caldis

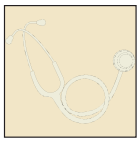
Kamal Baig

Timothy Dougherty

Marie Borum

RESEARCH MENTOR/ DEPARTMENT CHAIR

Marie Borum



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Are repeat outpatient ketamine infusions associated with cognitive dysfunction?

INTRODUCTION

Outpatient ketamine infusions can be effective in relieving severe neuropathic pain for a period of weeks or months. The NMDA receptor is involved in learning and memory and antagonists such as ketamine may be associated with cognitive impairment (1,2). The objective of this study is to investigate whether repeat outpatient ketamine infusions are associated with cognitive dysfunction as measured by the Manos 10-point clock test, a validated screening tool for cognitive dysfunction(3).

METHODS

With IRB approval, patients undergoing repeat outpatient ketamine infusions were asked to complete a Manos 10 point clock test before and after each ketamine infusion and on the follow up clinic visit 2 to 4 weeks after the last infusion. The clock is scored using the Manos 10 point clock drawing criteria. Intact cognition was a score of 10, probable cognitive deficit, less than 8, and severely impaired at less than 4.

Statistical analysis was done in two parts to evaluate the primary and secondary questions.

Mean clock score, BMI, age, and ketamine dose were calculated across days 1-3 and times (pre,post), so there would only be 1 clock score and 1 covariate score for BMI, age, and dose for each subject at each episode. For the primary question of whether there is a change in cognition associated with additional episodes of care, we used fixed effects mixed model regression, with clock scores as the dependent variable. We were particularly interested in the adjusted effect of episode of care with later episodes' clock scores being compared to episode 1. A significant effect would indicate that cognition changes over time within subjects. For the secondary questions, in order to determine whether the clock score pattern across episodes differed by age, ketamine dose, BMI, race, sex, or the presence of opioids or antidepressants, we used a random effects mixed model including each of the above variables as covariates, along with episode. If the term was significant, it meant that the pattern of clock scores across episodes of care differed across levels of the indicator variable.

RESULTS

Each patient was given ketamine infusions for 3 consecutive days constituting one episode. These episodes were repeated 4 to 16 weeks apart. Data from 60 patients, who collectively had 124+ repeat episodes, were collected. In the final adjusted fixed effects model, episodes 4 (p=.037) and 6 (p=.039) both had significantly lower clock scores than episode one. In the random effects mixed model, ketamine dose (mg/kg) was significantly positively associated with clock scores (p=.008): for each .1 mg/kg increase in dose, the clock score was .23 points higher. Other findings with the random effects model assessed use of adjuvant medications in the setting of the infusions. Clock scores among patients receiving opioids were significantly lower than those for patients without opioids starting with episode 4. Also those who did use antidepressants concurrently, had clock scores that declined more across episodes than those without antidepressants.

CONCLUSION

Ketamine use may be associated with decreased cognition. In our study, patients with neuropathic pain receiving repeat outpatient infusions showed lower cognitive test scores after the 4th episode likely due to outliers in the data given the small sample size for each episode after the 4th episode of infusion. Analysis with the random effects model showed that dose had a positive correlation with cognitive test scores, while concurrent use of opioids or antidepressants had a negative correlation.

STATUS

Medical Student

AUTHORS

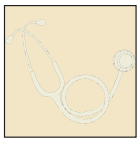
Shawn Chawla

May Chin

Richard Amdur

RESEARCH MENTOR/ DEPARTMENT CHAIR

May Chin



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Clarity or Confusion? A Comparative Analysis of the Usage of "Allow Natural Death" in State Polst Forms

Translating advance care planning discussions into actionable medical orders is a perennial challenge for providers caring for seriously ill patients. "Allow Natural Death" (AND) has been endorsed as an alternative to the traditional "Do Not Resuscitate" (DNR) order. Questions as to the clarity of its meaning exist however, and the frequency with which providers and institutions use AND is largely unknown. One place where AND terminology has been introduced is the Physician Orders for Life-Sustaining Treatment (POLST) form. State POLST forms were analyzed to quantify and objectively characterize uses of AND orders. POLST forms for all states with existing programs were assessed for use of the phrase "Allow Natural Death." Incidences of AND were categorized with respect to surrounding language, instructions for medical interventions, and clinical circumstances dictating activation of the order. 45 states were identified as having POLST programs; 6 state forms were undergoing revision or had been withdrawn from public circulation at the time of study. 23 of the 39 state forms in active use (59%) utilized AND at least once as a medical order. 21 states (91%) used AND synonymously with DNR or Do Not Attempt Resuscitation, while 2 states (9%) used AND synonymously with Comfort Measures Only, an order dictating a broader set of limitations to medical interventions. Among states using AND synonymously with DNR, 16 (76%) explicitly prohibited defibrillation, while the remaining 5 (24%) did not address it. 17 AND/DNR orders (81%) were specified as being applicable to a person without pulse and respiration, with the remaining 4 (19%) applicable to one without pulse or respiration. Allow Natural Death" orders are now employed by a majority of state POLST forms. Our results confirm the wide variability in the meaning and use of AND orders, specifically with respect to the scope of medical interventions they address and the clinical conditions under which they are activated. Ambiguity continues to exist with this new terminology; we advise caution to institutions and providers considering use of AND language in medical orders, as the aforementioned discrepancies may contribute to misunderstandings and induce critical errors during emergent clinical situations.

STATUS

Medical Student

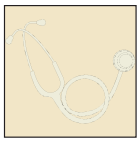
AUTHORS

Daniel Chen

Daidre Azueta

RESEARCH MENTOR/ DEPARTMENT CHAIR

Daniel Chen



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Is Androgen Excess Masked in Alopecia Areata Patients: a retrospective data analysis of 1,587 patients

Studies on the pathophysiology and comorbidities associated with alopecia areata (AA) are limited. The purpose of this study was to determine the prevalence of androgen excess in AA and its subtypes, in relation to demographics and comorbidities. Medical records of 1,587 Patchy AA, AT, AU, and ophiasis patients seen in the Department of Dermatology at the Cleveland Clinic Foundation in Ohio between 2005 and 2015 were reviewed. Out of this cohort, 226 patients met the inclusion criteria. There is evidence that patients with AA had significantly greater prevalence of polycystic ovary syndrome (PCOS) than the general population ($p<0.001$). Androgen excess was identified in 42.5% ($n=96$) of the 226 patients with AA or any subtype ($p<0.001$). The androgen excess group was significantly more likely to present with irregular menses, hirsutism, adult acne, PCOS, and/or ovarian cysts ($p<0.001$). This study was limited by being retrospective. Our study demonstrated that AA is associated with androgen excess.

STATUS

Medical Student

AUTHORS

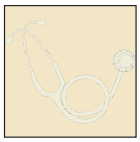
Cheyana Ranasinghe

Wilma Bergfeld

Melissa Piliang

RESEARCH MENTOR/ DEPARTMENT CHAIR

Wilma Bergfeld



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Elucidating the Mechanism of CXCL5 on Inducing Differentiation of Fibroblasts into Myofibroblasts in Pediatric CRS Sinus Mucosa

Submucosal glandular hyperplasia/hypertrophy (SMGHH) is the primary histopathological feature in pediatric and adult chronic sinusitis (CRS) and likely the major source of mucus hypersecretion. However, the mechanisms that lead to SMGHH are unknown. Our recent studies suggest that increased inflammatory proteins, fibrotic/myofibrotic changes, and extracellular matrix (ECM) protein deposition characterize the CRS sinonasal mucosa. These changes may be induced by chronic inflammation and contribute to the development of SMGHH. More importantly, we also found that the pro-inflammatory cytokine CXCL5, which promotes differentiation of prostate fibroblasts into myofibroblasts, is markedly upregulated in pediatric CRS sinus mucosa. However, it is unclear whether and how CXCL5 mediates myofibroblast phenoconversion and the ECM deposition necessary for the development of SMGHH in CRS. To address these questions, sinus mucosa tissue and primary sinus fibroblasts from CRS and non-CRS patients were characterized by immunofluorescence staining for myofibroblast markers, including α smooth muscle antigen (α SMA), collagen I and tenascin. The effect of specific CXC-type chemokines (CXCL5, CXCL8, CXCL12 and CXCL13) on regulating myofibroblast differentiation was evaluated by quantitating the mRNA and protein expression of α SMA and collagen I following exposure of primary fibroblasts to these chemokines. The mechanism of CXCL5 mediated myofibroblast phenoconversion was investigated using kinase inhibitors. Western blot analyses of signaling molecules showed dramatic fibrotic and myofibrobic changes in the basal lamina of pediatric CRS sinus mucosa and primary CRS fibroblasts exposed to CXCL5. Specifically, the mRNA levels of α SMA, collagen 1, TGF β and POSTN, an ECM protein, were induced in primary fibroblasts exposed to CXCL5. Moreover, CXCL5 mediated myofibroblast phenoconversion was repressed 67% by the PI3K kinase inhibitor, Ly294002. The phosphorylated AKT and GSK3β and the expression of the transcriptional factor, SNAIL, were significantly up-regulated in primary fibroblasts following exposure to CXCL5. These findings suggest that CXCL5 efficiently mediate myofibroblast phenoconversion through PI3K/AKT signaling pathway and also induce ECM protein expression, and may thereby promote fibrotic changes in sinus tissue architecture associated with the development and progression of SMGHH.

STATUS

Medical Student

AUTHORS

Alex Chua

Xiaofang Wu

Yajun Chen

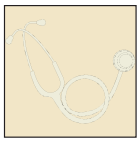
Mary Rose

Maria Pena

Diego Preciado

RESEARCH MENTOR/ DEPARTMENT CHAIR

Mary Rose



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Trying To Stay Healthy Can Sometimes Make You Sick: Vitamins At Mass Market Retail And Warehouse Stores Often Contain Gluten

INTRODUCTION

Celiac disease can cause nutritional deficiencies when there is exposure to gluten. Vitamin supplementation is often recommended to prevent malnutrition. However, it is important to evaluate all vitamins to determine if gluten is present. This study evaluated multivitamins available at mass market retail stores and a warehouse store to determine the frequency at which the vitamins contained gluten.

METHODS

A survey of multivitamins at two mass market retail stores and a national warehouse store was conducted. All available multivitamins were identified and the ingredients were reviewed. The vitamins were categorized as gluten-free or containing gluten. Vitamins were categorized as cautionary if they contained soy or were manufactured in a facility where there was potential for cross contamination with gluten-containing products. Vitamins without identified sources of gluten, but not labeled as gluten free, were placed in an uncertain category. A database was created using Microsoft Excel. Statistical analysis was performed using the Fisher Exact test, with statistical significance set at $p < 0.05$.

RESULTS

The first mass market retail store had 57 different multivitamins available, 25 (43.9%) categorized as gluten free, 5 contained gluten, 11 were cautionary and 16 uncertain. The second mass market retail store had 55 different multivitamins available, 22 (40%) categorized as gluten free, 6 contained gluten, 12 were cautionary and 15 uncertain. There was no significant difference ($p=0.7056$) in the rate at which gluten free vitamins were available at the mass market retail stores. The national warehouse store had 20 different multivitamins available, 10 (50%) categorized as gluten free, 1 contained gluten and 9 were uncertain. There was no significant difference in the rate at which the national warehouse store had gluten free vitamins compared to the first mass market retail store ($p=0.7947$) or the second mass market retail store ($p=0.5982$). Notably most of the brand vitamins of the first mass market retail store (100%), the second mass market retail store (67%) and the national warehouse store (100%) were gluten free.

DISCUSSION

The majority of vitamins available at the two mass market retail stores and half of the vitamins available at national warehouse store contained gluten, had the potential to be cross-contaminated with gluten products or it was uncertain if they contained gluten. Careful review multivitamin ingredients is important. Contacting vitamin manufacturers may be necessary to determine if a vitamin is gluten free. Individuals with celiac disease should be aware that many vitamins can contain gluten and may result in complications.

STATUS

Lab Intern

AUTHORS

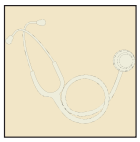
Michelle Corinaldi

Michael Corinaldi

Marie L. Borum

RESEARCH MENTOR/ DEPARTMENT CHAIR

Marie L.Borum



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Parents Must Be Cautious: Pediatric Multivitamins Can Contain Gluten

INTRODUCTION

Gluten enteropathy, also known as celiac disease, can affect 1 in 100 individuals. Increasingly, diagnoses are made in individuals who are asymptomatic. It has been reported that up to half of children with celiac disease may not be diagnosed. In effort to optimize health, parents often administer vitamins to their children. However, pediatric multivitamins can contain gluten which may adversely affect children with subclinical disease. This study evaluated pediatric multivitamins for gluten at mass market retail stores and a warehouse store.

METHODS

A survey of multivitamins at two mass market retail stores and a national warehouse store was conducted. Pediatric multivitamins were identified and ingredients were evaluated. The vitamins were categorized as gluten-free or containing gluten. Vitamins were categorized as cautionary if they contained soy or were manufactured in a facility where there was potential for cross contamination with gluten. Vitamins without gluten containing ingredients, but not labeled as gluten free, were placed in an uncertain category. A database was created using Microsoft Excel. Statistical analysis was performed using the Fisher Exact test, with significance set at $p<0.05$.

RESULTS

The first mass market retail store offered 17 pediatric multivitamins, 6 (35.3%) categorized as gluten free, 2 contained gluten, 7 were cautionary and 2 uncertain. The second mass market retail store offered 19 pediatric multivitamins, 10 (52.6%) categorized as gluten free, 3 contained gluten, 4 were cautionary and 2 uncertain. The national warehouse store offered 3 pediatric multivitamins, 2 (66.7%) categorized as gluten free and 1 contained gluten. There was no significant difference ($p=0.3351$) in the available gluten free pediatric multivitamins between the retail stores. There was no significant difference in the rate at which the national warehouse store had gluten free vitamins compared to the first mass market retail store ($p=0.5368$) or the second mass market retail store ($p=1.000$). Notably, the pediatric multivitamins containing gluten often had cartoon character labelling.

DISCUSSION

Parents should be aware that pediatric multivitamins with gluten can cause or exacerbate nutritional deficiencies in children with celiac disease. Children with celiac disease can often be asymptomatic, but may react to daily gluten exposure through vitamins. Awareness of vitamin ingredients is important to avoid unintentional gluten ingestion. Parents must be careful when selecting vitamins for their children.

STATUS

Lab Intern

AUTHORS

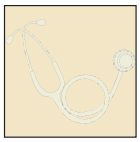
Michael Corinaldi

Michelle Corinaldi

Marie L. Borum

RESEARCH MENTOR/ DEPARTMENT CHAIR

Marie L. Borum



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Progression of Renal Disease and Arterial Stiffening in Type II Diabetes Mellitus

BACKGROUND

Type II Diabetes Mellitus has long been known to cause vasculopathy of both small and large vessels resulting in functional decline of vital organs especially the kidneys. Renal function of diabetics gradually declines with disease progression and can be assessed by determining the estimated glomerular filtration rate (eGFR). The effects of Diabetes on the vasculature can also be quantified by determining the degree of arterial stiffness in peripheral blood vessels such as the brachial or femoral arteries, using measured pulse wave velocity (PWV) as the assessment tool.

OBJECTIVE

In this study we attempt to evaluate the correlation between arterial stiffness and chronic kidney disease (CKD) stage in Type II diabetics.

METHODS

Subjects were diabetic patients diagnosed within the past 8 years, within the ages of 40-70 with an HbA1c between 6-9% being treated only with metformin. Once enrolled in the study each patient had blood drawn to calculate eGFR, and PWV of the femoral artery was measured using SphygmoCor CP system from ATCOR.

RESULTS

Comparing PWV between the two groups of patients with earlier stage CKD vs. stage 2 demonstrated that higher PWV are seen in the group with stage 2 CKD. The median PWV in patients with stage 1 CKD were 8.5 vs. 10.75 in the stage 2 CKD group.

CONCLUSIONS

Our data supports the hypothesis that there is an association between increasing arterial stiffness and progression of CKD in Type II diabetics. This data suggests that perhaps the mechanism underlying the development of macrovascular complications of larger blood vessels in diabetes may also contribute to the development of the microvascular complication of renal disease.

STATUS

Medical Student

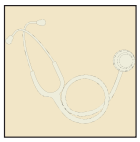
AUTHORS

Samuel Dengler

Sabyasachi Sen

RESEARCH MENTOR/ DEPARTMENT CHAIR

Sabyasachi Sen



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Falls-Related Emergency Department Visits Among Older Adults

Falls are the the leading cause of fatal and non-fatal injury in adults over the age of 65 years.[1] In fact, one in three adults in this age group experiences a fall each year, resulting in a large number of Emergency Departmenin more than 2.5 million emergency department visits[1,2] and a significant financial burden. As a Level I trauma center, the George Washington University Hospital anecdotally cares for many elderly patients after a fall. However, there is are no baseline demographic data for these types of injuries. This research aims to fill that void. This e study is a research will conductconduct a retrospective chart review of older adults (age 65 years and older) evaluated for a fall related injury who presented toat tThe George Washington University Hospital Emergency Department for evaluation of a fall related injury between February 1, 2014 and February 28, 2015. The information provided in data abstracted from the visit records will include parameters such as patient medical history, location of fall, as well as information regarding the Emergency Department work up. As this research is currently ongoing, there are no results available at this time. However, the Department of Emergency Medicine Center for Injury Prevention and control hopes the results will establish a baseline understanding of demographic and shed light on identify circumstances contributing to fall related injuries among older adults in our local population. Theseis is data are especially important given the agining population and possible need will contribute to the development for of additional research projects and or interventions.

REFERENCES

1 Centers for Disease Control and Prevention, National Center for Injury Prevention and Control. Web–based Injury Statistics Query and Reporting System (WISQARS) [online]. Accessed August 15, 2013.

2 Tromp AM, Pluijm SMF, Smit JH, et al. Fall-risk screening test: a prospective study on predictors for falls in community-dwelling elderly. J Clin Epidemiol 2001;54(8):837–844.

STATUS

Medical Student

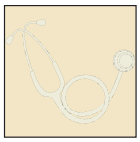
AUTHORS

Kate Douglass

Marie White

RESEARCH MENTOR/ DEPARTMENT CHAIR

Kate Douglass



SCHOOL OF MEDICINE AND HEALTH SCIENCES

A Case Report of an Endovascular Technique for Uterine Arteriovenous Malformations

PURPOSE

The purpose of this case study is to illustrate an interventional radiologic technique that can be used to temporarily reduce blood flow in a rare case of a large uterine arteriovenous malformations requiring hysterectomy.

CASE REPORT

A 36 year-old female with a history of two second-trimester spontaneous abortions presented for a pre-op appointment for planned hysterectomy after a pelvic MRI showed significant uterine AVM. Due to concern for hemorrhage during the surgery, bilateral iliac and bilateral ovarian arterial balloon catheters were placed under fluoroscopic guidance prior to surgery. After placement of balloon catheters under conscious sedation, the patient was transferred to the operating room. The patient was induced under general anesthesia. On diagnostic hysteroscopy, the patient had intrauterine scarring consistent with prior dilations and curettages. Balloons were inflated during surgical removal of the uterus and fallopian tubes. After hysterectomy and salpingectomies, the intra-arterial balloon catheters were deflated. The patient was hemodynamically stable and catheters were removed. She was discharged after a few days.

CONCLUSION

As this clinical case illustrates, percutaneous minimally invasive image-guided interventional techniques may be used in complex OB/GYN patients. It is important to recognize the importance of the multidisciplinary approach to the treatment of such patients.

KEYWORDS:

arteriovenous malformation, embolization, iliac artery, ovarian artery, bleeding, endovascular treatment/therapy, emergent procedure

STATUS

Medical Student

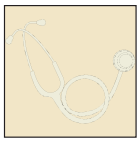
AUTHORS

Bradley Fox

Anthony Venbrux

RESEARCH MENTOR/ DEPARTMENT CHAIR

Anthony Venbrux



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Primary Care Providers Are Vital to Carrying out Hepatitis C Screening

BACKGROUND

Chronic Hepatitis C Virus (HCV) infection affects approximately 3 million Americans. The 1945-1965 birth cohort has the highest prevalence, estimated at 2%. In 2013, the United States Preventive Services Task Force (USPSTF) endorsed screening for HCV in this cohort with the goal of identifying cases and initiating treatment. However, a variety of obstacles to screening are suspected to contribute to low screening rates. This study evaluated the role of the primary care physician in completing recommended screening in an historically underserved community with a high prevalence of HCV.

METHODS

Individuals attending an August 2015 health exposition sponsored by the Rodham Institute completed an anonymous survey. The exposition was hosted in an urban setting where the population has historically been predominantly African American; currently 92% of residents identify as such. The survey included questions on demographic information, access to a PCP, insurance status, as well as knowledge of various topics related to Hepatitis C. Responses were excluded if they did not provide information on their history of screening. The university institutional review board approved the study. Statistical analysis was performed using Fisher's exact test, with significance set at $p<0.05$.

RESULTS

Ninety five responses were analyzed. Among them were 29 born in the 1945-1965 timeframe. All of members of this cohort reported having a primary physician and 27 (96.4%) had health insurance. Sixteen discussed HCV with their doctor and 12 of them (75.0%) were screened. Thirteen respondents had not discussed HCV; among them, three (23.1%) were tested for the virus. Having a discussion with the primary physician resulted in a significantly higher rate of HCV screening ($p=0.0092$).

CONCLUSIONS

The primary care provider is vital to implementing preventive health recommendations including those related to HCV screening. Our study showed that in a high-prevalence, insured cohort, patients who had discussed HCV with their primary physician were three times more likely to have been screened for the infection. The population studied all had health insurance and a primary care provider, so health care was broadly accessible. The study also suggests that some recent USPSTF guidelines may not have penetrated into community primary care practices as the screening rates were suboptimal.

STATUS

Medical Student

AUTHORS

Daniel Gaballa

Dan Gaballa

Shreya Chablaney

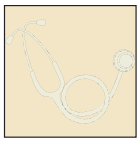
Justin Ertle

Timothy Dougherty

Marie L. Borum

RESEARCH MENTOR/ DEPARTMENT CHAIR

Marie L. Borum



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Comparing Emergency Department Resident and Patient Perspectives on Costs in Emergency Care

OBJECTIVES

Costs of care are increasingly important in healthcare policy and, more recently, clinical care in the Emergency Department (ED). We compare ED resident and patient perceptions surrounding the costs of emergency care, compliance, communication, and education.

METHODS

We conducted a mixed methods study using surveys and qualitative interviews in a single, urban academic ED. The first study population was a convenience sample of adult patients (>17 years of age), and the second was ED residents training at the same institution. Participants answered open- and closed-ended questions on costs, cost-related compliance, and communication. Residents answered additional questions on residency education on costs of care. Closed-ended data were tabulated and described using standard statistics while open-ended responses were analyzed using grounded theory.

RESULTS

Thirty ED patients and 24 ED residents participated in the study. Both ED patients and residents felt neutral regarding the importance of cost discussions and generally did not have knowledge of medical costs. Patients were comfortable discussing costs while residents were less comfortable. Additionally, some patients had cost concerns restricting compliance with treatment. Limitations to discussing costs included lack of time and perceived irrelevance. Generally, ED residents took costs into consideration during clinical decision-making, most commonly because of a feeling of personal responsibility to control healthcare costs. Nearly all ED residents agreed they had too little education regarding costs, and the most common suggestion for enhancing education was inclusion of price lists.

CONCLUSIONS

There were several notable differences in patient and resident perspectives on cost discussions in the ED in this sample. While patients do not see cost discussions to be important, they are generally comfortable discussing costs yet do not report having sufficient knowledge on what care costs. ED residents think costs are important, but are less comfortable discussing them, primarily because they lack education on medical costs.

STATUS

Emergency Medicine Chief Resident

AUTHORS

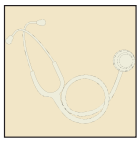
Stefanie K. Gilbert

Leana S. Wen

Jesse M. Pines

RESEARCH MENTOR/ DEPARTMENT CHAIR

Jesse M. Pines



SCHOOL OF MEDICINE AND HEALTH SCIENCES

The Significance of Red Blood Cell Antigen Matching on Bone Marrow Transplant Outcomes in Patients with Sickle Cell Disease

BACKGROUND

Hematopoietic stem cell transplant (HSCT) is the only potential curative therapy for sickle cell disease (SCD) currently. While significant research has been performed on the clinical impact of ABO-incompatible HSCT in patients with SCD, only preliminary studies have analyzed the outcomes of HSCT with non-ABO red blood cell (RBC) antigen discordance.

OBJECTIVES

To investigate the frequency and clinical significance of minor RBC antigen discordance on HSCT outcomes in patients with SCD.

DESIGN/METHODS

This study is a retrospective analysis of a cohort of patients with SCD who received a HSCT from 1995 to 2015, at a single institution.

RESULTS

Of the 48 patients with SCD who received HSCT, 17 (35.4%) had available data on minor RBC antigens for both donor and recipient. All 17 patients received transplants from HLA and ABO-matched related donors. There were 52.9% males, 88.2% African Americans, and mean age at time of transplant was 8.4 years old. Several different conditioning regimens were used, including reduced intensity regimens. The primary indications for transplant were history of stroke (47%), vasoocclusive crisis (29.4%), and acute chest syndrome (17.6%). Prior to transplant, alloantibodies were present in 35.3% of the subjects, the majority being anti-Rhesus-C.

The majority of patients (94.1%) had at least 1 minor RBC antigen discordant with their donor. Fourteen patients (82.4%) had 1-3 discordances. The most common discordant blood group systems were the Rhesus (47%), MNS (35.3%), and Dombrock (29.4%) systems. None of the subjects developed novel antibodies following HSCT, despite discordances.

Overall, there was little correlation between the number of minor RBC antigen discordances and HSCT outcomes (overall survival, graft failure, transfusion requirements, time to engraftment, time to transfusion independence, and complications). However, patients with two or more minor RBC discordances appeared to have more chronic GvHD, while patients with one discordance were more likely to develop acute GvHD.

CONCLUSIONS

There appeared to be a trend towards increasing cGVHD in patients who had greater numbers of discordant minor RBC antigens, but no other association with clinical HSCT outcomes; however, given the limited size of this cohort, further studies are required.

STATUS

Medical Student

AUTHORS

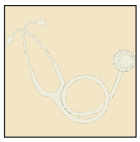
Samantha Hale

Jennifer Webb

Allistair Abraham

RESEARCH MENTOR/ DEPARTMENT CHAIR

Jennifer Webb



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Performance of Revised Geneva Score and Wells Score for Pulmonary Embolism in Inpatient Setting

INTRODUCTION

An analysis of 593 physician-reported hospital errors demonstrated pulmonary embolism (PE) as the number one missed/delayed diagnosis. Hospitalization is a known risk factor for thrombosis necessitating the use of pharmacologic or mechanical prophylaxis to prevent health-care associated venous thromboembolism (VTE). Several clinical prediction scores for suspected PE have been validated in patients presenting to the emergency department with suspected PE. Their use in inpatient risk stratification for pre-test probability of PE has not yet been validated.

OBJECTIVE

To validate the utility of Wells Score and Revised Geneva score (RGS) for risk stratification of inpatients with suspected PE.

METHODS/STUDY DESIGN

A retrospective study of all consecutive patients from March 2012 to Sept 2015 undergoing chest CT angiography (CTA) for suspected PE was conducted at the Veterans Affairs Medical Center Washington, DC. Patients who presented as an outpatient from clinic, emergency department, on therapeutic anticoagulation or had a hospital length of stay less than 48 hours from the time of CTA were excluded. Revised Geneva and Wells score were calculated based upon data entered by health care professionals in a computerized physician order entry system at the time of imaging.

RESULTS

542 consecutive CTA studies were performed. 85 of 170 inpatient subjects were excluded so 85 met inclusion criteria. The average age was 69 +/- 12 years. Of these 85 subjects, 19 (22.35%) were found to have PE on CTA which corresponded to the following RGS and Wells score respectively: low probability: 0%, intermediate probability: 89.9% (17/19) and 36.8% (7/19), high probability: 10.1% (2/19) and 73.2% (12/19). The remaining 66 patients without PE risk stratified to the following RGS and Wells score respectively: low probability: 7.6% (5/66) and 4.5% (3/66), intermediate probability: 84.8% (56/66) and 66.66% (44/66), high probability: 7.6% (5/66) and 28.8% (19/66).

CONCLUSION

The majority of patients in this study presented with intermediate probability RGS and Wells scores: 73/85 (85.9% CI: 78.5-93.3%, $p<0.05$) and 51/85 (60% CI: 49.6- 70.4%, $p<0.05$) respectively. Within this group, there was significant variability using the RGS for risk stratification—with 89.9% (77.9%-93.9%, $p<0.05$) of PE positive patients and 84.8% (CI: 75.2-92.8%, $p<0.05$) of PE negative patients within the intermediate risk category. This may indicate poor utility of the RGS in an inpatient population and need for clinical &/or laboratory marker with inpatient specific analogues to the D- Dimer that is utilized in the outpatient setting. Additional longitudinal data gathering and analysis are ongoing.

STATUS

Resident Physician

AUTHORS

Aneesha Hossain

Yevgeniy Vayntrub

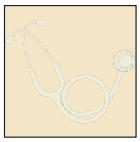
Nilo Avila

Nitin Seam

Dalia Abdelaziz Mobarek

RESEARCH MENTOR/ DEPARTMENT CHAIR

Jillian Catalanotti



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Validation of pneumonia and appendicitis genomic biomarkers using droplet digital PCR (ddPCR)

Droplet digital PCR (ddPCR) is a novel and improved molecular method that allows for absolute quantification of target transcript in copies per input samples. As such, its application in validation of high throughput screening with Microarray (MA) or Next Generation Sequencing may provide a cost-effective practical solution. To validate the MA identified genomic biomarkers of appendicitis and bacterial respiratory infections, we have applied the ddPCR on whole blood RNA from patients with acute appendicitis and respiratory infections, as well as on control subjects enrolled in the GWU IRB approved study. The MA transcript profiling identified 37 differentially expressed genes (DEG) in appendicitis versus abdominal pain patients and several strong biomarkers of respiratory infections were discovered during data analysis. The DEG list contained three major ontologies: infection-related, inflammation-related, and ribosomal processing. The detected transcripts were validated using ddPCR on 70 patients and confirmed the patterns detected by MA or NGS alone. ddPCR may serve as a robust tool for validation of large scale genomic biomarkers discovery experiments and could be implemented into clinical practice once the biomarkers are validated.

STATUS

Medical Student

AUTHORS

Priyanka Kamalapathy

Lakhmir S. Chawla

Ian Toma

Danielle Davison

Yndia Cooper

Andrew Meltzer

Khashayar Vaziri

Juliet Lee

Raymond Lucas

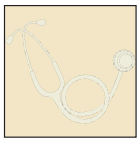
Michael G. Seneff

Aoibhinn Nyhan

Timothy A. McCaffrey

RESEARCH MENTOR/ DEPARTMENT CHAIR

Timothy A. McCaffrey



SCHOOL OF MEDICINE AND HEALTH SCIENCES

The effect of increased total daily dose of outpatient ketamine infusions on outcomes in chronic neuropathic pain patients

INTRODUCTION

Ketamine infusions have shown to provide significant relief in patients with chronic neuropathic pain. At our institution, patients have demonstrated improvement in mood and ambulation after treatment with four-hour outpatient ketamine infusions at subanesthetic doses. In this study, we compared four and five-hour infusions in the same patient to determine if a longer duration of infusion or a higher daily ketamine dose improved quality of life (QOL) outcomes.

METHOD

With IRB approval, we examined QOL outcome measurements in patients who received three consecutive days of four-hour ketamine infusions followed by three days of five-hour infusions months later. Ketamine doses did not exceed 1mg/kg/hr. Patients completed a Brief Pain Inventory assessing the impact of their chronic pain on QOL before each infusion session and again several weeks later. Four predictors (age, sex, race, and pre-treatment score) were used to evaluate any change in QOL due to demographics. To compare scores between four and five-hour infusion sessions, a paired t-test and multivariate generalized estimating equations were used.

RESULTS

Ten patients underwent four and five-hour ketamine infusions. There was no significant difference in QOL outcome measurements between the infusion sessions. The mean pain score did not show statistical significance when duration of infusion was increased.

CONCLUSIONS

Although patients infused with subanesthetic doses of ketamine over five hours reported improvement in level of pain, activity, mood, work, relationships and sleep, these results were not statistically significant. We will further evaluate the impact of dose and duration of infusion with a larger patient population.

REFERENCES

1 Schwartzman, Robert J RJ (03/2009). "Outpatient intravenous ketamine for the treatment of complex regional pain syndrome: a double-blind placebo controlled study." *Pain (Amsterdam) (0304-3959)*, 147 (1-3), 07.

2 Sigtermans, Marnix J MJ (04/2009). "Ketamine produces effective and long-term pain relief in patients with Complex Regional Pain Syndrome Type 1.". *Pain (Amsterdam) (0304-3959)*, 145 (3), 304.

STATUS

Medical Student

AUTHORS

Cathleen Kenary

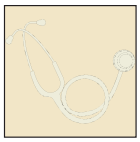
Ramon Go

May Chin

Richard Amdur

RESEARCH MENTOR/ DEPARTMENT CHAIR

May Chin



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Anterior Tibial Subluxation following Anterior Cruciate Ligament (ACL) Tears Increases with Time

INTRODUCTION

A complete ACL tear results in the loss of the primary restraint to anterior tibial subluxation. The extent to which tibiofemoral subluxation develops over time in the ACL-deficient knee is not well understood.

METHODS

In this retrospective cohort study, we assessed the anterior subluxation of the tibia relative to the femur using MRI studies of 74 patients diagnosed with complete ACL tears in both the medial and lateral compartments. The definition of chronicity was set at four months from injury. Standard t-tests with assumed equal variances were used to compare the means of the acute (≤4 months) and chronic (>4 months) populations.

RESULTS

The average medial compartment tibial subluxations among the acute and chronic groups were 0.06 cm and 0.37 cm, respectively (p=0.002). The average lateral compartment tibial subluxations among the acute and chronic groups were 0.25 cm and 0.50 cm, respectively (p=0.016). The average overall tibial subluxations among the acute and chronic groups were 0.16 cm and 0.44 cm, respectively (p=0.001).

CONCLUSION

Anterior tibial subluxation is greater among patients with chronic ACL injuries than among those with acute ACL injuries, the implications of which may favor earlier surgical intervention.

STATUS

Medical Student

AUTHORS

Ali Khan

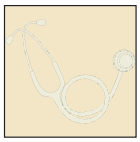
Rachel Lefebvre

Nicholas Rouse

Rajeev Pandarinath

RESEARCH MENTOR/ DEPARTMENT CHAIR

Rajeev Pandarinath



SCHOOL OF MEDICINE AND HEALTH SCIENCES

The Effect of Caudal Anesthesia on Spinal Cord Tissue Oxygenation as Assessed by Tissue Oximetry

BACKGROUND

During complicated procedures, perfusion to the spinal cord may be compromised, resulting in nerve damage and possible paralysis. Caudal injection of bupivacaine can have effects on mitochondrial oxygen consumption and the sympathetic system, which may increase or decrease spinal cord tissue oxygenation.

METHODS

20 patients up to 2 years of age undergoing surgery receiving a caudal injection of bupivacaine as part of their routine care were studied and compared with 20 patients that did not receive caudal injections for control. Near Infrared Spectroscopy (NIRS) monitor probes were placed on the lumbar region to measure spinal regional saturation (rSO_2) and on the forehead to measure cerebral oximetry as a control prior to injection of caudal anesthesia. Measurements of the regional saturations from the probes were recorded every five minutes for a minimum of 25 minutes.

RESULTS

Spinal rSO_2 and cerebral rSO_2 decreased over 25 minutes from baseline values in both groups. Furthermore, there was a more pronounced decrease in both spinal and cerebral rSO_2 in the caudal injection group compared to the control group. In the caudal injection group, cerebral rSO_2 decreased significantly (P=0.02); spinal rSO_2 also decreased but did not reach clinical significance. There were no significant changes in blood pressure or end tidal CO_2.

CONCLUSION

Caudal injection of bupivacaine decreased spinal cord tissue oxygenation. These results suggest either reduced local blood flow due to vasoconstriction, increased tissue oxygen consumption, or both. There appears to be no difference in immediate physiologic effects. Caudal injection-induced decline in rSO_2 could have implications in operative settings with ischemia or poor perfusion. Changes in rSO_2 also provide an opportunity to develop NIRS as a non-invasive tool to identify successful caudal injection.

STATUS

Medical Student

AUTHORS

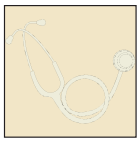
Alvin Kim

Neethu Chandran

Nina Deutsch

RESEARCH MENTOR/ DEPARTMENT CHAIR

Nina Deutsch



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Will She Recover? A Prolonged Hospitalization for a Comatose Female with Neuropsychiatric Lupus

CASE

A 25 year old African-American woman was brought into the ED by EMS after she was found unresponsive in her apartment. Police found the patient to be unconscious and unable to be aroused, lying in feces and urine, with no witnesses or medical history available. In the ED, physical exam showed an obtunded female with GCS of 6T. Neurological exam revealed a left eye gaze with horizontal nystagmus, absent Babinski reflex, 3+ reflexes in upper extremity, and 4+ reflexes in lower extremity bilaterally. CT head did not demonstrate acute hemorrhage or masses.

The patient was intubated to protect her and admitted to the ICU. She was started on empiric therapy for seizure with levetiracetam and for meningoencephalitis with ceftriaxone, vancomycin, and acyclovir. Lumbar puncture revealed no infection, and urine drug screen was normal. Brain MRI showed diffusion along the posterior frontal, parietal and temporal cortices bilaterally with diffuse pachymeningeal enhancement concerning for an autoimmune process.

Using the regional online health information exchange, we discovered that the patient had been diagnosed with SLE at a nearby hospital, two weeks prior to this admission. She had been started on steroids and hydroxychloroquine, and was discharged with plans for rheumatology follow-up. However, she missed that appointment, and medication compliance was unknown. Labs revealed a mixed lupus and Sjogren's picture, with evidence of renal and hematologic involvement of her SLE.

This patient was treated with levetiracetam, lacosamide, and pregabalin for seizures, and diagnostic EEG was performed. She was also started on pulse dose steroids and cyclophosphamide for SLE. Her neurologic status remained unimproved and her ICU course was marked by multiple complications, including massive hemoptysis at her tracheostomy site, prolonged seizures, and anoxia. Her chance of recovery was believed to be very poor given intensity of her condition. She was transferred to the medical floor on day 26 after passing tracheostomy collar trial, but she continued to have no purposeful movements.

Over the next two months, she slowly regained neurological function in her extremities, and was discharged to inpatient rehabilitation on oral prednisone and lacosamide. She returned home, and in the rheumatology clinic one month after discharge, had regained full neurological function. She began her third dose of cyclophosphamide and was continued on her seizure medications, and returned to work. She continues to follow with rheumatology and neurology.

DISCUSSION

SLE affects the neurological system by affecting inflammatory, vasculitic, thromboembolic, and meningeal pathways through a series of complex mechanisms. As a result, patient may experience a range of symptoms including stroke, seizures, cognitive dysfunction, and headaches. Risk factors for neuropsychiatric SLE include the presence of antiphospholipid antibodies, nephritis, young age, and African American ethnicity.

Recognizing neuropsychiatric manifestations of SLE are important as management involves treating both the neurological symptoms and the underlying SLE. Symptoms of neuropsychiatric SLE should be evaluated and treated just as in patients without lupus. Our patient presented with a likely seizure, and was treated empirically for seizure. Lupus patients with stroke should be treated as any other stroke patients. Airway, breathing, and circulation should always be assessed first when a patient presents with severe neurological symptoms. Once the patient has been stabilized and started on appropriate neurological treatments, SLE treatments such as pulse dose steroids should be initiated to help recover from the underlying disease. Neurological symptoms may persist longer in SLE patients, leading to a long and difficult hospital course. Our patient was initially thought to have a very low chance of regaining neurological function. Despite these concerns, she recovered fully after 68 hospital days and an additional 16 days in inpatient rehab. Because neuropsychiatric symptoms of SLE are often indistinguishable from non-SLE neurological symptoms, diagnosis can be difficult, requiring strong clinical suspicion and accurate medical history.

STATUS

Internal Medicine Resident

AUTHORS

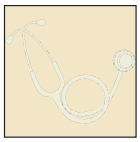
Srikar Kumar

Christian Geier

Jillian Catalanotti

RESEARCH MENTOR/ DEPARTMENT CHAIR

Jillian Catalanotti



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Detecting Sensitivity to Change of Forced Vital Capacity in Patients with Congenital Muscular Dystrophy

BACKGROUND

Congenital muscular dystrophies (CMD) comprise a group of phenotypically and genetically heterogeneous disorders characterized by progressive, early onset muscle weakness, contractures, and progressive respiratory insufficiency evidenced by a predictable annual rate of decline in forced vital capacity (FVC). Numerous measures exist to track disease progression in CMD; however their sensitivity to change is unknown in many cases. We want to determine if FVC is sensitive to change in this population. If it is, FVC can be used as a measure of disease progression in clinical and research settings.

METHODS

Prospective study with 24 genetically-confirmed CMD participants (14 with COL6-RD), ages 5.9-20. Pulmonary Function Tests (PFTs) were performed in the Pulmonary Function Laboratory of the National Heart, Lung, and Blood Institute at the National Institutes of Health. Testing included FVC in the sitting and supine positions, with results reported in both absolute values (in liters, L) and FVCpp.

RESULTS:

p-value for FVC sitting overall from years 1-3 was 0.009; from years 2-3 was 0.050. *p*-value for FVC COLVI sitting from years 1-3 was 0.055 and for LAMA2 supine from years 1-3 was 0.042.

DISCUSSION

Clinical trials need a robust N or need sufficient time to show a difference in FVC. More severe patients decline more rapidly, and this could help explain the significant difference in ΔFVC between years 2 and 3, but absent between years 1 and 2. Future studies could further explore muscle groups affecting each subtype to better understand why there was a significant drop in COLVI for sitting and LAMA2 for supine.

STATUS

Medical Student

AUTHORS

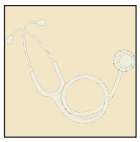
Melody Linton

K.G. Meilleur

C. Bonnemann

RESEARCH MENTOR/ DEPARTMENT CHAIR

Katherine G. Meilleur



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Environmental Factors Associated with Disease Flare in Juvenile and Adult Dermatomyositis

OBJECTIVE

To assess environmental factors in relationship to disease flare in juvenile and adult dermatomyositis (DM).

METHODS

An online survey was conducted for juvenile and adult DM patients from the US and Canada who were ≥ 1 year from diagnosis. Patients were recruited through myositis clinics and by a patient support group. The survey examined smoking, sun exposure, infections, medications, vaccines, stressful life events, and physical activity during the 6 months prior to disease flares, or in the past 6 months if the patient had not flared. Differences were evaluated by Chi-square and Fisher's exact tests. Residential locations prior to flare were correlated with the National Weather Service UV index.

RESULTS

Of 210 participants meeting probable or definite Bohan and Peter criteria (164 juvenile and 46 adult DM patients), 134 (63.8%) 103 juvenile and 31 adult DM) experienced a flare and 76 (36.2%) (61 juvenile and 15 adult DM) participants did not experience a disease flare within the past 2 years. For those reporting a disease flare, the mean duration to flare was 13 months for JDM and 10 months for DM. Patients with flare were less often 0-5 years of age compared to those who did not flare (2.2% vs. 15.8%, p=0.0004). Patients with a disease flare more often reported that their myositis worsened after sun exposure (44.4% vs. 28.6%, p=0.03, OR=2.0), but the use of photoprotective measures was similar between both groups. Infections were more frequently recorded in the preceding 6 months in those who flared vs. who did not, including UTI (10.2% vs. 0.0%, p=0.005, OR=16.4) and gastroenteritis (16.5% vs. 5.8%, p=0.04, OR =3.2). Patients who flared more frequently used NSAIDs (63.4% vs. 36.8%, p=0.0003, OR=3.0) or blood pressure medicines (12.7% vs. 3.9%, p=0.049, OR=3.5), or medicine for depression or mood changes (7.5% vs. 0.0%, p=0.001, OR 12.9). HPV vaccine was more frequent in those who flared vs. those who did not (8.2% vs. 0.0%, p=0.03, OR =10.0). Patients who flared tended to experience more frequent serious financial difficulties compared to those who did not (17.2% vs. 7.9%, p=0.06, OR=2.4) and to move to a new house (6.0% vs. 0.0%, p=0.05, OR 10.3). There was no difference in UV index between the two groups.

CONCLUSION

Sun exposure, certain infections, medications, and vaccines, which have been associated with illness onset, may also play a role in disease flares in patients with adult and juvenile DM.

STATUS

Faculty

AUTHORS

Gulnara Mamyrova

Lisa G. Rider

Olcay Y. Jones

Alison Ehrlich

Lauren M. Pachman

Robert W. Nickeson

Lisa G. Criscione-Schreiber

Frederick W. Miller

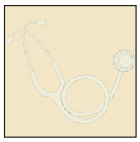
Lawrence K. Jung

Rodolfo V. Curiel

James D. Katz

RESEARCH MENTOR/ DEPARTMENT CHAIR

Victoria Shanmugam



COLUMBIAN COLLEGE OF ARTS AND SCIENCES

Scleroderma Wounds Exhibit Slower Healing than Wounds from Other Etiologies

INTRODUCTION

Scleroderma is an autoimmune disease characterized by inflammation, vasculopathy, and fibrosis of skin, vasculative and internal organs. Delayed wound healing is a known complication of scleroderma. The purpose of this study was to investigate whether chronic wounds in scleroderma patients heal more slowly than chronic wounds of other etiology.

METHODS

This research was conducted through the Wound Etiology and Healing Study (WE-HEAL Study). The WE-HEAL Study is a biospecimen and data repository approved by the George Washington University IRB (041408). Subjects gave written informed consent for collection of their data. Scleroderma cases with wounds (n=25) and age and sex matched control patients with chronic wounds from other etiologies (n=25) were selected for analysis. Baseline demographics, comorbidities, wound size, time to healing, and pain score were compared between the two groups. Scleroderma wounds were further analyzed based on scleroderma classification (localized vs. systemic; limited vs. diffuse). Statistical tests including T-test, Fisher's Exact and Chi Square were performed using GraphPad Prism 5.0.

RESULTS

While baseline total wound surface area (tWSA) was unchanged between the scleroderma and chronic wound groups, the tWSA at the last visit was significantly larger in the scleroderma group 24.80cm2 54.18 compared to the chronic wound group 0.18cm2 0.71 (p=0.028). Scleroderma wounds were significantly less likely to ultimately heal 52% compared to 84% (p=0.015). Pain scores tended to be higher in the subjects with scleroderma, but this did not reach statistical significance (4.08 ± 3.73 compared to 2.68 ± 2.90, p=0.145). Limited scleroderma wounds took longer to heal compared to wounds in patients with diffuse scleroderma suggesting the mechanisms of delayed wound healing in scleroderma may be more related to vasculopathy than ongoing inflammation.

CONCLUSION

Scleroderma patients exhibit delayed wound healing compared to patients with wounds from other etiologies. Scleroderma wounds are significantly less likely to ultimately heal than chronic wounds of other etiologies. There is an unmet need to further investigate the etiology of delayed wound healing in patients with scleroderma.

STATUS

Undergraduate Student

AUTHORS

Marissa Mangini

Sean McNish

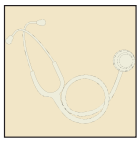
Anirban Banerjee

Jonathan Miller

Victoria K. Shanmugam

RESEARCH MENTOR/ DEPARTMENT CHAIR

Victoria K. Shanmugam



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Intraoperative administration of ε-aminocaproic acid (EACA) reduces blood loss in pediatric craniofacial reconstructive surgery

BACKGROUND

Surgical correction of craniosynostosis in pediatric patients is a complex procedure that results in significant blood loss and transfusion requirements. Antifibrinolytic agents have been shown to reduce blood loss in pediatric patients undergoing other types of major surgery involving significant blood loss. Two recent retrospective studies suggest the benefit of ε-aminocaproic acid (EACA) in reducing blood loss in pediatric craniofacial surgery.[1,2] Pharmacokinetic data in children undergoing craniofacial surgery recommends administering 100 mg/kg EACA loading dose followed by a continuous infusion at 40 mg/kg/hr in order to maintain target plasma EACA concentrations.[3] This study aims to provide further evidence supporting the use of EACA in pediatric craniofacial surgery using this specific dosing regimen.

METHODS

This is a retrospective study of children (4 months to 8 years of age) with craniosynostosis who underwent bifrontal orbital advancement or calvarial vault reconstruction surgery at out institution between July 2013 and December 2015. We compared intraoperative calculated blood loss, RBC transfusion volume, blood donor exposures, and postoperative surgical drain output between patients who received EACA and those who did not receive EACA.

RESULTS

A total of 44 patients were included in the study; 18 received EACA and 26 did not receive EACA. Both the EACA and non-EACA groups were analyzed for confounding characteristics and surgical variables and no significant differences between the two groups were found. The EACA group had a significantly lower calculated blood loss (37 ± 18 vs. 63 ± 45 mL/kg, $P = 0.004$) reduced RBC transfusion requirements (14 ± 12 vs. 30 ± 24 mL/kg, $P < 0.001$), and fewer intraoperative blood donor exposures (median 1, interquartile range 0-1 vs. median 1, interquartile range 1-1; $P = 0.002$) than the non-EACA group. There was no significant difference in the first postoperative 24-hour surgical drain output between the two groups.

CONCLUSION

EACA, administered at the recommended dosing regimen, is associated with decreased calculated blood loss, RBC transfusion requirements, and intraoperative blood donor exposures.

REFERENCES

1 Oppenheimer AJ, Ranganathan K, Levi B, Strahle JM, Kapurch J, Muraszko KM, Buchman SR. Minimizing transfusions in primary cranial vault remodeling: the role of aminocaproic acid. J Craniofac Surg 2014; 25(1):82-6.

2 Hsu G, Taylor JA, Fiadjoe JE, Vincent AM, Pruitt EY, Bartlett SP, Stricker PA. Aminocaproic acid administration is associated with reduced perioperative blood loss and transfusion in pediatric craniofacial surgery. Acta Anaesthesiol Scand 2016; 60(2):158-65.

3 Stricker PA, Zuppa AF, Fiadjoe JE, Maxwell LG, Sussman EM, Pruitt EY, Goebel TK, Gastonguay MR, Taylor JA, Bartlett SP, Schreiner MS. Population pharmacokinetics of epsilon-aminocaproic acid in infants undergoing craniofacial reconstruction surgery. Br J Anaesth 2013; 110:788-99.

STATUS

Medical Student

AUTHORS

Taylor Mann

Heather Gordish-Dressman

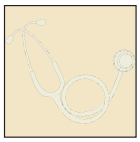
Tiffani DeFreitas

Robert F. Keating

Srijaya K. Reddy

RESEARCH MENTOR/ DEPARTMENT CHAIR

Srijaya K. Reddy



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Evaluation of family's willingness to pay and cost effectiveness for fertility sparing technology in prepubescent males undergoing gonadotoxic chemotherapy

INTRODUCTION

We are performing a cost-effectiveness analysis to determine the optimal experimental fertility preservation method to achieve fertility in prepubescent males who have undergone gonadotoxic chemotherapy. Each year in the United States, approximately 12,400 children and adolescents younger than 20 years old are diagnosed with cancer. The use of chemotherapy in treatment of these cancers often results in sterility. Cryopreservation of gonadal tissue in prepubescent males for use later in life via assisted reproductive technology is currently an investigational procedure, however the only possible option for this patient population. Although investigational, current techniques show great promise to be of clinical utility in the near future. In this study, we perform a cost-effective analysis to determine how efficacious cryopreservation followed by restored fertility and in vitro fertilization must be for families to find the cost acceptable.

METHODS

Decision Analysis (DA) is a quantitative approach that allows an investigator to break down a problem into a series of choices and outcomes. The results of such analysis have broad applications from individual treatment decisions to development of policies regarding groups of similar patients. In this study, an extension of DA called cost-effectiveness analysis is used which takes into account cost as a variable in choosing a treatment option.

We are currently using literature, institutional practice, and expert opinion to determine outcomes and costs of experimental fertility preservation protocols combined with intracytoplasmic sperm injection (ICSI). We will use these variables to fill in a decision tree incorporating various fertility sparing treatments: pluripotent stem cell culture (iPSC), xenotransplant, autotransplant, organ culture, and spermatogonial stem cell culture. All of these methods require ICSI to result in successful fertilization. We are modeling a cost-effectiveness analysis from the perspective of the patient.

RESULTS

Our goal is to determine the most cost-effective method of restoring fertility in cryopreserved tissue in order to aid future families in selecting a treatment method, as well as help direct the focus of developing these technologies. The results of our study will also dictate how efficacious restored fertility in prepubescent males must be in order for families to find the costs acceptable.

STATUS

Medical Student

AUTHORS

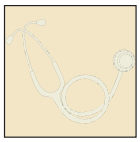
Steven Margolis

Michael Hsieh

Kelly Chiles

RESEARCH MENTOR/ DEPARTMENT CHAIR

Michael Hsieh



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Authorized Agent Controlled Analgesia Improves Pain Control in Critically Ill Adult Patients

LEARNING OBJECTIVES

The efficacy and safety of authorized agent controlled analgesia (AACA), also known as patient controlled analgesia by proxy, is documented in the pediatric literature. Most adult intensive care units do not offer this therapy. This study evaluates the efficacy and safety of AACA in the critically ill adult patient.

METHODS

A retrospective observational study was performed after an AACA protocol was introduced in a 42 bed mixed medical/surgical ICU. Patients requiring mechanical ventilation, frequent opioid dosing, or comfort care were independently placed on AACA by the ICU team. Nonverbal pain score and Richmond Agitation Sedation Severity Score (RASS) along with opioid and sedative use were abstracted 24 hours before and after intervention. Scores were compared using paired student t-tests. A mixed regression model adjusting for hour was used to control for change in pain over time. A random-effects mixed model was used to test whether the slope of pain scores differed from pre to post-AACA. A fixed effects mixed model was used to control for use of non-narcotic medications.

RESULTS

Among the 46 patients studied, the mean number of pain score evaluations was 9.3±5.0 pre- and 10.4±4.5 post-AACA. Mean change in pain score was -3.4±2.0 (95% confidence interval -4.0 to -2.7). This represented a significant 70% drop in mean pain score ($p<0.0001$), from a pre-AACA mean of 4.8±1.8 to a post-AACA mean of 1.5±1.6. Examination of the slope of pain scores by hour found little change within the pre- and post-AACA period, with a large drop from pre- to post-AACA. Mean RASS score decreased significantly (-0.2±1.9 v -1.6±1.3, $p<0.0001$), but in the model controlling for use of sedatives and analgesic medications, the effect of AACA on pain scores (pre- vs post-) remained significant ($p<0.0001$). No patient required naloxone.

CONCLUSIONS

Use of AACA is associated with a significant reduction in pain scores in critically ill patients. Larger studies are warranted to confirm these findings.

STATUS

Medical Student

AUTHORS

Jonathan Messing

Madelyn Hernandez

Joseph Aburahma

Richard Amdur

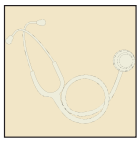
Sarah Sirajuddin

Danielle Davison

Babak Sarani

RESEARCH MENTOR/ DEPARTMENT CHAIR

Babak Sarani



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Patients Transferred for Upper Extremity Amputation: Do All Level I Trauma Centers Participate?

HYPOTHESIS

Level I trauma centers are required to provide specialized services, including hand surgery and microsurgical capability 24 hours a day. We hypothesize that patients are transferred to our academic, tertiary care center for management of upper extremity amputations despite the availability of approved, capable, closer level I facilities.

METHODS

Medical records were reviewed from October 2010 to June 2015 to evaluate patients transferred to our level I, academic institution for upper extremity amputation. Patients who presented with an ICD-9 code demonstrating amputation of an upper extremity were included the study. Patient demographics, type and presence of medical insurance, injured extremity, dominant extremity, number of extremity amputations, trauma designation of transferring facility, and zip code of transferring facility were recorded. Patients from 6 states were transferred to our facility and distances from each patient's transferring facility to all 13 level I trauma centers in these 6 states was computed by compiling straight-line distances (in miles) from the zip code of the transferring facility to the zip code of each level I trauma center.

RESULTS

Out of 261 patients with eligible ICD-9 codes transferred to the MGH, 250 (91.2% male, 8.8% female) had available data. Of these, patients were transferred from hospitals in 6 surrounding states: Massachusetts (163), Maine (31), Vermont (7), New Hampshire (21), Rhode Island (27), and Connecticut (1). For 112 patients our hospital was the nearest level I trauma center, however for the remaining 138 patients other trauma facilities were located closer to the referring hospital and were bypassed to get to our hospital. Among these 138 patients, an unpaired student t-test showed that the mean distance of the transferring facility to the nearest level I trauma center (mean= 30 miles; SD= 27 miles) was significantly different from the mean distance of the transferring hospital to our facility as a more distant level I trauma center (72 miles; SD= 60 miles) ($P< 0.001$). An average of 4 (range 1 – 10) level I trauma centers were bypassed before patients arrived at our center.

CONCLUSION

55% of patients transferred for upper extremity amputation from 6 surrounding states had a level I trauma center closer to their injury than our institution. Patients with upper extremity amputations are referred to our regional center despite the proximity of closer level I trauma centers. This suggests that regional microsurgical expertise is recognized and may be independent of ACS trauma accreditation.

STATUS

Graduate Student

AUTHORS

Shantum Misra

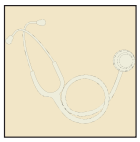
Suzanne C. Wilkens

Neal Chen

Kyle R. Eberlin

RESEARCH MENTOR/ DEPARTMENT CHAIR

Kyle R. Eberlin



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Outpatient Follow-up as Predictor of Readmission Rates and Glucose Control in Patients Hospitalized for Diabetes

BACKGROUND

Diabetes is a chronic disease with increasing prevalence. We hypothesize that a significant percent of patients with a primary diagnosis of diabetes/diabetes-related complications after hospitalization at George Washington University Hospital (GWUH) would have no specific follow-up and overall glucose control would be poor after discharge.

METHODS

This is a retrospective study evaluating the rate of follow-up for diabetes after hospitalization at GWUH for a primary diagnosis of diabetes/diabetes-related complications. There were 4266 GWUH admissions with a primary/secondary diagnosis of diabetes from June 2014 to June 2015. Chart review of patients (289) with a hospital admission for a primary diagnosis of diabetes/diabetes-related complications was conducted with assessment of readmission rates and overall glucose control after discharge. Discharge instructions/summaries from the hospital were reviewed for instructions/arranged appointments for follow-up. Follow-up rate was evaluated. Hemoglobin A1c during admission or within 180 days of admission as well as 90-180 days post-admissions were assessed. Hospital readmission rates were assessed at 30, 60, 90, and 180 days.

RESULTS

The readmission rate for a primary diagnosis of diabetes was 7.27% at 30 days and 28.02% at 90 days while overall readmissions for any cause at 30 days was 15.2% and at 90 days was 30.1%. 78.9% patients had A1c within 180 days of admissions/during admission. 21.8% had A1c > 10% and 21.5% >8%. Concerning follow-up, 71.47% had directions to follow-up with primary care providers. 67.08% patients has follow-up arranged with primary care providers prior to discharge; 40% of those that had follow-up arranged actually followed up compared to 17% that actually followed up when follow-up was not arranged (P = .0036). Of the 319 patients, 200 had follow up. Hemoglobin A1c within 90-180 days after admission. A1c was >10% for 37.1% and 59.6% for >8%.

DISCUSSION

Although limited by the review at a single institution in a metropolitan center with multiple health care systems, our data showed a significant percent of patients with a primary diagnosis of diabetes/diabetes-related complications were re-admitted, often did not have specific follow-up or complete follow-up as instructed, and overall glucose control remained poor following admission.

CONCLUSION

To improve long term health outcomes in hospitalized patients with diabetes, protocols to ensure follow-up need to be implemented.

STATUS

Medical Student

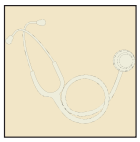
AUTHORS

Nathaniel Nguyen

Nicole Ehrhardt

RESEARCH MENTOR/ DEPARTMENT CHAIR

Nicole Ehrhardt



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Optimzing the Medicine Admitting Officer Role

BACKGROUND

Patients who are being admitted to the General Medicine floor from the Emergency Department wait a great deal of time before a bed becomes available. There is often a delay because patients are triaged to the wrong team or do not need to be admitted in the first place. The Medicine Admitting Officer (MAO) role was created this academic year to help triage patients more appropriately and improve their time to floor. The role of the MAO is to hold the medicine admitting pager, and receive pages directly from the ED regarding possible admissions. The MAO then sees the patient and determines if the patient is appropriate for the general medicine floor vs the pulmonary team, or possibly even the cardiac service or the Intensive Care Unit. The Medicine Admitting Resident works with the Emergency Medicine Team to evaluate and come up with an admission (or no admission) plan for the patient by helping with chart review and talking to medicine attendings and consultants.

PROBLEM

As this is a new role, the role has not been fully studied. Is it an effective use of resident's time? Does it contribute to resident education? Are there any obstacles that the MAO faces? These are just some of the questions that arose with the execution of the position.

One particular problem that arose is who admits during the time there is overlap between the day admitting team and the night admitting team.

The survey completed by the Internal Medicine Residents indicated that they preferred that the Medicine Admitting Officer decide who admits the admissions between the overlap hours of 6 and 8 pm.

METHODOLOGY

The Intervention was the MAO deciding who admits the patient.

The effectiveness of this was judged by surveys done by both residents who did the MAO role prior to the change, as well as after the change. The surveys were a series of questions on how well they thought the intervention worked from a score of 1 thru 5.

RESULTS

The results of the survey was still pending at time of this abstract submission.

IMPLICATIONS

The exact role of the MAO will become clearer defined, and more optimized using input from fellow residents. The overlap time of 6 to 8 PM, which is the busiest will in theory, run smoother, with one person taking charge and assigning patients to residents. Future changes and interventions can be made from this to better optimize this new role.

STATUS

Resisdent Physician

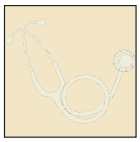
AUTHORS

Faryal Osman

Nika Safaie

RESEARCH MENTOR/ DEPARTMENT CHAIR

Nupur Mehta



SCHOOL OF MEDICINE AND HEALTH SCIENCES

An Unusual Case of A Blue Finger

INTRODUCTION

Acute discoloration and paresthesia of a distal extremity is concerning for an ischemic event or a manifestation of underlying systemic disease. Achenbach syndrome is an infrequent, but benign etiology of an acute blue finger that needs to be recognized clinically. We present a case to increase awareness.

CASE

A 57-year-old Caucasian female presented to rheumatology clinic for "bruising digits." She described four episodes of spontaneous segmental, blue discoloration of varying digits over the past two years. Each episode was isolated to a single digit and preceded by 10-15 minutes of throbbing with the digit then turning white and numb. These prodromes were followed by a feeling of "blood vessel popping" with subsequent "bruising" and mild swelling. Resolution of discoloration ranged from several hours to several days. There was no association with exposure to cold temperatures and warming the fingers would not alleviate the symptoms, nor abort the course. Past medical history includes Raynaud's disease diagnosed in her twenties. Her current symptoms feel distinctly different from usual Raynaud's episodes. She is a non-smoker and takes no medications. Family history is non-contributory.

Physical exam was unremarkable at presentation and follow up. Photos from the recent episode were available, revealing blue discoloration involving the volar surface of the right 3rd digit at the PIP extending 1cm on either side of the joint with mild swelling, sparing of the distal phalange and no abnormalities of the surrounding digits.

Work-up for Raynaud's included anti-nuclear antibodies and its sub-serologies, anti-phospholipid serologies, complements, complete blood count and complete metabolic panel. These studies were unremarkable and no autoimmune process was identified. The patient also underwent MRA of the right upper extremity, which was non-revealing. Based on the clinical presentation, a diagnosis of Achenbach syndrome was made and the patient was reassured.

DISCUSSION

Achenbach syndrome is a benign, self-limiting cause of spontaneous blue finger discoloration that is commonly misdiagnosed as vascular problems, including Raynaud's. Unlike Achenbach syndrome, Raynaud's episodes may involve multiple fingers simultaneously, is temperature related and warrants further work-up. In contrast, case studies and case series of Achenbach syndrome suggest futility of angiography and extensive rheumatologic work-up and have not demonstrated any significant disease associations over time. Despite the concerns raised by acuity and appearance, knowledge of Achenbach syndrome along with careful history taking will direct the physician to the correct diagnosis and avoid unnecessary, costly testing.

STATUS

Staff

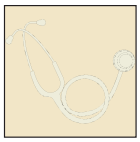
AUTHORS

Gregory Piech

Bita Shakoory

RESEARCH MENTOR/ DEPARTMENT CHAIR

Bita Shakoory



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Creating Emergency Department Point-of-Care Testing Protocols: An Expert Panel and Delphi Process

In recent years, point-of-care (POC) testing has gained popularity in emergency departments (EDs) to facilitate rapid laboratory test results 1 2 3 4 . Despite increasing popularity, few studies have addressed POC use early in ED care, specifically around ED triage. Availability of laboratory testing may help risk-stratify patients by providing additional information early in ED care. In a prospective study, triage POC testing changed patient management in 14% of cases, Emergency Severity Index (ESI) triage level in 15%, and 56% found POC testing to be helpful in the triage process [5] . In addition, POC may hasten ED care through early ordering of symptom appropriate diagnostic tests—a process called rapid posttriage assessment [6 7] .

In this project, we convened an expert panel to identify priorities for ED POC testing and created 2 protocols intended for early care of ED patients. One protocol focuses on early prioritization for time-sensitive conditions, and a second is a rapid posttriage assessment POC protocol.

We convened a technical expert panel and used a Delphi process to create 2 protocols for ED POC testing. The goal was to seek input to develop these protocols using a consensus-seeking methodology using expert guidance followed by multiple rounds of structured questionnaires. In our study, we used 2 rounds of structured questionnaires to solicit opinions; resolve areas disagreement; and, where possible, achieve consensus. The protocols were designed to aid nurses in deciding which POC to order for ED patients with specific symptoms.

STATUS

Medical Student

AUTHORS

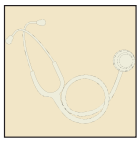
Jesse Pines

Mary Elizabeth Buchanan

Mark Zocchi

RESEARCH MENTOR/ DEPARTMENT CHAIR

Jesse Pines



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Renal failure due to Proteinase-3 antibody positive ANCA-associated glomerulonephritis in a patient with Bartonella quintana endocartitis

BACKGROUND

Bartonella species can cause culture-negative bacterial endocarditis (BE). However, their role in pathogenesis of organ-threatening ANCA-associated vasculitis is not well recognized. Our case depicts this unusual association and the importance of accurate diagnosis, which would dramatically alter the treatment strategies and disease outcome.

CASE DESCRIPTION

A 55 year old African-American male with past medical history of hepatitis-C and alcoholism presented with dyspnea, fever, weight loss, and lower extremity edema to an outside hospital and was noted to be in acute renal failure with creatinine of 5.5, and hypertension. Echocardiography demonstrated severe aortic and mitral valve vegetations. Blood cultures, ANA, HCV PCR, HIV, cryoglobulins, SPEP, C4 were normal. Intensive search for an infectious etiology revealed elevated Bartonella henselae and B. quintana IgG and elevated Bartonella quintana IgM. Patient also had positive C-ANCA/anti-proteinase 3 antibodies and low C3 complement. Drug and toxicology screening were negative except for ethanol. Renal biopsy demonstrated pauci-immune proliferative glomerulonephritis (GN). Subsequently, the patient was treated with IV antibiotics and pulse IV steroids. Treatment with Rituximab was considered but patient refused further therapy and was discharged on Rifampin, Doxycycline, and Prednisone. Ten days later he presented to our hospital with acute respiratory distress and was noted have worsening renal function and pulmonary edema. His echocardiogram showed worsening ejection fraction (65% -> 35%) with aortic valve vegetations. Patient declined aortic valve repair. C-ANCA –associated glomerulonephritis was attributed to Bartonella infection and more aggressive immunosuppressive therapy was withheld. Patient had significant recovery of cardiac and renal function with antibiotics and supportive care.

DISCUSSION

Positive c-ANCA/ proteinase-3 antibodies (PR3) is one of the diagnostic features of Wegener's/Granulomatosis with polyangiitis (WG/GPA). Glomerulonephritis in GPA is "pauci-immune". Therefore, presence of immune-complex and C3 complement deposits in renal biopsy is atypical for GPA but has been reported in ANCA-associated-GN due to cocaine, hydralazine and other drugs. Our patient had consistently tested negative for these drugs. In the two other cases described in the literature, presence of IgG/ IgM/ C3 complexes in renal biopsy of ANCA-associated-GN ,can help distinguish glomerulonephritis seen with WG/GPA from renal involvement caused by Bartonella. Failing to distinguish Bartonella induced infectious glomerulonephritis from Wegener's/GPA glomerulonephritis, would lead to aggressive immunosuppressive therapy with rituximab or cyclophosphamide, which may potentially lead to catastrophic consequences.

STATUS

Medical Student

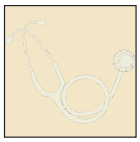
AUTHORS

Hamza Rahimi

Mandan Hashefi

RESEARCH MENTOR/ DEPARTMENT CHAIR

Mandan Hashefi



SCHOOL OF MEDICINE AND HEALTH SCIENCES

70 Years of Progress: History of the D.C. Rheumatism Society, 1946-2016

In the aftermath of the Second World War, medical practice was at a turning point. Antibiotic therapy with penicillin and anti-inflammatory therapy with aspirin had just reached mainstream use. The National Institutes of Health had just been established, creating a place for young investigators to discover novel solutions to intractable problems in medicine. Multiple national societies appeared for the benefit of countless diseases, encouraging innovation and discovery. In the midst of this national engagement, a local special interest group, the Rheumatism Society of the District of Columbia (D.C. Rheum or the Society), became one of the first local rheumatological professional society. Founded in 1946, the Society aimed "to stimulate interest in and increase the knowledge of rheumatic diseases among physicians and laymen." Originally a collection of physicians from various fields of medicine (including cardiology, pediatrics, and orthopedic surgery), D.C. Rheum grew to be a meeting place for the capital's foremost intellectual contributors to the state of the art in the developing specialty of rheumatology. This paper uses primary sources gathered from PubMed, family archives, and the Society's archive of meeting minutes in order to characterize the historical contribution and development of D.C. Rheum. In addition to describing how the Society evolved over time, this study contextualizes the activities of D.C. Rheum in the overall milieu of the science of rheumatology and aims to create a sense of the ways in which local professional societies interact with rapidly evolving scientific progress.

STATUS

Medical Student

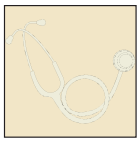
AUTHORS

Sonia Silinsky Krupnikova

Victoria Shanmugam

RESEARCH MENTOR/ DEPARTMENT CHAIR

Victoria Shanmugam



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Retinal Vasculitis as an Initial Presentation of Synovitis, Acne, Pustulosis, Hyperostosis, Osteomyelitis/Chronic Recurrent Multifocal Osteomyelitis (SAPHO/CRMO)

STATUS

Medical Student

AUTHORS

Pragya Singh

Tim Brady

RESEARCH MENTOR/ DEPARTMENT CHAIR

Pragya Singh

BACKGROUND AND PURPOSE

This is a case of a patient with chronic sternoclavicular pain presenting with retinal vasculitis found to have synovitis, acne, pustulosis, hyperostosis, osteomyelitis (SAPHO)/chronic recurrent multifocal osteomyelitis (CRMO) spectrum disorder. SAPHO syndrome is a rare chronic condition commonly involving the bones of the anterior chest with concomitant dermatological manifestations. CRMO is an aseptic inflammatory bone disease similar to SAPHO syndrome but lacks joint and cutaneous involvement. In more recent literature, SAPHO syndrome and CRMO are often described as a single clinical spectrum. This case illustrates the potential of a rare disease to masquerade as common process, thus delaying adequate treatment.

METHODS/CASE DESCRIPTION

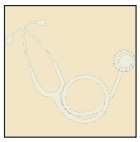
The patient is a 37-year-old female who presented with years of recurrent episodes of sternoclavicular pain responsive to non-steroidal anti-inflammatory drugs (NSAIDs). Initial biopsy revealed reactive bone and fibrosis and she was told she had "costochondritis." She began experiencing floaters in her left eye and initial workup revealed elevated C-reactive protein (CRP) and estimated sedimentation rate (ESR), normocytic anemia, and regions of vascular leakage on fluorescent angiography. Further investigation included a CT showing sternal hyperostosis and sclerosis and a PET/CT showing sclerotic and partially lytic lesions in the sternum and bilateral clavicular heads. This was particularly concerning for a neoplastic process but a re-biopsy showed chronic inflammation without evidence of malignancy. Sternoclavicular pain continued and months later, the patient reported an episode of pustular skin lesions in a dermatomal distribution on the right chest wall.

RESULTS/CASE DISCUSSION

Given the presence of pustulosis, hyperostosis, and chronic inflammation on biopsy, a diagnosis of SAPHO/CRMO spectrum disorder was made and immunosuppressive therapy was initiated. Following treatment with oral prednisone 40mg, her symptoms improved and CRP and ESR levels returned to normal. Decreasing the prednisone to 10mg resulted in the return of sternal pain and the cessation of prednisone completely resulted in a re-elevation of inflammatory markers. Pustular skin lesions and retinal vasculitis have not returned.

CONCLUSION/SIGNIFICANCE

While bone pain can be a common complaint, serologic and radiographic evidence of inflammation should prompt one to exclude a malignant process prior to initiating treatment. This case demonstrates a unique scenario where a mundane process reveals to be something more sinister. SAPHO/CRMO spectrum disorder describes the clinical spectrum of sterile inflammatory bone disease with the commonly concurring disorders of synovitis, acne, pustulosis, hyperostosis, and osteomyelitis. In addition to the typical manifestations, this presentation is particularly unique involving retinal vasculitis.



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Treatment Outcomes following Traumatic Optic Neuropathy

An association between facial trauma and blindness has long been recognized, but it was not until 1845 that Nuhn recognized that visual impairment was associated with optic nerve scarring. Traumatic optic neuropathy can be either direct or indirect. Direct traumatic optic neuropathy results from anatomical disruption of the optic nerve, whereas indirect traumatic optic neuropathy is caused by the transmission of forces from a site distant from the optic nerve.The occurrence of traumatic optic neuropathy is 0.4 to 2.5 percent in facial trauma,which has limited large-scale investigations. Nevertheless, a comprehensive understanding of orbital frac- ture patterns, load-bearing, and mechanistic skeletal impact studies has elucidated that the mechanistic processes leading to traumatic optic.

BACKGROUND

Traumatic optic neuropathy is characterized by sudden loss of vision following facial trauma leading to variable visual de cits. The purpose of this study was to evaluate recent institutional trends in the treatment of traumatic optic neuropathy, evaluate the outcomes of different treatment strategies, and identify factors associated with improved vision.

METHODS

Institutional review board approval was obtained to retrospectively review patients diagnosed with traumatic optic neuropathy at a high-volume trauma center from 2004 to 2012. Pretreatment and posttreatment visual acuity was compared using quantitative analysis of standard ophthalmologic conversion.

RESULTS

A total of 109 patients met inclusion criteria (74.3 percent male patients), with a mean age of 38.0 ± 17.5 years (range, 8 to 82 years). Management of traumatic optic neuropathy involved intravenous corticosteroids alone in 8.3 percent of patients (n = 9), 56.9 percent (n = 62) underwent observation, 28.4 percent (n = 31) had surgical intervention, and 6.4 percent (n = 7) underwent surgery and corticosteroid administration. Only 19.3 percent of patients returned for follow-up. Vision improved in 47.6 percent of patients, with a mean follow-up of 12.9 weeks. Patients younger than 50 years had a trend toward higher rates of visual improvement, 60 percent versus 16.7 percent (p = 0.15).

CONCLUSIONS

The majority of traumatic optic neuropathy patients are unikely to return for a follow-up examination. Optic nerve decompression has fallen out of favor in the authors' institution, and observation is the most common management strategy. Outcomes following corticosteroid administration and observation are comparable. (*Plast. Reconstr. Surg. 137: 231, 2016.*)

STATUS

Medical Student

AUTHORS

Michael Sosin

Sean Y. Saadat

Eduardo Rodriguez

Carla De La Cruz

Gerhard S. Mundinger

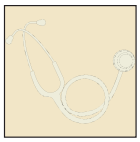
Arthur J. Nam

Paul N. Manson

Michael R. Christy

RESEARCH MENTOR/ DEPARTMENT CHAIR

Eduardo Rodriguez



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Pedal Lymphangiography Remains a Valuable Tool for Percutaneous Thoracic Duct Embolization

LEARNING OBJECTIVES

We intend to describe and visually demonstrate the use of bipedal lymphangiography as a viable technique to visualize the lymphatic circulation. We will also demonstrate its utility for percutaneous thoracic duct embolization (TDE).

BACKGROUND

Pedal lymphangiography was first described by Kinmonth in the 1950's and remains the gold standard for accessing the lymphatic circulation today. In the past, pedal lymphangiography was used to image lymph nodes for cancer staging but now is primarily used to identify chylous leaks for subsequent percutaneous TDE. Given the relatively low incidence of chylous leaks, pedal lymphangiography is a skill that few newly trained interventional radiologists learn and even fewer have opportunity to master. Several strategies have been suggested to gain access to the lymphatic circulation such as direct nodal injection and retrograde cannulation of the thoracic duct, however, these methods are not without complication.

CLINICAL FINDINGS / PROCEDURE DETAILS

Direct nodal lymphangiogram was attempted as described by Itkin in 2012. Under ultrasound guidance, suitable lymph nodes in the groin were accessed, however, the needle repeatedly became dislodged due to the patient's slender body habitus and the direct nodal injection was abandoned in favor of traditional bipedal lymphangiography.

Bipedal lymphangiography begins with injection of methylene blue into the web spaces between the toes. The subcutaneous tissue of the dorsal foot is infiltrated with lidocaine and a superficial transverse incision is made. Lymphatic vessels, now a vibrant blue, are gently isolated from the subcutaneous fat and cannulated. Ethiodized oil is infused and periodic fluoroscopy performed to demonstrate progression of contrast to the level of the cisterna chyli.

Once visualized fluoroscopically, a 21 gauge Chiba needle is used to puncture the cisterna chyli and the thoracic duct is accessed with a stiff guidewire and microcatheter. Embolization is achieved with coils and a liquid embolic agent such as Onyx (EVOH copolymer).

CONCLUSION AND/OR TEACHING POINTS

Pedal lymphangiography is a valuable tool in the interventional radiologist's toolbox. The technique of direct nodal injection used in TDE may theoretically decrease procedure times, however, this technique may be technically more difficult in patients with thin body habitus necessitating the use of pedal lymphangiography.

STATUS

Medical Student

AUTHORS

Matthew Stib

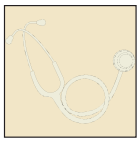
Michael Secrist

Kermit R. Rust III

Anthony C. Venbrux

RESEARCH MENTOR/ DEPARTMENT CHAIR

Anthony C. Venbrux



SCHOOL OF MEDICINE AND HEALTH SCIENCES

The Use of Silgel STC-SE, a Topical Silicone Gel for the Treatment and Reduction of Hypertrophic and Keloid Scars

INTRODUCTION

A Single centre study assessing the efficacy of Nagor's Silgel STC-SE silicone gel, to reduce the appearance of hypertrophic and keloid scars.

METHODS

A 16-week controlled study of 36 patients with hypertrophic or keloid scars. The subjects were divided between two cohorts one assessing recently healed scars (<6 months) and one assessing older scars (6 months to 2 years) in order to determine the effectiveness of Silgel. Both cohorts were prescribed a 20ml tube of Silgel and instructed to apply sparingly to the scar, twice daily, for 16 weeks. The efficacy of the Silgel on the scar was evaluated by skin hydration, skin moisture evaporation, skin elasticity, basic scar measurements (length, width, and height), subjective patient questionnaire data, and image analysis. All subjects, from both cohorts, had data collected at baseline and weeks 1, 4, 8, 12, and 16. Photographs were taken for image analysis at baseline, week 8, and week 16. Statistical analysis was conducted on all data in order to show any statistical significance.

RESULTS

Of the 29 patients that completed the study, 90% of patients reported marked improvements in their scar appearance. Patient subjective questionnaire data showed great satisfaction with the product. Image analysis showed visual improvement with statistically significant reduction of the 'red' colour of scars. Overall, scar dimensions were significantly reduced. There was a significant decrease from baseline levels in terms of average scar length. Skin elasticity did not significantly change from baseline. Skin hydration and skin moisture evaporation also did not change significantly from baseline. Skin moisture evaporation significantly decreased from week 8 to week 16.

CONCLUSIONS

The results of this study indicate that Silgel has been found to be an effective treatment in reducing the appearance and red colour of hypertrophic and keloid scars up to two years old.

STATUS

Medical Student

AUTHORS

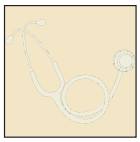
Erica Tafuro

Sharon Stewart

Greig Dougall

RESEARCH MENTOR/ DEPARTMENT CHAIR

Sharon Stewart



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Neonatal Intensive Care Unit (NICU) Management during Treatment for Type 1 Retinopathy of Prematurity and Eye Outcomes

INTRODUCTION

Retinopathy of prematurity (ROP) is caused by abnormal retinal blood vessel development in premature infants and requires treatment of severe Type 1 disease to prevent ophthalmic complications such as scarring, retinal detachment, and blindness. However, even with treatment, many become blind or are affected by myopia, strabismus, or visual impairment. Currently, there are no published guidelines for NICU medical management during laser treatment for Type 1 ROP. The purpose of this study was to evaluate NICU care during ROP laser treatment and determine eye outcomes associated with treatment circumstances in order to better prevent medical and ophthalmic complications.

METHODS

We historically reviewed neonates with Type 1 ROP treated between January 2009 and June 2015 at Children's National Medical Center (CNMC) which is a Level IV NICU.[1] For infants receiving their first laser treatment at CNMC, we assessed demographics, intubation requirements, treatment duration, median time to return to respiratory and feeding baselines, and eye outcomes at ≥6 months of follow-up. Incidence of grade 3 or 4 intraventricular hemorrhage (IVH), hydrocephalus, sepsis anytime prior to treatment, necrotizing enterocolitis (NEC), and bronchopulmonary dysplasia (BPD) were noted as indicators of medical disease burden.

RESULTS

Of the 51 infants reviewed, 2 were excluded due to first treatments at other hospitals. Six others were excluded because they received anti-VEGF injection as ROP treatment. For the 43 infants treated with laser, mean age at treatment was 37.0±2.7 weeks (range 32.0-42.4), gestational age was 24.1±1.6 weeks, and birth weight was 684.5±284.7g. Incidence of sepsis anytime prior to the procedure was high at 88% (38), with BPD at 86% (37), NEC at 42% (18), and grade 3 or 4 IVH at 23% (10). Nine infants (21%) were intubated at baseline (base-ETI), 10 (23%) were electively intubated before laser (elect-ETI), 3 (7%) required urgent intubation during treatment due to respiratory distress (urg-ETI), and 21 (49%) received no intubation (no-ETI). Treatment duration for no-ETI was shorter (0.8 hours) than all intubated groups (base-ET 1.0, pre-ET 1.4, urg-ETI 2.0). Return to respiratory and feeding baselines were markedly prolonged for elect-ETI at median 90.0 hours and 75.0 hours, respectively, compared to base-ETI (16.8, 3.0), urg-ETI (51.7, 30.0), and no-ETI (11.0, 5.9) (Figures 1 and 2). Eye outcomes included macular scar (14%), retinal detachment (8%), legal blindness (17%), and strabismus (28%) with elect-ETI having poorest outcomes (20%, 30%, 40%, 40%, respectively).

DISCUSSION

For extremely low-birth-weight infants with Type 1 ROP, elect-ETI prolonged return to respiratory and feeding baselines, and eye outcomes were poorest for this group. In contrast, urg-ETI was associated with shorter return to baselines despite increased procedure duration. Given these surprising findings, there may be cause to avoid elective intubation for laser treatment when neonates are stable as longer ventilation can lead to respiratory morbidity and delayed feeding in this population of infants with an already high disease burden.

REFERENCES

1 Miller MM, Revenis ME, Lai MM, et al. Risk and Clinical Course of Retinopathy of Prematurity in 78 Infants Gestational Age 22 to 25 weeks. J AAPOS 2014;18:266-70.

STATUS

Medical Student

AUTHORS

Laura Tiedemann

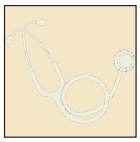
Lamia Soghier

Robert McCarter

Marijean M. Miller

RESEARCH MENTOR/ DEPARTMENT CHAIR

Marijean M. Miller



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Glycemic Control as a Function of Breakfast Macronutrients and Physical Activity Timing in Young Children with Type 1 Diabetes

BACKGROUND

Incidence of T1D is increasing in young children (< 7 years). During this sensitive developmental period, daily medical regimens are needed to prevent T1D complications commonly seen later in life. Diabetes management for young children relies solely on parents, and factors related to glycemic control and variability have not been well studied in this age group.

OBJECTIVE

To characterize blood glucose (BG), energy expenditure, diet and physical activity (PA) patterns in a small cohort of young children with type 1 diabetes (T1D).

METHOD

10 children aged 3-7 years (Mage= 5.88, 80% female) with T1D for at least 1 yr (2.78 ± 1.55 years) participated. For five days, participants wore blinded continuous glucose monitors (CGM) and actigraphs as objective measures of BG and PA, respectively, and parents completed daily 24 hour interviews (e.g., diet, BG monitoring). Parents also completed the Physical Activity Questionnaire (PAQ). Medical chart review was completed for the year prior to participation.

RESULTS

Glycemic control was overall good: M A1c = 7.27%± 0.69; six participants' A1c's ≤ 7.5 (within the 2015 American Diabetes Association (ADA) pediatric targets). Participants completed 6.32±2.15 BG checks/day and spent an average of 61% of the 5 day period above the ADA suggested BG range of 90-150 mg/dL and 18% below range. All parents reported satisfaction with their child's PA; however, results showed kids received significantly less PA than the 60 minutes per day recommended by American Academy of Pediatrics (Average PAQ score = 2.46 ±0.61; actigraph = 19.51 moderate to vigorous min/day ±24.67). Participants consumed a mean of 1530.91± 331.08 kilo calories/day (46% carbohydrates, 18% protein, and 15% fat) generally in line with recommendations for healthy children. There was no association between moderate-vigorous PA and time spent in low BG excursions ($r = 0.27$, $p = 0.45$). Participants who engaged in PA during the morning as well as afternoon trended toward less time in overall BG excursions ($\rho = 0.55$, $p = 0.06$).

CONCLUSIONS

Even young children meeting targets for A1c spend a significant portion of their day outside of the recommended BG range. Young children are more sedentary than parents perceive, and even short amounts of PA after each meal may have an impact on glycemic control for the remainder of the day.

STATUS

Medical Student

AUTHORS

Miriam Toaff

Carrie B. Tully

Loretta DiPietro

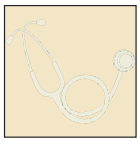
Celia Henderson

Fran Cogen

Randi Streisand

RESEARCH MENTOR/ DEPARTMENT CHAIR

Randi Streisand



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Volume Averaging of Spectral-Domain Optical Coherence Tomography Impacts Retinal Segmentation in Children

PURPOSE

To determine the influence of volume averaging on retinal layer thickness measures acquired with spectral-domain optical coherence tomography (SD-OCT) in children.

METHODS

Macular SD-OCT images were acquired using three different volume acquisition settings (i.e., ART 1, 3, and 9 volumes) in children enrolled in a prospective OCT study. Total retinal, retinal nerve fiber layer, ganglion cell layer, inner plexiform layer, inner nuclear layer, and outer plexiform layer thicknesses were measured around an ETDRS grid using beta version automated segmentation software for the Spectralis. The magnitude of manual segmentation required to correct the automated segmentation was classified as either minor (less than 12 lines adjusted), moderate (>12 and <25 lines adjusted), severe (>26 and < 48 lines adjusted) or fail (> 48 lines adjusted or could not adjust due to poor image quality). The frequency of each edit classification was assessed for each volume setting. Thickness, paired difference and 95% limits of agreement of each anatomic quadrant were compared across volumes.

RESULTS

75 subjects (median age 11.8 years, range 4.3- 18.5 years) contributed 75 eyes. Less than 5% of the 9 and 3 volume scans required more than minor manual segmentation corrections, compared to 71% of 1 volume scans. The inner (3mm) region demonstrated similar measures across all layers, regardless of volume number. The one volume scans demonstrated greater variability of the RNFL thickness, compared to the other volumes in the outer (6mm) region.

DISCUSSION

In children, a minimum acquisition setting of ART 3 for SD-OCT volumes should be obtained to reduce retinal layer segmentation errors.

STATUS

Medical Student

AUTHORS

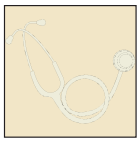
Carmelina Trimboli-Heidler

Kelly Vogt

Robert A. Avery

RESEARCH MENTOR/ DEPARTMENT CHAIR

Robert A. Avery



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Cost-Effectiveness Analysis of Early Point-of-Care Lactate Testing in the Emergency Department

OBJECTIVES

To determine the cost-effectiveness of implementing a Point-of-Care (POC) Lactate program in the ED for patients with suspected sepsis to identify patients with occult hypoperfusion who can benefit from early resuscitation.

METHODS

We constructed a cost-effectiveness model to examine an ED with an average volume of 30,000 patients annually. We evaluated a POC Lactate Program in which patients with SIRS and suspected infection are screened for an elevated lactate ≥ 4 mmol/L. Using the POC program, those with severe sepsis and elevated lactate levels are resuscitated and their lactate clearance is evaluated by serial POC lactate measurements. Patients with adequate lactate clearance are admitted to the general medical floor, whereas those without adequate clearance are admitted to the intensive care unit (ICU). In the base-case we assumed 68% of patients with severe sepsis and an elevated lactate identified in the ED would have adequate lactate clearance to allow for medical floor admission with a 2% overall mortality reduction. The POC Lactate Program was compared with a Usual Care Strategy in which all patients with severe sepsis and an elevated lactate are admitted to the ICU. Costs were estimated from the 2014 Medicare Inpatient and National Physician Fee schedules, and hospital and industry estimates. We conducted one- and two-way sensitivity analyses across pre-determined ranges for each variable.

RESULTS

In the base-case, an ED with 30,000 visits per year had 5,340 patients with suspected sepsis, of which 207 had severe sepsis and 44 with a lactate ≥4 mmol/L. The POC Lactate Program cost $39.53 to screen each ED patient with suspected sepsis, perform serial lactate testing on those with an elevated lactate, and their subsequent admission costs. This was compared with the Usual Care Strategy which had a cost of $33.20 per patient for lactate testing. In the POC arm, 14 of the 44 patients had inadequate lactate clearance and were admitted to the ICU, and the remaining 30 patients were admitted to a medical floor after adequate lactate clearance. The screened patients in the POC arm had 9.3784 quality-adjusted life years (QALYs) of life expectancy remaining compared with 9.3782 for the Usual Care Strategy for an incremental effectiveness of 0.0002 QALYs per patient screened for the POC Lactate Program, or 1.07 total QALYs gained across the entire screened population. The POC arm had an incremental cost-effectiveness ratio of $31,590 per QALY gained, well below accepted willingness-to-pay-thresholds.

CONCLUSIONS

Implementing a POC Lactate Program for screening ED patients with suspected sepsis is a cost-effective intervention for ED patients to identify severe sepsis responsive to early resuscitation.

STATUS

Medical Student

AUTHORS

Michael Ward

Wesley Self

Gregory Jasani

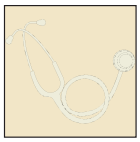
Adam Singer

Danielle Lazar

Jesse Pines

RESEARCH MENTOR/ DEPARTMENT CHAIR

Jesse Pines



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Race Does Not Affect the Prevalence of Sporadic Adenomas in Inflammatory Bowel Disease

BACKGROUND

Sporadic adenoma formation found on surveillance colonoscopies in patients with inflammatory bowel disease (IBD) represents a significant risk for cancer. Certain racial groups like African Americans (AA) are at increased risk of developing colorectal cancer (CRC), but there is conflicting literature on differences in sporadic adenoma formation. Some data suggests AA are at increased risk for large adenomas, more proximal lesions, and increased prevalence. These data, however, are studying the general population and to our knowledge no study has looked at differences in adenoma formation by race in IBD patients. The present retrospective study analyzes the prevalence of adenomas in IBD patients.

METHODS

All IBD patients who received a surveillance colonoscopy within the past year were included in the present study. Sporadic adenomas included serrated, tubular, villous, and tubulovillous adenoma formation. A database was created using Microsoft Excel and identifying information was eliminated to ensure anonymity. Statistical analysis was performed using Fisher's Exact Test, with statistical significance set at $P<0.05$.

RESULTS

One hundred and thirty six patients with IBD were included, 34 (25%) of which were AA, 68 (50%) Caucasian, and 34 (25%) classified as other. Of the 136 patients, 58 had Crohn's disease and 78 patients had ulcerative colitis. A total of 12 (8.8%) sporadic adenomas were found, 8 of which were serrated and 4 tubular. The incidence of sporadic adenomas were 4/34 (11.8%) among AA and 8/68 (11.8%) for Caucasians. The calculated P-value between these two groups is 1.0 ($P<0.05$) using Fisher's Exact Test. The average age of AA with adenomas was 44.7 years and 50.4 years in Caucasians. Average disease duration was 16.3 years in AA and 17.9 years in Caucasians.

DISCUSSION

IBD is known to increase the risk of developing colorectal cancers, especially through the inflammation-dysplasia pathway. Well-studied risk factors for CRC in IBD include duration, severity and extent of colitis, but a relationship between race and CRC risk has only been demonstrated in the general population, not IBD patients. There is even less data regarding the difference in sporadic adenoma formation between different races in IBD patients. While some literature suggests a difference in the prevalence of sporadic adenomas among AA and Caucasians in the general population, the present study found no such difference for our population of colitis patients. Additionally, the two groups did not differ greatly in average age or disease duration, which could have potentially served as confounding variables.

The study of sporadic adenoma formation in IBD is still in its early stages. While differences in risk have not yet been well-characterized, further understanding of the molecular mechanisms underlying adenoma development might allow us to stratify risk more appropriately. At present, race does not seem to be an independent risk factor, so we should maintain a high index of suspicion of pre-neoplastic lesions in all IBD patients.

STATUS

Medical Student

AUTHORS

Najeff Waseen

Samah Nassereddine

Alexis Payle

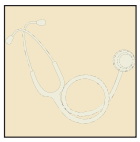
Jennie Zhang

Timothy Dougherty, Jr.

Marie L. Borum

RESEARCH MENTOR/ DEPARTMENT CHAIR

Marie L. Borum



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Risk Factors for Compartment Syndrome in Treatment of Supracondylar Humerus Fractures

PURPOSE

Ischemia secondary to vascular injury or compartment syndrome (CS) potentially complicates management of supracondylar humerus (SCH) fractures. Prompt recognition and treatment prevents irreversible muscle damage. We aimed to determine risk factors associated with the development of CS in patients with SCH fractures.

METHODS

A retrospective chart review was performed of all patients surgically treated for displaced Gartland Type III SCH fractures from 2007-2014 at a single tertiary care pediatric hospital. Baseline demographics included age, injury type (open vs. closed), and mechanism of injury. Vascular status, defined by presence or absence of a palpable pulse and hand perfusion, was recorded at all time-points through care, along with existence of neurologic deficit. Multiple pre-, intra-, and post-operative variables were gathered and two groups, CS and non-CS, were compared. The data was analyzed with a two-tail significance level of 0.05 to determine risk factors contributing to the development of CS.

RESULTS

Of the 733 patients included, 7 (0.95%) developed CS requiring fasciotomy. Three patients presented acutely, three patients in the early postoperative period, and one patient in a delayed fashion. Open fractures occurred at a higher frequency in the CS group compared to non-CS group (2 vs 9, p=0.004). Patient and fracture demographics were similar between the groups. Time to surgery had no effect on the outcome. The mean operative time was greater in patients who developed CS than those who did not (89.1 min vs 40.5 min, p=0.0051); however, 5 of 7 patients had concomitant procedures including fracture debridement or fasciotomy at the time of reduction. Vascular status and nerve injury were not significant risk factors associated with CS.

CONCLUSION

Previous research identified the clinical finding of a pulseless hand as a risk factor for vascular injury and associated complications. Our study suggests that an open fracture pattern may represent another feature with a higher risk of developing CS, potentially related to degree of initial soft tissue trauma. Increased operative time observed in our CS group was likely related to surgical complexity and need for associated procedures as opposed to prolonged traction or manipulation necessary to achieve fracture reduction.

SIGNIFICANCE

CS is a rare but potentially devastating complication occurring in patients with SCH fractures. Identification and close observation of patients with specific clinical indicators fated for a poorer outcome may improve early detection and treatment of CS and prevention of long-term sequelae. Awareness that symptoms of ischemia warranting treatment can evolve prior to fracture stabilization, during the early postoperative period or in a delayed fashion is important for proper diagnosis.

STATUS

Medical Student

AUTHORS

Megan Young

Rijo Maracheril

Benjamin Martin

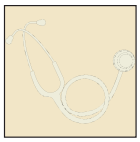
Matthew Oetgen

Yunfei Wang

Allison Matthews

RESEARCH MENTOR/ DEPARTMENT CHAIR

Megan Young



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Beer Potomania: A Challenging Case of Hyponatremia

Beer potomania is a syndrome of hyponatremia associated with excessive beer drinking. Little or no salt content of beer, and suppression of protein breakdown by the carbohydrate and alcohol content of beer, result in marked reduction in the solute load to the kidney. This leads to impaired water clearance and a dilutional hyponatremia. Beer potomania is difficult to recognize especially in the presence of other factors commonly affecting sodium excretion.

A 66 year-old man with history of alcoholism and alcoholic cardiomyopathy presented to the emergency room with tremors of his upper and lower extremities. History dated back to 6 days prior to presentation when he developed tremors of all four extremities, and was unable to walk. He had a significant history of alcohol consumption, usually drinking 4 to 5 cans of beer per night for the past 34 years. In addition, he had consumed a fifth of a vodka bottle the day before presentation. He had a pattern of often skipping meals though was compliant with both his diuretics medications: furosemide 40 mg once daily and spironolactone 25 mg daily. He was not on any antipsychotic or antidepressant drugs. His history was negative for seizures, confusion or somnolence. He denied diarrhea, vomiting, cold intolerance, shortness of breath, swelling, or excessive water intake. On physical exam, he was euvolemic with no JVD, lower extremity edema or pulmonary crackles. Neurological exam revealed resting tremors of both his hands. Labs were remarkable for plasma sodium of 122, BNP of 474, serum osmolality of 268, urine osmolality of 223, and urine sodium of 20. Patient was assessed to have severe euvolemic hypotonic hyponatremia. The combination of euvolemic hyponatremia with history of excessive beer drinking made beer potomania very likely. His urine osmolality and urine sodium, however were higher than expected in beer potomania. These could be explained by the two diuretics that the patient was taking. Furthermore, patient's poor nutritional intake added to the severity of his hyponatremia. History, physical exam and lab testing excluded SIADH and hypothyroidism. Patient was managed with fluid restriction, appropriate nutritional and sodium intake and withholding of his diuretics. Plasma sodium slowly corrected to 130 over the course of 3 days.

This case illustrates the condition beer potomania, an infrequent cause of hyponatremia. Findings in hyponatremia do not always point in one direction, especially with the concomitant use of diuretics. Understanding of pathophysiology can be useful in interpreting lab results. Recognition of beer potomania as a separate entity of hyponatremia is critical. Management should be tailored for this specific etiology, as if unrecognized can lead to serious neurologic sequelae and even death. Patient education and alcohol related counseling, is essential to prevent recurrence.

STATUS

Staff

AUTHORS

Raza Yunus

Hind Rafei

Parvinder Khurana

RESEARCH MENTOR/ DEPARTMENT CHAIR

Parvinder Khurana

DRUG ABUSE

SCHOOL OF NURSING

Adverse childhood experiences and binge drinking as an adult

BACKGROUND

Binge drinking is a significant public health problem and 25% of American adults are binge alcohol users. While adverse childhood experiences (ACEs) have been linked to many unfavorable health outcomes, little is known regarding relationship between ACEs and later binge drinking. It is therefore important for the nursing community to identify which ACEs are associated with later binge drinking behavior.

OBJECTIVES

The purpose of this study was to determine whether exposure to ACEs is predictive of later binge drinking, using data from the Behavioral Risk Factors Surveillance System (BRFSS).

METHODS

Data were obtained from the 2011 BRFSS, an annual cross sectional survey. Four states utilized the ACE module and 52,836 met the inclusion criteria. Logistic regression and linear regression were used to determine whether 11 ACEs (Lived with depressed person, drinker, illegal drug user, jailed person, divorce, and whether parents hit each other, hit you, swear at you, touch you inappropriately, made you touch them, or have sex with them) are associated with self-reported binge drinking.

RESULTS

Overall, 10 of 11 ACE variables (all except forced sex) were significant predictors of binge drinking and all 11 were significant predictors of binge drinking frequency (each $p < .05$), either in isolation or after accounting for demographic variables. Further, the total number of ACE categories experienced was a significant predictor of binge drinking, such that each additional ACE category was associated with an additional 0.14 binge drinking event each month.

CONCLUSIONS

ACEs increase the risk for later binge drinking. It is therefore important for the nursing community to include ACEs in the assessment at patient encounter when caring for patients with binge drinking problems.

STATUS

Graduate Student

AUTHOR

Ann Hoffman

RESEARCH MENTOR/ DEPARTMENT CHAIR

Qiuping Pearl ZHou

SCHOOL OF MEDICINE AND HEALTH SCIENCES

The Impact of See the City You Serve Fieldtrip: An educational tool for teaching the Social Determinants of Health

PURPOSE

Despite a call to action to address the social determinants of health in the United States, there has been limited evaluation of specific tools for teaching the social determinants of health to our medical learners. This study evaluates the See the City You Serve Fieldtrip as a tool for teaching the social determinants of health to incoming medical interns.

METHODS

85 incoming interns from The George Washington University School of Medicine and Health Sciences Graduate Medical Education programs participated in a bus tour of Washington, D.C. guided by community partners. The fieldtrip introduced trainees to the neighborhoods where their patients will come from. Each participant completed a pre and post activity survey. The pre and post-test values were compared for each participant using a two-sided, paired t-test. Qualitative reflection responses were recorded and coded for recurrent themes.

RESULTS

In our study population, 21% of the interns were from D.C. and 93% had experience working with underserved populations. Basic knowledge of D.C. disparities increased after the activity as compared to baseline as noted by the greater percentage of interns who correctly identified the number of D.C. wards (65% vs. 100%, p=0.000), the wards with the lowest per-capita income (46% vs. 100%, p=0.000), and the degree of cancer mortality disparities in D.C. (53% vs. 97%, p=0.000). Furthermore, as compared to baseline, post-activity a greater percentage report being at least somewhat comfortable understanding the neighborhoods from which their patients come (58% vs. 89%, p=0.000), identifying challenges to health care that affect low income patients (74% vs. 90%, p=0.001), describing community resources (29% vs. 67%, p=0.000), and referring patients to local community resources outside of GWU (25% vs. 64%, p=0.000). Interns recurrently reported that this experience would change the way they practice medicine through improved awareness of the social determinants of health, improved understanding of local resources to assist in patient care, and improved understanding of local patients' background.

CONCLUSION

We found that, among incoming residency interns, a brief bus tour guided by community partners during orientation week improved knowledge of local disparities, improved understanding and comfort addressing the social determinants of health, and inspired physicians to change the way they practice medicine. These sorts of experiences linking community resources and trainees can and should be woven into residency curriculum as part of ongoing resident education regarding population health and utilizing community resources to address the social determinants of health.

STATUS

Faculty

AUTHORS

Aileen Chang

Tracie Bass

Monique Duwell

Jeffrey Berger

Raksha Bangalore

Nancy Lee

Jehan El-Bayoumi

RESEARCH MENTOR/ DEPARTMENT CHAIR

Alan Wasserman

EDUCATION/HEALTH SERVICES

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

A Public Health Approach to the Planning and Implementation of an Exercise Support Group for Veterans

BACKGROUND

Poor musculoskeletal health is a public health issue disproportionately affecting the veteran population. VA Strong, a health initiative developed from the partnership of the Muscle Morphology, Mechanics, and Performance Laboratory (3MAP Lab) at the Washington DC VA Medical Center (DC VAMC) and the Catch-A-Lift Fund (CAL), targets veteran DC VAMC employees interested in both maintaining a fitness regimen and contributing to the well-being of fellow veterans within the local community. 3MAP Lab has the core mission of improving the musculoskeletal health of veterans through exercise-based rehabilitation, and CAL has the primary goal enhancing the well-being of returning veterans through strength training and peer-to-peer support. Therefore, the founding principles of the VA Strong program are: self-efficacy, volunteerism, and community engagement.

METHODS

Application of public health theory will allow the VA Strong program to identify program components that align well with its central activities. Logic models will be applied to determine the program's inputs, activities, and outputs, and their relationship to one another: 1) The Health Belief Model best explains the fitness component of the program and will serve to best identify how veteran perceptions of musculoskeletal health will affect their participation and adherence to an exercise regimen. 2) Social Learning Theory will provide a framework for the peer-to-peer volunteerism aspect of the program. This element of VA Strong will be used to engender the participation of DC VAMC employees in CAL-sponsored community activities to support subsidized community fitness center memberships for returning veterans. 3) Grounded Theory will be utilized to better understand how veterans perceive common research outcomes concerning musculoskeletal health, functional performance, and caregiver burden. Feedback from veterans will inform the use of patient-centered outcomes and shape future research endeavors at the DC VAMC.

RESULTS

The use of integrated logic models will provide a conceptual framework for the VA Strong program and its component activities. Moreover, this approach will provide the opportunity for DC VAMC stakeholders to evaluate the program's effectiveness in attaining its targeted outcomes concerning self-efficacy, volunteerism, and community engagement.

CONCLUSION

Overall, this conceptual framework is informed by previous research on community engagement, and the barriers to physical fitness among the veteran population. The application of public health theory to the implementation and evaluation of the VA Strong program will maximize veteran adherence to the exercise regimen, foster participation in veteran volunteer programs associated with CAL, and identify patient-centered outcomes for exercise-based rehabilitation research.

STATUS

Graduate Student

AUTHORS

Laura Falcon

Brian M. Hoover

Michael O. Harris-Love

RESEARCH MENTOR/ DEPARTMENT CHAIR

Michael O. Harris-Love

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Teaching Internal Medicine Residents about Genetics: One topic at a Time—Breast Cancer

BACKGROUND

Currently, the field of medicine is experiencing rapid changes in genetics and genomics information. While medical school curricula all include some genetics education, the content may vary from one school to another, leaving Internal Medicine (IM) residents with different skills and knowledge. In an IM residency where residents come from different medical schools, presenting an organized genetics curriculum may have value. Patients expect their physicians to be knowledgeable and current about their specific disease, including the genetic components and expect that they can inform them about terminology, inheritance, diagnostic testing, risks and benefits of testing. Physicians will need education about how to find current information about genetics factors in many diseases, and how to inform and counsel their patients using web-based tools.

PURPOSE

The purpose of this project was to identify baseline genetics knowledge of Internal Medicine (IM) Residents at The George Washington University, and to determine if a 1-hour presentation can be used to improve their knowledge.

METHODS

We performed a literature review of currently available information on genetics curriculum for IM residents and residency programs in other specialties. Although there is no standardized curriculum in genetics for IM residents, we did identify a proposed curriculum in genetics for IM[1].There has also been research in education about genetics in other residencies including Pediatrics, Obstetrics and Gynecology, Psychiatry and Surgery[2,3,4,5,6,7,8,9].

We propose to deliver a one-hour presentation about genetics and breast cancer to IM residents and medical students at GWU during Grand Rounds. The presentation will include concepts in genetics, as well as specific information about breast cancer and guidelines for testing. We plan a pre-test to assess knowledge about genetics and breast cancer, a one-hour presentation and a post-test. Pre-test and post-test scores will be compared using student's t-test.

CONCLUSION

We plan to evaluate the efficacy of a one-hour presentation for teaching genetics and use it as a possible model for other genetics education for IM residents. Possible topics for monthly presentations could include: colon cancer, ovarian cancer, emphysema, cardiology—long and short QT, among others.

REFERENCES

1 Riegert-Johnson, D.L., Korf, B.R., Alford, R.L., Broder, M.I., Keats, B.J., Ormond, K.E., … Watson, M.S. (2004). Outline of a medical genetics curriculum for internal medicine residency programs. *Genetics in Medicine: Official Journal of the American College of Medical Genetics,* 6(6), 543-547. doi: 00125817-200411000-00015 [pii]

2 Macri CJ, Gaba ND, Sitzer LM, Freese L, Bathgate SL, Larsen JW Jr. Implementation and evaluation of a genetics curriculum to improve obstetrician-gynecologist residents' knowledge and skills in genetic diagnosis and counseling. Am J Obstet Gynecol. 2005 Nov;193(5):1794-7. PubMed PMID:16260236.

3 Ready KJ, Daniels MS, Sun CC, Peterson SK, Northrup H, Lu KH. Obstetrics/gynecology residents' knowledge of hereditary breast and ovarian cancer and Lynch syndrome. J Cancer Educ. 2010 Sep;25(3):401-4. doi: 10.1007/s13187-010-0063-4. PubMed PMID: 20186516.

4 Kershner MA, Hammond EA, Donnenfeld AE. Knowledge of genetics among residents in obstetrics and gynecology. Am J Hum Genet. 1993 Dec;53(6):1356-8. PubMed PMID:8250052; PubMed Central PMCID: PMC1682504. Winner JG, Goebert D, Matsu C, Mrazek DA. Training in psychiatric genomics during residency: a new challenge. Acad Psychiatry. 2010 Mar-Apr;34(2):115-8. doi: 10.1176/appi.ap.34.2.115. PubMed PMID: 20224020.

5 Hoop JG, Savla G, Roberts LW, Zisook S, Dunn LB. The current state of genetics training in psychiatric residency: views of 235 U.S. educators and trainees. Acad Psychiatry. 2010 Mar-Apr;34(2):109-14. doi: 10.1176/appi.ap.34.2.109. PubMed PMID: 20224019.

6 Layde JB, Roberts LW. Education on genetics for psychiatric residents. Acad Psychiatry. 2010 Mar-Apr;34(2):85-6. doi: 10.1176/appi.ap.34.2.85. PubMed PMID: 20224009.

7 Finn CT. Increasing genetic education for psychiatric residents. Harv Rev Psychiatry. 2007 Jan-Feb;15(1):30-3. PubMed PMID: 17364971.

8. Stratakis CA, Cavuto NJ, Nelson D, Rennert OM. Molecular genetics in pediatric training: how much do we really know? Md Med J. 1995 Mar;44(3):210-3. PubMed PMID: 7707858.

9 Stoner J, Qi Y, Erdman SH, Attard TM. A web-based assessment of pediatrics resident medical knowledge in childhood hereditary gastrointestinal cancer predisposing syndromes. J Cancer Educ. 2009;24(4):254-6. doi:

10 1080/08858190902972921. PubMed PMID: 19838880.

STATUS

Medical Student

AUTHORS

Maria Henry

Andrew Nance

Charles Macri

RESEARCH MENTOR/ DEPARTMENT CHAIR

Charles Macri

SCHOOL OF NURSING

The Impact of an Advance Care Planning Simulation on the Communication Skills of Palliative Care Nurse Practitioner Students

BACKGROUND

Effective communication is the cornerstone of a therapeutic relationship, especially when dealing with serious, life threatening illness. Decisions based upon a patient and family's wishes, goals and values need to be guided by clinicians equipped to engage in complex advance care planning (ACP) conversations. Given its importance, communication skill proficiency has been identified as a core competency for the Advanced Practice Registered Nurse (APRN) in palliative care. Although simulation utilizing a standardized patient model has been employed for communication skills training in healthcare education, little is known about its usefulness in preparing palliative care nurse practitioner students for these challenging ACP discussions.

OBJECTIVES

The purpose of this pilot study was to evaluate the impact of advance care planning simulations upon the communication skills and self-efficacy of palliative care nurse practitioner students enrolled in a college of nursing.

METHODS

A prospective, quantitative study using a one-group pretest-posttest design was implemented to measure student communication skills and self-confidence. A convenience sample (N=19) of students enrolled in New York University's College of Nursing was obtained for the study. Students engaged in two ACP discussion simulations with actors playing the role of a newly diagnosed oncology patient. In addition to demographic information, the participants completed a self-confidence tool prior to the first and after the second simulation. An independent faculty member scored the students' performances for each simulation using a communication skills checklist based on the SPIKES protocol. Statistical analysis of the study variables was performed using paired t test and Wilcoxon signed-rank test measurements. Statistical significance was set at $p < .05$.

RESULTS

The majority of participants were between the ages of 20-30, had 4-10 years of nursing experience and reported having exposure to patient discussions surrounding healthcare proxy, code status and breaking bad news during their clinical rotations. Fifty-six percent (n =5) of the participants demonstrated improvement in communication skills ($t = -.098$, $p = .924$), while ninety-three percent (n = 14) reported increased self-confidence ($t = 4.725$, $p< .001$) after completion of the second simulation encounter. Statistical significance for nine of the 14 self-confidence tool items was confirmed by the Wilcoxon signed-rank test. Study limitations included attrition, sample size, intervention timing and scheduling.

CONCLUSION

Despite mixed results, this pilot provided key insights into the potential for repetitive simulation in communication skills education and the feasibility for future research of this pedagogy in the palliative care nurse practitioner student population.

STATUS

Doctoral Student

AUTHORS

Rose Anne Indelicato

Deborah Chapa

Dorothy Wholihan

RESEARCH MENTOR/ DEPARTMENT CHAIR

Deborah Chapa

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Clinical Public Health Integration in Medical School Curriculum: Transitioning Medical Problems to Health Solutions

The current chronic disease burden, growing health disparities, and evolution of our healthcare system require that medical students be equipped with basic public health education to effectively manage patients, navigate the healthcare system, and advocate for health[1,2,3,4,5,6]. The Institute of Medicine and the AAMC emphasize the need for physicians to be trained in public health[1,8]. The inaugural year of the revised curriculum at The George Washington University School of Medicine and Health Sciences (GW SMHS) represented a first step at the institution to integrate clinical public health into medical education. As part of this process, the Clinical Public Health (CLiPH) Working Group, a student formed curriculum advisory board, was created to give real time feedback and assess the Public Health & Health Policy theme curriculum in the first year at GW SMHS. The project objectives were:

1) To review and evaluate the effectiveness of the public health theme curriculum in the first year of the revised curriculum, including first year medical students' perceptions and knowledge of the public health theme.

2) To develop a proposal to maximize opportunities and achieve better integration of the public health theme into the curriculum.

The group aims toward clinical public health integration across the four year medical degree curriculum and better collaboration with the Milken Institute School of Public Health at the George Washington University to create an expanded scope of practice within public health for practicing physicians. Over the summer, the working group engaged with multiple stakeholders to forward the clinical public health agenda at GW SMHS. To conduct the curriculum assessment, the students developed a template and the group reviewed over fifty sessions, in the Public Health & Health Policy Theme, Clinical Skills and Reasoning Course (CSR), and intersession activities. Outside research was done to supplement resources to recommend and improve integration of the clinical public health material into the revised preclinical curriculum. Recommended revisions and developments were sent to faculty stakeholders as resources for the revision process of the curriculum. Future work to revise the curriculum should include study of the evolution of students' knowledge, attitudes, and beliefs surrounding clinical public health and the impact it has on their development as a physician. To better inform the development of the curriculum and how best to engage students with clinical public health, major stakeholders, such as health departments, community stakeholders, public health experts, and most importantly students should continue to be a part of the dialogue.

REFERENCES

1 Hernandez, L, Munthali, A, Solyst, M, Martinez R. *Training Physicians for Public Health Careers*. Washington, DC; 2007:1–4. Available at: https://www.iom.edu/~/media/Files/Report Files/2007/Training-Physicians-for-Public-Health-Careers/Trainingphysiciansreportbrief.pdf.

2 Berwick DM, Finkelstein J a. Preparing medical students for the continual improvement of health and health care: Abraham Flexner and the new "public interest". *Acad Med*. 2010;85(9 Suppl):S56–65. doi:10.1097/ACM.0b013e3181ead779.

3 Frenk J, Chen L, Bhutta Z a, et al. Health professionals for a new century: transforming education to strengthen health systems in an interdependent world. *Lancet*. 2010;376(9756):1923–58. doi:10.1016/S0140-6736(10)61854-5.

4 Kaprielian VS, Silberberg M, Mcdonald MA, et al. Teaching Population Health: A Competency Map Approach to Education. *Acad Med*. 2014;88(5):626–637. doi:10.1097/ACM.0b013e31828acf27.Teaching.

5 Fineberg H V. Public health and medicine where: the twain shall meet. *Am J Prev Med*. 2011;41(4 Suppl 3):S149–51. doi:10.1016/j.amepre.2011.07.013.

6 Cohen JJ. Will Changes in the MCAT and USMLE Ensure That Future Physicians Have What It Takes ? 2015;310(21):2253–2254.

7 Finkelstein J a, McMahon GT, Peters A, Cadigan R, Biddinger P, Simon SR. Teaching population health as a basic science at Harvard Medical School. *Acad Med*. 2008;83(4):332–7. doi:10.1097/ACM.0b013e318166a62a.

8 Mann S. After Reform, More Medical Schools Emphasize Public Health. *AAMC Reporter*. https://www.aamc.org/newsroom/reporter/170156/public_health.html. Published January 1, 2011.

STATUS

Medical Student

AUTHORS

Ashtin Jeney

Bridget Huysman

Jamie Majdi

Kent Aje

Madeline Taskier

David Popiel

Lawrence Deyton

Karla Bartholomew

RESEARCH MENTOR/ DEPARTMENT CHAIR

David Popiel

EDUCATION/HEALTH SERVICES

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Tracking 50 plus years of growth in scholarly output in the School of Medicine and Health Sciences, the Milken Institute School of Public Health, and the School of Nursing

The Himmelfarb Health Sciences Library serves the School of Medicine and Health Sciences, the Milken Institute School of Public Health, and the School of Nursing. Over the last half century, the School of Medicine and Health Sciences, and the more recently incorporated Schools of Public Health and Nursing, have experienced substantial growth in their research enterprise and a corresponding increase in scholarly communications. Using statistics and metrics derived from bibliographic databases, this poster will track the growth in scholarly output from 1960 to the present. Number of publications will be tracked and additional metrics will be explored. These metrics include influential papers as measured by citation analysis, key author affiliations, and global reach. Journals and subject areas in which faculty regularly publish will also be identified. Trends over time will be analyzed and emerging methods of exploring impact will be highlighted. This poster hopes to highlight a strong record of growth in scholarship among the three schools served.

STATUS

Faculty

AUTHORS

Anne Linton

Tom Harrod

Paul Levett

RESEARCH MENTOR/ DEPARTMENT CHAIR

Rich Simons

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Development and Evaluation of a Web-based Chest and Abdominal Radiology Game for Fourth Year Medical Students

BACKGROUND

The educational potential of non-traditional computer-assisted models to enhance knowledge acquisition and retention, has been recognized across many disciplines, including medicine. In particular computer-based games allow for the incorporation of multimedia, provide access to learning material in a time and place convenient for the student, and give interactive feedback critical for active self-assessment. Studies of these interactive games, which appear to engage the student in an informal way, have demonstrated the ability to stimulate greater individual learning with improved retention of the material and a desire for self-improvement. Most studies conducted, however, have assessed the effectiveness of the game systems using subjective student feedback. More empirical data is needed to confirm their efficacy in knowledge acquisition and retention. Further, computer-based instruction is particularly well suited to image-based disciplines such as radiology. Radiology is integral to clinical management as a physician, and its role continues to expand as fast as new technologies grow. Studies have shown, however, that long-term retention of specific structures on chest radiographs between the second year and fourth year of medical school was poor despite evidence documenting good short-term retention of tested information. A need for more effective teaching methods to improve chest and abdominal radiology knowledge retention has been identified. This project proposes to study knowledge acquisition and retention of abdominal and chest imaging in fourth year medical students enrolled in a diagnostic radiology elective courses at George Washington University School of Medicine and Health Science.

METHODS

Fourth year medical students who enroll in a four week clinical diagnostic radiology elective course from July 2016 to November 2016 will be recruited for the study, and randomly assigned to complete either the online-game or the traditional lecture course. Students assigned to complete the online-game will progress through three levels of increasing complexity: beginning with basic structure identification and orientation, then diagnosis of common pathologies, finally introduction to more complex and rare cases. After completion of each level of the game, students must correctly answer five questions before progressing to the next level, which will assess knowledge acquisition in real time. One month after completion of the module, students in the control and experimental groups will complete a 10 question quiz on the material to assess knowledge retention.

SIGNIFICANCE

We hypothesize that compared to traditional didactic teaching, students who participate in the gaming format lesson will demonstrate greater knowledge acquisition and long-term knowledge retention.

REFERENCES

Roubidoux, M., Chapman, C., & Piontek, M. (2002). Development and Evaluation of an Interactive Web-Based Breast Imaging Game for Medical Students. Academic Radiology, 1169-1178.

Feigin, D., Magid, D., Smirniotopoulos, J., & Carbognin, S. (2007). Learning and Retaining Normal Radiographic Chest Anatomy. Academic Radiology, 1137-1142.

Jeffrey, D., Goddard, P., Callaway, M., & Greenwood, R. (2003). Chest Radiograph Interpretation by Medical Students. Clinical Radiology, 478-481.

STATUS

Medical Student

AUTHORS

Laura Linville

Jocelyn Rapelyea

RESEARCH MENTOR/ DEPARTMENT CHAIR

Jocelyn Rapelyea

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Design of an Online Histopathology Atlas in the New Medical Curriculum

BACKGROUND

The purpose of this project is to help develop a comprehensive histology and pathology online database that would aid students throughout their pre-clinical years. With the modern systems-based approach that GW's own medical school adopted, it becomes a necessity that students learn and integrate both normal and disease processes throughout the various organ blocks. Students need a resource they can utilize as a reference to learn these two disciplines, since the curriculum has a heavy component of self-teaching. The Microanatomy and Pathology Atlas (MAPA) helps to address this need as it contains specifically labeled histology and pathology image sets that are cross referenced with the traditional laboratory instructions and objectives from the two courses. These clearly labeled images are made interactive, which allows students to self-test for better assessment and understanding. Future plans to add clinical vignettes will help students consolidate problem solving skills and relevant multidisciplinary information.

METHODS

First and second year medical students were sent online surveys that asked a variety of "yes" and "no" questions about the atlas – ease of use, accessibility, and correlation with course material, both in lecture and lab. Students could also submit their own comments as they used the atlas.

RESULTS

Preliminary results have shown that 92% of students are in favor of using the tool and 62% strongly favor further use. Current data collected in the fall of 2015 shows that the atlas has a positive correlation with the material in classes, both in terms of comprehension and proficiency. 88% of students have stated that the tool has complemented their studies, while another 66% would strongly recommend it to other peers. The data suggests that 50% of students strongly found the level of information appropriate for coursework. Students have already commented on the ease of using the atlas and its utility for self-quizzing in learning microanatomical structure.

CONCLUSIONS

The project is still ongoing with data collection. Preliminary results have been very promising in terms of student feedback and growth for further improvement. The atlas will continue to be updated, based on this input. Other organs systems and vignettes will be incorporated. Current results indicate students identify MAPA as a valuable tool for improving comprehension of histology and pathology. We hope that it will become a central resource that students in upcoming classes can use.

STATUS

Medical Student

AUTHORS

Varun Moktan

P. Latham

J. Wade

M.S. Davis

A. Mills

G. Butera

J. Krum

R.A. Jurjus

RESEARCH MENTOR/ DEPARTMENT CHAIR

Rosalyn A. Jurjus

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Optimizing Electrocardiogram Interpretation and Catheterization Laboratory Activation in ST-Segment Elevation Myocardial Infarction: A Teaching Module for Medical Students

BACKGROUND

To achieve the 90-minute reperfusion goal in ST-segment elevation myocardial infarction (STEMI) care, providers must diagnose STEMIs from electrocardiograms (ECGs) obtained upon emergency room arrival and appropriately activate the catheterization lab. To enhance early STEMI care, we sought to improve medical student STEMI recognition and diagnostic accuracy with a teaching module we designed and developed.

METHODS

Through a literature review, we identified evidenced-based criteria for classic STEMI patterns, STEMI-equivalents with non-classic STEMI patterns including hyperacute T-waves, STEMI with existing left bundle branch block (LBBB) and Wellens' syndrome and non-ischemic STEMI-mimics such as known LBBB, pericarditis, ventricular aneurysm, pulmonary embolism, left ventricular hypertrophy, hyperkalemia, Brugada syndrome, early repolarization and takotsubo cardiomyopathy. We reviewed cases from George Washington University Hospital and compiled the 24 best ECGs with clinical information, diagnostic ECG criteria and imaging including cardiac catheterization, echocardiography and computed tomography into the teaching module. We then conducted a prospective education validation trial with fourth-year medical students. We administered pre- and post-tests comprised of exemplary cases of STEMIs, STEMI-equivalents and STEMI-mimics from our case review. Participants studied the module for two weeks and received a didactic module-based lecture prior to the post-test. Students served as their own control. The primary end point was STEMI recognition, measured by appropriate catheterization lab activation. The secondary endpoint was correct ECG diagnosis. Paired t-tests were used to compare pre- and post-training scores.

RESULTS

Appropriate catheterization lab activation mean score was 61% (SD 0.14) and improved to 76% on post-test (SD 0.18, $p<0.0001$). Accurate ECG diagnosis mean score was 59% (SD 0.14) and improved to 74% on post-test (SD 0.16, $p<0.0001$). A sample size of 26 achieved more than 99% power.

CONCLUSIONS

The module significantly improved student STEMI recognition, appropriate catheterization lab activation and diagnostic accuracy.

STATUS

Medical Student

AUTHORS

Alexander E. Sullivan

Mortada A. Shams

P. Jacob Varghese

Abudureyimu Shajidan

Bassel Hassouna

Vimala V. Jayanth

RESEARCH MENTOR/ DEPARTMENT CHAIR

Marco Mercader

EDUCATION/HEALTH SERVICES

SCHOOL OF MEDICINE AND HEALTH SCIENCES

A Medical Mission Trip to the Himalayas: Bhutan Cancer Registry

Upon receiving the GW School of Medicine and Health Sciences Health Services Scholarship, and a grant from the American Bhutanese Associates for Health (ABAH) foundation, the summer of 2014 was spent designing the Bhutan Cancer Registry project. The project is a digital cancer data registry designed to address the country's need of surveillance on its growing prevalence of stomach cancer, and tailored to the unique requirements of the Bhutanese healthcare system. Two weeks were spent in the Kingdom of Bhutan assessing requirements for the registry by meeting with Bhutanese physicians and health policy officials at the local hospitals and the Royal Ministry of Health. The mission trip was enriched by many first hand experiences with the Bhutan's unique healthcare system, such as their universal healthcare, traditional herbal medicine, basic health units, the strong influence of Buddhist compassion in their medical practices, and their growing need for medical equipment, especially in diagnostic radiology. The knowledge of the Bhutanese healthcare system was brought back to the United States, and implemented in a prototype of a digital cancer registry which was electronically delivered to Dr. Ugen Dophu, the Director General of Medical Services at Bhutan's Ministry of Health. The general information about the Bhutanese healthcare system gathered during this mission trip was also presented to the United States Department of States and Project Health, an NGO, to help move forward ABAH's humanitarian efforts to obtain donations of medical equipment to Bhutan.

STATUS

Medical Student

AUTHOR

Ke Sun

RESEARCH MENTOR/ DEPARTMENT CHAIR

Robert Morrow

SCHOOL OF MEDICINE AND HEALTH SCIENCES

synDRME: A Synthesis of Digital Resources for Medical Education

BACKGROUND

Across the world, many low to middle income countries are dealing with a critical shortage of physicians. This problem is exacerbated by a shortage of trained faculty to educate future physicians in meeting the needs of their country. Meanwhile, advances in Internet technology have opened the modality of "e-learning" to a global audience. These online resources serve as valuable tools for supplementing resource starved medical schools with needed educational tools, however the wide array of choices make it difficult to select the most effective resource. New efforts are needed to increase the number of teaching faculty in these countries and to find ways to deliver the required curriculum in innovative and cost-effective ways.

OBJECTIVES

The objective of synDRME is to collect, catalog, and evaluate e-learning resources for medical schools. Specifically, to evaluate how available educational resources would function in, and their usefulness to, medical schools with limited resources. In addition, a new website was built to allow for easy access to evaluations and resources.

METHODS

Online resources were compiled and evaluated. An evaluation rubric was developed by an interdisciplinary team to assess each e-learning resource according to its cost, appropriateness for patient population, required technological infrastructure, website loading speed, time demands on faculty, learning value, and comprehensiveness of content. Based on evaluation, a score between 1 and 4 stars (4 being highly recommended) was awarded to each resource. Detailed resource evaluations were then hosted on our synDRME website.

RESULTS

A new website was developed to host resource evaluations and for easier access. A total of 268 online resources were evaluated covering 15 traditional medical school courses (e.g. anatomy, pediatrics). These evaluations and links to resources have been uploaded to the synDRME site.

CONCLUSIONS

We were able to provide recommendations for 268 existing educational resources that can substitute for faculty-lead classroom experiences. This is an ongoing project, and the course evaluations are being compiled on a website and made available online via www.syndrme.org. What is most important is that we have established a comprehensive rubric to guide medical school deans and faculty in the developing world so they can rate and compare the usefulness of these new resources for their students.

STATUS

Medical Student

AUTHOR

Jason Teng

Holden Spivak

RESEARCH MENTOR/ DEPARTMENT CHAIR

James Scott

EDUCATION/HEALTH SERVICES

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Integrating a Curriculum for Otolaryngology in Undergraduate Medical Education

It has been well identified in previous literature that there is a lack of otolaryngology teaching for general practitioners. There is not currently a standardized curriculum for otolaryngology in undergraduate medical education or during residency for those pursuing a general field such as Emergency Medicine, Internal Medicine, Pediatrics or Family Medicine. While the need for more exposure to otolaryngology within these fields has been well documented, as 25% of primary care complaints are otolaryngology related, little has been done to identify the best method for educational intervention. Important topics for inclusion in such a curriculum have been identified and methods of teaching (online learning modules, case-based group learning sessions, physical exam skills, simulation activities, etc) have been proposed. This study will expand on prior research by surveying internal medicine residents and otolaryngology residency program directors for their opinions on how to incorporate a curriculum for otolaryngology. Residency program directors were chosen due to their experience with the nature, volume and content of referrals from primary care. Internal medicine residents were chosen due to their unique perspective on how to deliver a subspecialty curriculum within the scope of their current training. This data will further inform the ideal setting and format for an otolaryngology curriculum and identify how to incorporate it into primary care training. Improving education, and therefore confidence, in management of common otolaryngic conditions amongst general practitioners will ultimately enhance patient care.

STATUS

Medical Student

AUTHOR

Arielle Thal

RESEARCH MENTOR/ DEPARTMENT CHAIR

Philip Zapanta

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Attitudes Toward Academic Dishonesty in Physician Assistant Students

PURPOSE

The purpose of this study was to assess Physician Assistant (PA) students' attitudes and experiences toward academic dishonesty during training and to determine whether PA students self-report cheating during PA school.

METHODS

An anonymous, quantitative, exploratory, descriptive survey was sent to clinical-year PA students enrolled in PA programs accredited by the Accreditation Review Commission on Education for the Physician Assistant (ARC-PA).

RESULTS

A sample of 493 self-selected PA students in their clinical year of training responded to the survey. Only 3% of clinical-year PA students self-reported cheating during PA school. Males self-reported significantly higher rates of cheating in PA school than females. The most common cheating behavior that clinical-year PA students reported either observing or hearing about in PA school was receiving information about an exam prior to its administration (70.9%). The attitudinal statement that respondents most strongly agreed to was "cheaters in PA school just end up hurting themselves in the long run." The strongest predictor for cheating in PA school was a history of cheating as an undergraduate.

CONCLUSION

This study confirmed previous research indicating that academic dishonesty exists in PA education. It also determined that clinical-year PA students attitudes toward and experiences with academic dishonesty vary.

STATUS

Faculty

AUTHORS

Marianne Vail

Suzanne Coleman

Mark Johannsson

Karen Wright

RESEARCH MENTOR/ DEPARTMENT CHAIR

Karen Wright

EDUCATION/HEALTH SERVICES

SCHOOL OF NURSING

Evaluation of an Education Module that Addresses Patient Hesitancy and Refusal of Vaccines

Immunizations have been a major reason for the decrease in vaccine preventable diseases in the United States. Recently there has been an upsurge in vaccine hesitancy and refusal due to concerns about safety, efficacy and necessity of vaccines and vaccine misinformation reported in the media. There is limited research on educating health care providers on strategies to address vaccines issues. Primary health care providers (including nurses and nurse practitioner students) need additional knowledge and effective communication skills to address the issue of patient vaccine hesitancy/refusal.

The purpose of this pilot study was twofold. The first was to develop and evaluate an on-line, interactive, learning module to enhance knowledge of nurses/nurse practitioner students on issues of vaccine hesitancy/refusal. The second purpose was to evaluate nurses/ nurse practitioner students' knowledge of communication skills utilizing motivational interviewing concepts to address issues of vaccine hesitancy /refusal.

An on-line interactive education module was developed with specific content on issues in vaccine refusal, provider strategies and motivational interviewing communication techniques. A pre-test/post-test design was used to assess the change in knowledge and communication skills of nurses/nurse practitioner students to address the issue of vaccine hesitancy/refusal.

Data analysis is in process. Results of this study will serve to inform future study of the use of interactive education programs for health care providers to address vaccine hesitancy/refusal in clinical practice.

STATUS

Graduate Student

AUTHOR

Margaret Venzke

RESEARCH MENTOR/ DEPARTMENT CHAIR

Christine Pintz

EDUCATION/HEALTH SERVICES

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Review of Strategic Thinking Approaches and Tools Used in Healthcare Administration Education and Practice

BACKGROUND

With an ever-changing, complex landscape, the healthcare industry must be able to strategically manage and respond to challenges. Strategic thinking is often regarded as the precursor and underlying mechanism of strategic management, and is an essential skill for healthcare leaders. The strategic thinking process relies on synthesis, implementation and evaluation. While the value of strategic thinking is well recognized, it is unclear what formal educational approaches are used to develop strategic thinking. Identifying what tools, methods, and techniques exist to develop strategic thinking can inform healthcare administration education and professional development for current and future healthcare leaders.

OBJECTIVE

The objective of this literature review is to identify and describe educational tools used to teach strategic thinking to healthcare students and managers. By building on earlier works and addressing gaps in literature, this paper aims to contribute to the understanding, development and education of strategic thinking in current and future healthcare leaders.

Methods: A systematic literature review of formal educational tools for strategic thinking was conducted using the PRISMA guideline. Pertinent studies were searched in four databases: ABI/Inform Complete Plus, CINAHL Plus, ERIC, and MEDLINE Complete using specific inclusion and exclusion criteria. The search was limited to titles or abstracts and studies published between 1994 and January 2016.

Search terms consisted of a combination of four domains:

1) Topic of interest (strategic thinking);

2) Approach (e.g. “education,” “tools,” “methods”);

3) Target group (e.g. “students”, “managers,” “leaders”); and

4) Industry/setting (e.g. “healthcare,” “healthcare administration program,” “hospital”).

RESULTS

We identified 12 studies that met the inclusion criteria. The studies featured a variety of practical approaches to develop strategic thinking, including formalized instruction, specific work experiences; and utilization of system archetypes.

CONCLUSION

In our literature review, we identified a limited number of formal educational tools to train healthcare leaders in strategic thinking. Given the importance of strategic thinking ability in the healthcare management literature, this finding is surprising. Several explanations may support this finding. First, strategic thinking development may occur more informally or in hands-on field experiences not reported in the literature. Second, educational tools may focus on particular sub-components of strategic thinking (synthesis, implementation and evaluation). Finally, we excluded terms related to strategic thinking (e.g. strategic planning, strategic marketing, strategic management), which are often used interchangeably despite certain distinctions. Overall, there are few tools, methods, and techniques identified in the literature to help develop strategic thinking in current and future healthcare leaders.

STATUS

Graduate Student

AUTHOR

Jacklynn Wong

RESEARCH MENTOR/ DEPARTMENT CHAIR

Wayne Psek

SCHOOL OF MEDICINE AND HEALTH SCIENCES

ALiEM AIR-Pro Series: Identifying quality content from blogs and podcasts for the senior emergency medicine resident

INTRODUCTION

In 2008, the Accreditation Council for Graduate Medical Education endorsed a change such that EM residency programs can now decrease their synchronous conference experiences by up to 20% in exchange for asynchronous learning termed Individualized Interactive Instruction (III). Identifying quality online resources that would also fulfill III's reporting criteria (program director monitoring, evaluation component, faculty oversight, program effectiveness) is challenging.

Using crowdsourced expertise, the Approved Instructional Resources (AIR) series from Academic Life in Emergency Medicine (ALiEM) was created in 2014 to provide a credible method to identify quality educational blogs and podcasts. The identified resources, however, focused on basic content with limited utility for more senior residents. We thus created the AIR-Pro series in 2015, an offshoot of the original AIR series, aimed to cover more advanced concepts.

METHOD

The AIR-Pro series is a continuously building curriculum covering a new subject area every 2 months. For each area, 6 EM Chief Residents identify 3-5 advanced clinical questions. Using FOAMsearch.net to search blogs and podcasts, relevant posts are scored by 8 reviewers from the AIR-Pro Board (faculty and chief residents at various institutions). The scoring instrument contains 5 measurement outcomes (7-point Likert scale): recency, accuracy, educational utility, evidence based, and references. The AIR-Pro Approved label is given to posts with a score of ≥28 (out of 35) points and these are featured in the blog posting. For scores of 26-27, an Honorable Mention label is given if Board members collectively felt that they were valuable.

For each AIR-Pro subject area, a multiple choice quiz is written based on the featured posts. Educator dashboard access of the Google Drive quizzes is given to program directors for monitoring. If approved by their program director, EM residents receive official III credit upon completion of each quiz.

CURRICULUM/TOOL/MATERIAL

As of Jan 1, 2016, there have been 2 modules published on ALiEM with 1,220 (Cardiovascular) and 1,059 (Trauma) pageviews worldwide. Although early in development, 21 different institutions are using the AIR-Pro Series with over 150 residents completed the cardiovascular and trauma quizzes. We anticipate more because the original AIR Series has over 73 programs using it for III credit.

CONCLUSIONS

The AIR-Pro series is a novel, objective, crowdsourced approach towards identifying quality, educational, social media content for the advanced EM resident.

STATUS

Graduate Student

AUTHORS

Fareen Zaver

Michelle Lin

RESEARCH MENTOR/ DEPARTMENT CHAIR

Michelle Lin

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Urinary Tin, Cadmium and Lead and Associations with Body Mass Index and Waist Circumference: National Health and Nutrition Examination Survey 2011-2012

INTRODUCTION

The role that endocrine disrupting compounds play in fat metabolism and fat storage remains unclear. Organic tin compounds interact with peroxisome proliferator–activated receptors (PPARs), which are intimately involved in the regulation of fat cell growth and production as well as other processes related to glucose and lipid regulation. Although the effects of organic tin compounds have been examined in animal studies, few human studies have examined organic tin compounds in relation to weight and obesity. In this study, we evaluate whether urinary total tin and other toxic heavy metals are associated with body mass index (BMI) and waist circumference (WC) among a nationally-representative sample.

METHODS

We conducted a cross-sectional study on 1790 adolescents (aged 6-19) and adults (aged 20-59) using the 2011-2012 cycle of the National Health and Nutrition Examination Survey (NHANES) and examined whether urinary total tin, lead, and cadmium independently predicted waist circumference and body mass index.

RESULTS

Results showed that higher quartiles of urinary tin, lead, and cadmium were associated with lower BMI and WC (ptrend <0.05), based on multiple linear regression models adjusted for race, age, gender, SES, physical activity, dietary factors, and urinary creatinine. There were significant decreases in log-transformed WC across the four quartiles of urinary tin exposure (beta = -0.049, -0.076, and -0.095 for 2nd, 3rd, and 4th quartiles, respectively; $p<0.05$), and similar statistically significant downward trends occurred for lead and cadmium for both BMI and WC outcomes. These results were weighted to be representative of the US population.

CONCLUSIONS

Exposure to certain heavy metals such as tin, lead, and cadmium, may influence waist circumference and body mass index. In addition to further insight into heavy metal pharmacokinetics, the role of toxic heavy metals in the environment and their influence on fat metabolism and storage need further study.

STATUS

Graduate Student

AUTHORS

Francesca Branch

Zhen Chen

Melissa J. Perry

RESEARCH MENTOR/ DEPARTMENT CHAIR

Melissa J. Perry

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Pregnant Women's Health Consequences following exposure to PBDEs

PBDEs (Polybrominated diphenyl ethers) are chemicals introduced by industry in the 1970s to serve as flame-retardants on common consumer products like electronics, plastics, and foam in furniture. They are also suspected to disrupt thyroid activity during pregnancy, which is a time of increased demand on the thyroid gland. Maternal thyroid fluctuations and disease as a result of exposure to PBDEs are therefore a concern. This systematic review aimed to capture all of the relevant peer-reviewed literature investigating the association between PBDEs and maternal thyroid activity. Use of the PRISMA checklist (Preferred Reporting Items for Systematic Reviews and Meta-Analyses), a best practice standard for conducting systematic reviews, guided the search. Twelve relevant studies resulted from searching the online medical databases PubMed, Scopus, and Clinical Key with the terms 'PBDE', 'pregnant', and 'thyroid'. Studies' results varied on whether PBDE exposure increased or decreased thyroid activity, but nine of the twelve studies reported significant associations between PBDE exposure during pregnancy and thyroid activity, especially with two PBDEs: BDE 47 and BDE 99. While it is unclear which PBDEs have a negative or positive association with thyroid activity and more research is needed, many PBDEs are significantly associated with thyroid activity so caution is warranted, especially around BDE 47 and BDE 99. With this information, policymakers could push to ban BDE 47 and BDE 99, ban them only if other PBDEs can be safely substituted, or push for more research. Additional research could elucidate which PBDEs are associated with increased or decreased thyroid activity and at what levels they adversely affect thyroid health. Regardless of how policymakers and industry move forward, an interim awareness campaign for pregnant women may help protect them from thyroid health consequences.

STATUS

Graduate Student

AUTHOR

Alison Chiaramonte

RESEARCH MENTOR/ DEPARTMENT CHAIR

Ami Zota

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Quality of Life Improvements for Residential Permanent Relocation Following the Fukushima Nuclear Power Plant Accident

The accidental release of nuclear radiation from the Fukushima Dai-chi Nuclear Power Plant (FDNPP) resulted in the evacuation of over 100,000 residents in the Fukushima Prefecture. Residents who returned to their homes following the cancellation of the evacuation orders (six months after the incident) could be susceptible to increased health impacts from long-term radiation exposure. To assess the quality of life improvements for women and children who permanently move away from the FDNPP evacuated zones, long-term radioactive exposures for residents who returned to their homes were compared to the health effects of residents who permanently moved away. A systematic review was conducted to examine the various exposures and health effects citizens encountered following the FDNPP incident, including mental health assessments. Nine months after the FDNPP incident, the median annual dose of radiation was below the Japanese federal recommended allowable dose limit for the public (1 mSv/y). Federal countermeasures to radiation exposure included providing residents with non-local food and bottled water. Mental health impacts of returning to the evacuated areas included concerns for children and future generation's health, obtaining acute radiation syndrome and living in areas with low ambient radiation exposure. Mental health improvements were the main quality of life improvement that people would experience if they permanently moved away from the Fukushima Prefecture, following the FDNPP incident. This finding will have implications on the future economy of both the Fukushima Prefecture and the surrounding communities, international medical emergency response methods, and public education about radiation exposure risks. Future studies should focus on individual exposure levels, long-term, low-dose radioactive exposures, and the length of time federal countermeasures to local food consumption should be provided.

STATUS

Graduate Student

AUTHOR

Megan Christian

RESEARCH MENTOR/ DEPARTMENT CHAIR

Lance Price

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Community Exposure to E-waste Pollutants in Developing Countries and Associated Health Outcomes: A Systematic Review

As global production and consumption of electronic goods continues to increase, there becomes a growing need to examine e-waste management and health implications associated with prolonged exposure to e-waste pollutants. The aim of this systematic review was to synthesize evidence on the association between exposure to e-waste pollutants and adverse health outcomes in developing countries, in those residing in towns with e-waste sites compared to those residing in towns without e-waste sites. A comprehensive search for original research using Scopus and PubMed databases was conducted on the association between e-waste toxicant exposure and health outcomes, of which 16 were included for substantial review following application of inclusion/exclusion criteria. Results indicated an overall association between residence in e-waste processing towns and increases in negative health outcomes. Exposure to PAHs, PCBs, PBDEs, and lead were correlated with deficiencies in neonatal development. Similarly, PBDEs and PAHs were associated with physical and neurodevelopmental deficits in children. Lead, cadmium, chromium, PCBs, and PAHs were associated with increased DNA oxidative stress and damage along with other genotoxic effects. Finally, PCBs and PBDEs were found to influence thyroid hormones. Communities living in close proximity to e-waste sites or conducting home e-waste dismantling procedures may be at increased risk for adverse health effects associated with exposure to e-waste toxicants and by-products. Additional epidemiological research conducted over longer study periods are recommended in effort to further evaluate the associations presented in this review.

STATUS

Graduate Student

AUTHORS

Emily Hsu

Jay Graham

RESEARCH MENTOR/ DEPARTMENT CHAIR

Jay Graham

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Predicting Long Term Risk Values from Short Term Chemical Exposure Tests

Environmental and public health organizations including the World Health Organization (WHO) and the U.S. Environmental Protection Agency (USEPA) develop human health reference values (HHRVs) that set 'safe' levels of exposure to non-carcinogens. This research investigates whether the results of short-term animal studies can reasonably provide a quantitative estimate of a long term point-of-departure (POD) allowing faster development of chronic HHRVs. Currently the development of HHRVs can be slow and cumbersome, leaving chemicals unanalyzed and in the environment. The goal is a methodology to predict the doses associated with the long-term health effects of chemicals that have short-term data but do not have long-term data. Data from the National Toxicology Program's (NTP) technical reports have been extracted and used to compare best fits for points of departure (PODs) for 41 chemicals tested both long-term and short-term between 2000 and 2012. The analysis focuses on non-neoplastic lesions, final mean body weight and mean organ weight. Using these data, statistical modeling techniques are being performed to determine the predictability of short-term data in determining long-term PODs. Comparisons will be made by chemical, within specific test animal groups (e.g., female mice) and by lesion site or type. The results are hypothesized to be models for estimation of long-term PODs from short-term data and an estimation of uncertainty in these relationships. Preliminary data suggest there are quantitative relationships between exposures causing non-neoplastic effects in short-term tests and those causing effects in long-term toxicity tests.

STATUS

Graduate Student

AUTHOR

Jessica Kratchman

RESEARCH MENTOR/ DEPARTMENT CHAIR

George Gray

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Associations between Body Mass Index and Semen Parameters among men from the Washington D.C. Metropolitan Area

PURPOSE

Infertility affects an estimated 15 percent of couples worldwide, and male factor infertility accounts for approximately 40 to 50 percent of infertility cases. Obesity affects more than a third of adults in the U.S.; African-Americans have the highest age-adjusted rates of obesity, followed by Hispanics. There is mounting evidence that male obesity may play a role in reducing fertility and embryo health. Semen parameters are the most commonly used biological indicators of male fecundity. U.S. studies examining obesity and semen parameters have reported inconsistent results, often finding an inverse association with increased Body Mass Index (BMI) and some, but not all, parameters. In most male reproductive health studies, African-American and Hispanic men have been largely underrepresented.

This descriptive analysis summarizes the semen parameters of 114 men from the Greater Washington, D.C. area receiving treatment at the George Washington University Medical Faculty Associations. Participants were recruited among the men seeking treatment from the Assisted Reproduction, Endocrinology, or Adult Medicine Clinics. It provides an exploratory look at sperm health among DC area men and examines associations between sperm health and BMI.

METHODS

Analysis was conducted on self-reported demographic, lifestyle and environmental data collected from two questionnaires. BMI was self-reported and categorized as underweight and normal (<25), overweight (25-29.9) and obese (≥30). Semen parameters were analyzed continuously as well as categorically based on a priori classification, by BMI, race, and additional demographic and lifestyle factors.

RESULTS

Preliminary results show that mean age of the study population was 41 years old, and the racial distribution was: 46.4% Caucasian, 25.5% African-American, 12.7% Hispanic, and 15.4% Other. Overweight men constituted 41.3% of the population, while obese men constituted 42.2%. Mean sperm motility for African-American men was significantly lower compared to Caucasian and Hispanic men (ptrend<.05). Mean sperm morphology for Hispanic men was significantly higher compared to African-American men (p<.05). Mean sperm motility was significantly lower for obese men compared to underweight and normal weight men (p<.05).

CONCLUSION

These early data indicate that there were a few statistically significant differences in some semen parameters in this population when examining them by race and BMI. Future analyses will examine parameters categorically and incorporate multiple regression models to control for potential confounders.

STATUS

Graduate Student

AUTHORS

Nathan McCray

Francesca M. Branch

GiaLinh N. Nguyen

Melissa J. Perry

RESEARCH MENTOR/ DEPARTMENT CHAIR

Melissa J. Perry

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Consumer product chemicals in indoor dust: a quantitative meta-analysis of US studies

Commercial chemicals from consumer products have been shown to collect in indoor dust. However, most dust exposure studies focus on a single class of chemicals among a small, convenience sample. In this study, we synthesized the literature on phthalates, replacement flame retardants (RFRs), perfluoroalkyl substances (PFASs), fragrances, and phenols in indoor dust and assessed the implications for human health. First, we systematically collected U.S. indoor dust literature since 2000. We included 31 papers and 2 unpublished datasets. Next, we estimated pooled geometric means (GMs) and 95% confidence intervals for 45 chemicals measured in ≥3 datasets. From these estimates, we calculated residential intake from dust ingestion, inhalation, and dermal uptake from air. We used hazard traits from the Safer Consumer Products Candidate Chemical List to assess health implications. Phthalates occurred in the highest concentrations in dust, followed by phenols, RFRs, fragrance, and PFASs . Several phthalates and RFRs had the highest residential intakes. The hazard assessment showed that many chemicals in dust share adverse effects, such as reproductive and endocrine toxicity. Our results indicate that U.S. indoor dust consistently contains many consumer product chemicals, from multiple chemical classes, at varying concentrations. Safety assessments, biomonitoring, and regulations should reflect the likelihood of consumer exposure to chemical mixtures.

STATUS

Staff

AUTHORS

Susanna Mitro

Robin E. Dodson

Veena Singla

Gary Adamkiewicz

Angelo F. Elmi

Monica Kaitz

Ami R. Zota

RESEARCH MENTOR/ DEPARTMENT CHAIR

Ami R. Zota

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Semi-Automated Scoring of Triple-Probe FISH in Human Sperm Using Confocal Microscopy

Aneuploidy, or an abnormal number of chromosomes, is found in human gametes and is caused by errors during meiosis. Although most human fetuses conceived from aneuploid gametes do not survive to term, some aneuploid conceptuses do result in offspring with compromised phenotypes. Kleinfelters, Turners, and XYY syndromes are examples of well-characterized chromosomal disorders resulting from aneuploid conceptuses. To study sperm aneuploidy and its impacts on fertility and reproduction, fluorescence in situ hybridization (FISH) is used to quantify the frequency of aneuploidy in sperm and requires the scoring of thousands of nuclei. Traditional manual scoring of FISH sperm can be time consuming, which can lead to scorer fatigue and increased error. Semi-automated methods that rely on computer software to objectively count fluorescence signals using specified criteria are needed.

In this validation study, we used a Zeiss LSM 710 confocal microscope combined with the Zen software (Zeiss, Jena, Germany) for image acquisition. Application of online spectral linear unmixing allowed for effective separation of the four fluorochromes used to identify chromosomes X, Y, 18 and the nuclei. Image processing, segmentation, classification, and scoring were performed using custom analysis software developed in MATLAB®.

The semi-automated results were compared with manual scoring results in 10 slides. In comparing percent disomy calculated by each scoring method for each slide, a significant difference was found on one slide for XX18 (0.62% automated vs 0.05% manual). For the other 9 slides, XX18 estimates were comparable by method, as were the YY18 and XY18 estimates across all 10 slides. These results demonstrate that semi-automated methods using spectral imaging on a confocal microscope are a feasible approach for analyzing numerical chromosomal aberrations in sperm, and are comparable to manual methods.

STATUS

Staff

AUTHORS

GiaLinh Nguyen

Francesca M. Branch

Anastas Popratiloff

Sheena E. Martenies

Heather A. Young

Glen Deloid

Melissa J. Perry

RESEARCH MENTOR/ DEPARTMENT CHAIR

Melissa J. Perry

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Increased risk of renal cell carcinoma following exposure to metalworking fluids among autoworkers

OBJECTIVES

Metalworking fluids (MWF), used to cool and lubricate metal in occupational settings, have been linked to several cancers but data on kidney cancer is limited. MWF is generally classified as of straight (neat or mineral oils), soluble (mixture of oil and water-based), and synthetic (water-based, no oil), reflecting different compositions over time and for different operations. We examined how oil- and water-based MWF influenced rate of kidney cancer overall and renal cell carcinoma (RCC) specifically.

METHODS

From a cohort of Michigan autoworkers, 33,421 subjects were eligible for follow-up between 1985 and 2009. The cohort was linked to the National Death Index and the Michigan Cancer Registry, which identified new cases of kidney cancer and histologically confirmed RCC. We analyzed all kidney cancer and RCC alone in relation to cumulative exposure to each specific type of MWF, with a 15-year lag. Penalized splines with Cox Proportional Hazards Regression were used to estimate Hazard Ratios (HRs) and 95% confidence intervals (95% CIs), controlling for age, gender, race, calendar year, year hired, time since hire, plant, and other MWF types.

RESULTS

There were 135 incident cases (83 RCC). A linear increase in the log-HR was observed for kidney cancer incidence with increasing cumulative exposure to each type separately and for all three types pooled into a single variable. The association was strongest for White males and RCC specifically. At the mean cumulative exposure to total MWF exposure, the estimated HR was 1.11 (95% CI 1.04, 1.19) for kidney cancer and 1.16 (95% CI 1.05, 1.27) for RCC only.

CONCLUSIONS

Our results signal a dose-dependent association between all types of MWF and kidney cancer and the RCC histologic type, although the influence of possible components in MWF needs to be determined. The better understanding of components and contaminants of MWF as well as molecular indicators of kidney damage that better define pathways leading to kidney cancer deserves further research.

STATUS

Postdoctoral Student

AUTHOR

Deepika Shrestha

RESEARCH MENTOR/ DEPARTMENT CHAIR

Kate Applebaum

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Attitudes toward Environmental and Reproductive Health among Men of Color

PURPOSE

African-Americans have been historically underrepresented in environmental and reproductive health studies. This lack of inclusive research participation threatens the validity of findings and weakens generalizability to potentially at-risk populations.

METHODS

The objective of this study was to use qualitative methods to explore attitudes toward reproductive health, environmental health, research participation and research recruitment. Three semi-structured focus groups were conducted with 24 African-American male participants, aged 25-64, recruited from the greater Washington, DC area. Data were analyzed using thematic content rooted in Grounded Theory.

RESULTS

For environmental health, participants expressed an overall knowledge of key issues such as air quality and environmental health threats, but felt there were few ways to avoid negative environmental exposures. For reproductive health, participants highlighted that having previously fathered a child was a key to engagement in their own personal reproductive health status. Participants also were concerned about the potential for research misconduct and also expressed that cases of infertility were often met with stigma and a lack of community support. For health research recruitment, the major themes that emerged were the importance of incentives for motivating participation, relevant subject matter, and culturally sensitive recruiters.

CONCLUSION

It is important to engage men of color in a culturally relevant manner, and researchers can begin by better framing the health issues and educating on how various research topics relate directly to the African-American male community. For reproductive health research, concerns about the secure handling of their biological samples including sperm, mistrust of researchers, and the negative stigma toward male infertility in the African-American community all exist as potential obstacles to recruitment that have to be addressed. Researchers will have to use more effective recruitment strategies that include relatable recruiters, succinct proposals, and transparency in the research intent. Effectively engaging African-American males and targeting them for recruitment in all areas of research is essential for creating positive changes in health outcomes for the many ethnically and racially diverse members of the American population.

STATUS

Graduate Student

AUTHORS

Lance Thompson

Francesca M. Branch

Nicholas D. Porter

Nathan McCray

Melissa J. Perry

RESEARCH MENTOR/ DEPARTMENT CHAIR

Mellissa J. Perry

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Effects of Urbanization on Health Status Among China Migrant Workers: A Systematic Review

China's rapid urbanization and economic prosperity galvanized one of the largest worker migrations from rural-to-urban cities. A major driver of this population shift is an increase in job opportunities found in industries, such as construction or manufacturing. In addition to the financial and societal stress of moving to a new city, rural-to-urban migrant workers face many barriers, including a lack of worker knowledge in industrial settings, little-to-no safety training in hazardous positions, and lack of affordable health care. Because of these upstream factors that hinder migrant workers' ability to protect themselves, a systematic review was conducted to identify migrant workers' overall health status and needs compared to non-migrant workers in China. Three databases were used: Scopus, CINAHL, and PubMed. Twelve articles remained after applying the inclusion criteria. Seven of the twelve articles examined mental health status, four examined health service utilization and awareness, and one examined work ability amongst migrant workers. Of the seven mental health studies, three found that migrant workers exhibited better mental health whereas four found worse mental health indicators when compared to their urban counterparts. Four studies found health service utilization to be lower compared to non-migrant workers. Lastly, one study found the work abilities of migrant workers to be affected by social support and mental health. Across the studies, age and social support were common factors that had a strong influence on migrant workers' mental health status, health service utilization, and work ability. The presence of the "healthy worker effect" may lead to an underestimation of the findings on migrant workers' health status and needs; thus, warranting the critical need for additional longitudinal studies. Overall, this study provides a better understanding of migrant worker health, and a strong foundation to support future research in this growing field.

STATUS

Graduate Student

AUTHOR

Wendy Fan

RESEARCH MENTOR/ DEPARTMENT CHAIR

Melissa Perry

EPIDEMIOLOGY

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Using the Inverse Maximum Ratio-Λ as a Technique to Quantify Surface Uniformity

BACKGROUND

Techniques used in data variability assessment are subsequently used to draw conclusions regarding the "spread"/uniformity of data curves. Due to the limitations of these techniques, they are not adequate for circumstances where data manifest with multiple peaks (bimodal, multi-modal). As such manifestations of data are common in various fields, a sound mathematical approach to quantify the uniformity of such data could prove to be useful in a number of different ways. Extrapolating such an approach to quantify the uniformity of surfaces in 3-dimensional space could further expand its utility.

METHODS

We proposed and validated a new mathematical metric, the Inverse Maximum Ratio, to quantify the uniformity behavior of bimodal and multi-modal data in 2 dimensions. Firstly, a universal mathematical definition of the Inverse Maximum Ratio (Λ) was derived and its expected value and variance were examined under various conditions. The performance of Λ was then assesed under various uni-modal, bimodal and multimodal data conditions, and the finite bounds of the metric were examined. The utility of Λ in quantifying the uniformity of surfaces in 3-dimensional space was then examined using several simulated surfaces with various 'non-uniformity' manifestations.

RESULTS

In both 2 and 3-dimensions, _ performed consistently across all tested conditions. The range of the metric was determined to be within [0, 1] and estimates closer to the upper bound indicated more 'uniform' presentations of data. From derivations of its expected value and variance as well as from graphical assessments, it's performance was determined to be distribution independent and reliabile across various manifestations of data (unimodal, bimodal, multi-modal in 2 dimensional conditions). Λ was also determined to be superior to commonly used variability assessment techniques in capturing the uniformity of data curves. Further, Λ was also determined to be equivalently useful in 3-dimensional space to quantify the uniformity of various surfaces. The bounds, behavior and consistency of the metric was identical in 2 and 3-dimensional conditions.

CONCLUSION

We believe that the proposed metric not only performs consistently across all presentations of data in both 2 and 3-dimentions, but also that it outperforms the standard techniques in bimodal and multi-modal presentations of data. This metric's consistent performance in all tested conditions make it a reliable tool for use in fields such as biomechanics, immunology, material sciences etc. where such presentations of data are common.

STATUS

Graduate Student

AUTHORS

Derek Brown

Avinash Chandran

Loretta DiPietro

Jerome Danoff

RESEARCH MENTOR/ DEPARTMENT CHAIR

Loretta DiPietro

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Time Trends in Incidence and Severity of Injury among NCAA Soccer Players, 1990-1996 and 2004-2009

BACKGROUND

A number of socio-cultural and environmental changes have occurred over the past several decades that may affect the risk of injury among young athletes playing soccer. PURPOSE: To identify trends in injury incidence and severity between two time periods (1990-1996 and 2004-2009) in both male and female NCAA soccer players.

METHODS

Data were analyzed from the National Collegiate Athletic Association (NCAA) Injury Surveillance System (ISS). As per the data collection guidelines, injury incidence was defined as: 1) any injury event that occurred during participation in an intercollegiate game or practice; 2) that required medical attention; and 3) restricted participation or performance for >1 day beyond the event. To account for varying levels of playing exposure and contribution to injury occurrence among the athletes, we calculated Athlete-Exposure (AE), defined as a single athlete participating in a single practice or competition with any probability of injury. Incidence density (ID) then was calculated as the number of events per 1000 AE within each time period. The rate ratio (RR), along with the 95% Wald confidence interval (CI), compared incidence density in 2004-2009 relative to that in 1990-1996.

RESULTS

Overall sex-pooled injury rates were significantly lower in the 2004-2009 cohort compared with the 1990-1996 cohort [RR=0.88 (95%CI=0.86, 0.91)] and this was true for almost every category of injury studied. The lower rates were especially noticeable for recurrent injuries [RR=0.62 (95%CI=0.57, 0.68)], short-term injuries [RR=0.69 (95%CI=0.67, 0.72)] and for injuries requiring surgery [RR=0.35 (95%CI=0.29, 0.41)]. There was also a significant reduction in injuries occurring during games, particularly for injuries occurring during the second half [RR=0.69 (95%CI: 0.66, 0.73)]. In contrast, we observed a significant increase in rates of long-term (>7 days pf lost time) injuries between 1990-1996 and 2004-2009 [RR=1.33 (95%CI=1.27, 1.40)].

CONCLUSIONS

These surveillance data show decreasing trends in collegiate soccer injuries. Whether these decreases are attributable to greater resources being allocated toward athlete health, injury management, or toward the safety of the playing environment cannot be determined. Given the prominence of soccer play in the United States, public health efforts should promote the use of this surveillance system to better inform and evaluate injury prevention practices and policies directed toward player safety.

STATUS

Faculty

AUTHORS

Avinash Chandran

Mary J. Barron

Beverly Westerman

Loretta DiPietro

RESEARCH MENTOR/ DEPARTMENT CHAIR

Loretta DiPietro

EPIDEMIOLOGY

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Does Obesity Make Children More Vulnerable to Injuries When Involved in Motor Vehicle Collisions?

BACKGROUND

Motor vehicle collisions (MVC) impose significant risk for morbidity and mortality on children. The impact of obesity on body injuries in children involved as passenger in a MVC is unknown.

OBJECTIVE

1) To examine whether obesity is protective against body injury sustained in a motor vehicle collision in non-driving children not using car seats and 2) to see what type of injury is the most frequent in obese children involved in a motor vehicle collision.

METHODS

The Nationwide Emergency Department Sample (NEDS) produced by the Health Cost and Utilization Project (HCUP) was analyzed for the years 2010 and 2011. The NEDS is a database of all-payer Emergency Room visits collected from all over the United States. We included all records of children between the ages of 3 to 14 involved in a Motor Vehicle Collision (MVC). Groups were then created demarcating between obese and non-obese children using International Classification of Diseases, Ninth Revision, (ICD-9) diagnostic codes. Each group was assessed for different types of body injury through the use of disease-specific diagnostic codes. Data was analyzed using chi square to calculate odds ratios and multivariate logistic regression to control for possible confounding factors including sex, age, income quartile, type of insurance and whether or not the MVC occurred on a weekend.

RESULTS

There were 352,568 children ages 3-14 reported by the NEDS involved in a motor vehicle collision in 2010 and 2011, of them 474 had an ICD-9 codes for overweight or obesity. After controlling for confounders, it was found obese and overweight children were 1.564 (95% CI: 1.30-1.88) times more likely to have an injury compared to non-obese non-overweight children. Obese and overweight children were also 5.946 (95% CI: 4.652 – 7.600) times more likely to sustain two or more injuries, 11.42 times more likely (95% CI 8.38-15.54) to sustain a lower extremity injury and 4.74 (95% CI: 2.98 – 7.53) to sustain a more serious skull or face fracture compared to non-obese non-overweight children. However, obese and overweight children were more likely to be protected against concussions, 0.36 (95% CI: 0.14 – 0.92), when compared to non-obese non-overweight counterparts.

CONCLUSIONS

There was a correlation between obesity or overweight status and increased risk of injury among children involved in a MVC. Obese and overweight children were most at risk for lower extremity injuries as well as sustaining multiple injuries. Further studies should be completed to restructure the recommendations for safety restraint laws. Limitations include small sample size, prevalence of mortality, long-term complications and lack of ability to identify type of restraint child was using or if they were restrained at all.

STATUS

Graduate Student

AUTHORS

Brittany Christopher

Mohamed Mohamed

RESEARCH MENTOR/ DEPARTMENT CHAIR

Mohamed Mohamed

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Psychosocial disparities experienced by recently arrived Latino immigrant youth

Upon arriving in the US, immigrant youth experience significant stress adjusting to a new culture and lifestyle, which in turn affects health status. Previous research has documented the burden that the immigration process can have on families, yet few have focused on recently arrived youth. Understanding psychosocial differences in youth that recently immigrated, compared with those living in the US for five or more years, informs policy change that can address potentially detrimental health consequences. Analyses were based on data from a cross-sectional community survey of Latino youth aged 12-17 years (n=360) in 2012, born outside of the US. Validated measures included English preference, psychological distress, acculturative stress, and stressful life events. After adjusting for age, youth who immigrated to the US more recently had significantly higher acculturative stress ($p < .05$). Specifically, they felt more discriminated against, that their behavior was interpreted based on Latino stereotypes, and misunderstood in daily situations because of their English skills. Recently arrived youth also reported significantly ($p < .05$) more stressful life events within the past year, including moving residence, having a family member deported, and divorce. No differences were observed for measures of depression or future expectations. The development of culturally and linguistically appropriate prevention and intervention programs that address these psychosocial factors identified by this study as putting recently arrived immigrants at substantial risk are warranted. Further, interventions should promote social integration, family reunification, and job readiness, which will benefit immigrant youth, their families, and the community as a whole.

STATUS

Graduate Student

AUTHORS

Sean Cleary

R. Snead

T. Karver

E.K. O'Brien

E. Andrade

M.C. Edberg

RESEARCH MENTOR/ DEPARTMENT CHAIR

Sean Cleary

EPIDEMIOLOGY

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Continued Sex-Differences in the Rate and Severity of Knee Injuries among NCAA Soccer Players, 2004-2009

BACKGROUND

Studies continue to report a greater risk of knee injury in female, compared with male athletes; however, there are no comparable data on injury severity.

PURPOSE

We extend previous analyses and examined sex-differences in the rate and severity (lost days of participation, need for surgery) of knee injuries among collegiate soccer players between 2004 and 2009, while controlling for several covariables previously linked to injury occurrence.

METHODS

Data from the National Collegiate Athletic Association Injury Surveillance System (NCAA-ISS) were used to calculate injury incidence density (ID) per 1000 athletic exposures (AE). As per the data collection guidelines of the surveillance system, injury incidence was defined as: 1) any injury event involving the knee that occurred during participation in an intercollegiate game or practice; 2) that required medical attention and/or surgery; and 3) restricted participation or performance for > 1 day beyond the event. The rate ratio (RR), along with the 95% Wald confidence interval (CI), compared incidence density among female, relative to male soccer players (the referent group). Multivariable regression and multivariable negative binomial regression modeling then tested the relation between sex and knee injury incidence and severity among all injured soccer players, while controlling for contact, setting, and division level, as well as for the interactions among these variables.

RESULTS

Between 2004 and 2009, the sex-specific rate of knee injuries was 1.20 per 1000 AEs in women and 0.90 per 1000 AEs in men [RR =1.45, 95% CI = (1.27, 1.64)]. In the multivariable modeling, women continued to experience significantly higher odds of knee injury compared with men [aOR =1.44, 95% CI = (1.27, 1.63)]. Also, the adjusted odds of a knee injury that resulted in surgery remained higher in women compared with men [aOR = 1.61, 95% CI= (1.00, 2.58)]. From the negative binomial modeling, we observed that women also experienced significantly more lost time from participation, independent of contact, competition level, and surgery (beta=0.129; p=0.05).

CONCLUSION

Given the prominence of soccer play in the United States, continued efforts to evaluate and improve knee injury prevention practices and policies may be especially important for female players.

STATUS

Faculty

AUTHORS

Loretta DiPietro

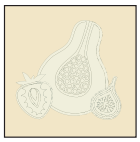
Dara Fulstone

Avinash Chandran

Mary J. Barron

RESEARCH MENTOR/ DEPARTMENT CHAIR

Loretta DiPietro



MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Effects of three-times daily diet soda consumption for one week on the composition of the gut microbiome in healthy young adults

Epidemiologic studies report associations between artificial sweetener (ASW) consumption and metabolic abnormalities, yet well-designed human intervention studies in humans are limited. Given that ASW contain no or few calories, one potential mechanism through which ASW may influence metabolic risk is through altering the gut microbiota. As alterations in the gut microbiota are known to be implicated in the development of metabolic disease, the purpose of this study was to investigate the effects of one week of three times daily diet soda (with ASW) consumption on the gut microbiota in healthy college students. We hypothesized that participants randomized to consume diet soda would have lower microbial diversity following consumption of diet soda, while microbial composition in the control group would be similar before and after the intervention. Healthy adults (n=22) were asked to provide a stool sample at three study visits, each one week apart. After the first visit, participants were instructed to avoid all ASW-containing substances for seven days (week 0). A second fecal sample was then collected (day 7), and a third was collected after one week of three times daily diet soda or carbonated water consumption (day 14) to evaluate changes in gut microbiota. DNA and RNA were extracted and samples were run on a single lane of an Illumina HiSeq. Metagenomics was performed using PathoScope™ and Censuscope™ and compared against a knowledgebase of normal gut microbiome data. Changes in read counts over the three time points were then compared between the two study groups. Twenty participants underwent randomization (n=11 diet soda, n=9 carbonated water), eighteen of whom completed the two-week study. While data analysis is ongoing, our preliminary data (n=2) suggest that ASW may in fact reduce microbial diversity. We observed a relative increase in species within the Bacteriodetes phylum and relative decreases in other phyla analyzed (Actinobacteria, Verrumicrobia, Proteobacteria, and Firmicutes) following diet soda exposure (n=1), but not following the carbonated water control (n=1). These preliminary data support our hypothesis that repeated ASW exposure may reduce the diversity of the gut microbiota and are consistent with findings of Suez et al., who also reported an increase in Bacteriodetes following saccharin exposure. However, a larger sample size and additional analyses are needed to confirm these findings. If ASW are found to adversely influence microbial diversity, this may have clinically relevant effects on metabolism, body weight, and health, which requires further study in humans.

STATUS

Undergraduate Student

AUTHORS

Jenna Abdelhadi

Domenica Simone

Charles Hadley King

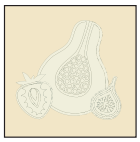
Raja Mazumder

Keith A. Crandall

Allison C. Sylvetsky (Meni)

RESEARCH MENTOR/ DEPARTMENT CHAIR

Allison C. Sylvetsky (Meni)



MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Effects of an incentive program on participants' attendance at farmers' markets in DC

INTRODUCTION

Healthy food incentive programs at farmers' markets offer an opportunity to improve food access, promote healthy eating, and enhance economic viability of markets. The Produce Plus program offers low-income Washington, DC residents the opportunity to receive one $10 voucher/family/market/week for fruits and vegetable purchases at participating markets. We examined the effect of Produce Plus on participants' frequency of attendance and use of additional money/benefits at markets.

METHODS

Program participants were surveyed at participating farmers' markets across the District between June and September 2015. Survey questions included frequency with which the participants shopped at farmers' markets and whether they used additional money/benefits beyond the program benefits. Descriptive statistics were used to summarize the data.

RESULTS

Of the 288 survey respondents, 58.0% reported having attended a farmers' market >3 times in the past month, 70.6% reported that they came to the market specifically because of Produce Plus, and 84.8% reported attending farmers' markets more frequently because of Produce Plus. Only 33.6% of participants reported spending additional money at the market, of which 57.5% used their own money and 35% used SNAP benefits. Among participants reporting attending markets more frequently because of Produce Plus, the majority (59%) reported not spending additional funds at the market.

CONCLUSION

Our findings indicate that healthy food incentive programs are a strategy for increasing attendance at farmers' markets, but most program participants only spend incentive program benefits at the market.

STATUS

Graduate Student

AUTHORS

Anna Bost

Meghan McGonigle

Sara Pellegrino

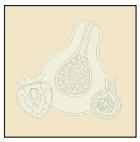
Lillie Rosen

Uriyoan Colon-Ramos

Kim Robien

RESEARCH MENTOR/ DEPARTMENT CHAIR

Kim Robien



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Diet as a Risk Factor in Obstructive Sleep Apnea

RATIONALE

Obstructive sleep apnea (OSA) is a common disease affecting approximately 2% of women and 4% of men. It is independently associated with cardiovascular disease and metabolic syndrome. Established risk factors for OSA include obesity, male gender, post-menopausal state, smoking and increased neck circumference. Sleep deprivation, a common occurrence in OSA, is associated with weight gain and cravings for carbohydrates. Preference for fatty foods has been documented in sleep deprivation. Studies using mouse models have suggested that high fats diets increase the severity of sleep apnea independent of BMI (body mass index). We hypothesized that dietary habits, especially increased fatty food intake, are independently associated with severity of OSA.

METHODS

104 patients, diagnosed with obstructive sleep apnea and presenting to the George Washington-Medical Faculty Associates Center for Sleep Disorders, completed a validated diet survey, Rapid Eating Assessment for Patients (REAP). Apnea-hypopnea index (AHI) was used as a measure of the severity of OSA. Subjects were divided using BMI in to obese (BMI > 30 kg/m2) and overweight (BMI > 25 but < 30 kg/m2) categories. Regression analysis was performed to predict severity of OSA from gender, BMI, age, % energy from fat, and the individual dietary components of REAP.

RESULTS

Subjects with a BMI <30 who consumed a diet high in fat (>35% of their total diet) had twice the severity of sleep apnea (AHI 18.2 ± 10.1 vs. 36.6 ± 27.5; p = 0.001). There was a statistically significant difference (p= 0.04) in OSA severity between subjects eating processed meats “often” [AHI 42.5 ± 30.7] versus those eating “rarely/never” [AHI 28.9 ± 22.7], even after adjusting for BMI. Conversely, eating greater than 2 servings of dairy per day conferred protection against sleep apnea [AHI 26.2 ± 15.6 vs. 39.7 ± 31; p = 0.04].

CONCLUSIONS

Dietary components may confer increased risk for worsening severity of OSA. Based on these find¬ings, unhealthy dietary patterns warrant further study of their role in OSA associated cardiovascular diseases and metabolic syndrome development.

STATUS

Medical Student

AUTHORS

Caitlin Bove

Vivek Jain

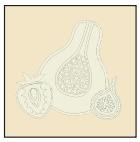
Naji Younes

Marijane Hynes

RESEARCH MENTOR/ DEPARTMENT CHAIR

Marijane Hynes

EXERCISE & NUTRITION SCIENCES



MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Characterizing the Gut Microbiota in Healthy Young Adults

OBJECTIVE/BACKGROUND

Trillions of micro-organisms reside in the gastrointestinal tract, and play a critical role in the host's physiology. Recent evidence has demonstrated that these micro-organisms, referred to collectively as the gut microbiota, are intricately involved in the development of obesity, diabetes and other metabolic diseases. Factors including route of delivery (i.e. vaginal birth vs Caesarean), infant feeding practices (i.e. breastfeeding vs formula feeding), diet (e.g. vegetarian vs. low-fat, high fiber diet vs. Western diet), physical activity, medication use, and smoking influence the gut microbiota and contribute marked variability in microbial composition between individuals, yet little is known about what constitutes a "healthy" gut microbiome. Given the emerging importance of the gut microbiota in human health and disease, the objective of this study is to evaluate the associations between lifestyle factors, metabolic biomarkers, and gut microbiome composition, in order to determine whether one or more patterns of "healthy microbiome composition" exists. In addition, we aim to evaluate the intra-individual reproducibility of gut microbiome composition.

METHODS

Young adults (18-35 years of age) participate in a study visit where they are instructed to collect a stool and urine sample, and complete a detailed diet history questionnaire, a validated physical activity questionnaire, a lifestyle habits questionnaire, a validated perceived stress questionnaire and validated sleep index. During the visit, participants also undergo anthropometric measurements including height, weight, and waist circumference, and provide a fasting blood sample to evaluate metabolic markers including blood glucose levels, lipid profiles, and inflammatory cytokines. Participants are then asked to record their diet, physical activity, and sleep patterns and are also asked to provide two additional stool samples, over a period of seven days following their study visit.

RESULTS

Data collection is currently in progress. To date, we have screened 65 volunteers and have enrolled 11 participants (9 male, 2 female, mean age 22.09).

CONCLUSIONS

In investigating the reproducibility of repeated measures of microbial composition and in determining what constitutes a 'healthy' microbiome, our study will provide important data, which will advance the human microbiome field. Findings of this study will enable us to develop rigorously-designed future studies aimed at elucidating the role of the human gut-microbiota in the prevention and treatment of metabolic disease.

STATUS

Undergraduate Student

AUTHORS

Colby Carlone

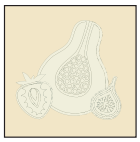
Raja Mazumder

Keith Crandall

Allison Sylvetsky Meni

RESEARCH MENTOR/ DEPARTMENT CHAIR

Allison Sylvetsky Meni



VETERANS AFFAIRS MEDICAL CENTER

The Association of Lower Extremity Strength with Step Ascent and Descent Performance in Men with Knee Osteoarthritis

BACKGROUND

Knee osteoarthritis (OA) is a chronic disease characterized by articular cartilage damage, pain, and muscle weakness. Ambulating stairs is a leading source of pain in people with OA, and disease progression may be marked by asymmetrical gait abnormalities. The primary objective of this study was to determine the relationship between knee peak torque and Step-Up-and-Over (SUO) test performance in individuals with knee OA. The secondary objective was to assess asymmetries in the study participants based on knee peak torque and OA severity.

METHODS

Twenty-one male Veterans with knee OA (age = 59.8 yrs. ±4.5) from the Washington DC VA Medical Center enrolled in the study. The severity of knee OA was determined by a radiologist using the Kellgren–Lawrence (K-L) grading system during the assessment of participant x-rays. Functional performance was assessed via the SUO test, which involves ascending/descending an 8-inch box on a force plate. The SUO test outcomes included movement time and force-time parameters representing step-up force (concentric muscle control), step-down force (eccentric muscle control), and force-time curve smoothness (lower-limb motor coordination). Peak torque of the knee extensors and flexors were measured using isokinetic dynamometry (180°/s). Correlation analysis was used to determine the association between strength and SUO test outcomes. Paired t-tests were used to assess bilateral differences in peak torque and the K-L grades.

RESULTS

The mean within-participant difference in the K-L score was 0.7 ±0.6. Normalized knee peak torque was not significantly greater in the less involved leg (mean = .32 ±.14) compared to the more involved leg (mean = .27 ±.11; $p > .05$), but was greater in the dominant leg (mean = .34 ±.13) versus the nondominant leg (mean = .25 ±.11; $p = .001$). Movement time during the SUO test was associated with knee extensor strength ($r = -.41$, $p = 0.009$), but not flexor strength ($r = -.30$, $p = .056$). Movement time was the only parameter measured during the SUO test that was associated with peak torque.

CONCLUSIONS

Preliminary findings suggest that strength and OA severity asymmetries were minimal within the sample. Gross measures of knee extensor strength are associated with the movement time of the step ascent/descent task. However, the SUO force-time parameters may be associated with motor coordination rather than peak torque generation. Future work is needed to determine whether motor coordination improves independently of changes in knee strength over the course of OA treatment.

STATUS

Staff

AUTHORS

Tomas I. Gonzales

Haniel J. Hernandez

Bryant A. Seamon

Donte Pennington

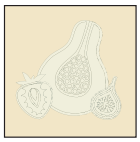
Valerie McIntosh

Marc R. Blackman

Michael O. Harris-Love

RESEARCH MENTOR/ DEPARTMENT CHAIR

Michael O. Harris-Love



MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Four Days of Caffeine Withdrawal in Caffeine Consumers Lowers Strength in Knee Flexors and Extensors

There is strong evidence supporting the ergogenic properties of caffeine with aerobic exercise, but potential ergogenic benefits to anaerobic activities remain in question. These studies of anaerobic exercise have varied designs and equivocal results. It is also unclear how caffeine withdrawal can affect performance.

PURPOSE

To study the effects of caffeine withdrawal on peak torque (PT), average power, perceived exertion (RPE) and perceived pain index (PPI) during exercise with an isokinetic dynamometer in habitual caffeine consumers.

METHODS

Physically active subjects (n=33; 30 female, 3 male; age: 21±1; mass: 60.25±6.79 kg) performed anaerobic exercise tests before and after 4 days of caffeine withdrawal. Isokinetic PT and average power were tested in the subjects' dominant leg at 60°·s^{-1}, 180°·s^{-1}, and 300°·s^{-1}. Short duration endurance was assessed in 30 repetitions at 180°·s^{-1}. Isometric PT was measured at 30° and 90° flexion. Data were analyzed with either paired t-tests or repeated measures ANOVA with an alpha of 0.05 and presented as means ± SD.

RESULTS

Following caffeine withdrawal, knee extension PT at 60°·s^{-1} decreased by 7.5 N-m (92±21 vs. 84 ± 25 N-m; p=0.006); 30 repetitions PT at 180°·s^{-1} decreased from 69±16 to 65±14 N-m (p=0.016); isometric PT at 30° of knee flexion decreased from 54±16 to 48±10 N-m (p=0.005); and isometric PT at 90° of knee flexion declined by 8.2 N-m (102±39 vs. 94±38 N-m; p<0.001). Knee flexion PT at 180°·s^{-1} decreased by 2.8 N-m (40±12 vs. 37±10 N-m; p=0.049) and during 30 repetitions at 180°·s^{-1} decreased from 40±9 to 37±10 N-m (p=0.04). Average power for extension at 60°·s^{-1} decreased 6.6 N-m (78±23 N-m vs. 72±19 N-m; p=0.015) and flexion average power at 180°·s^{-1} decreased from 86±37 to 78±29 N-m (p=0.05) following caffeine withdrawal. For 30 repetitions at 180°·s^{-1}, knee extension average power decreased 6 N-m (135±35 vs. 129±31 N-m; p=0.039) and flexion average power decreased 7.5 N-m (68±24 vs. 61±22 N-m; p=0.02). No significant differences in RPE or PPI following withdrawal were observed in response to the exercises.

CONCLUSION

The current study demonstrates that caffeine withdrawal significantly decreases isokinetic and isometric torque and power in moderate-to-high caffeine consumers.

STATUS

Graduate Student

AUTHORS

Tara Hannings

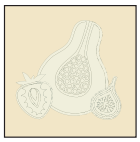
G.M. Hudson

A.J. Visek

L. DiPietro

RESEARCH MENTOR/ DEPARTMENT CHAIR

Geoffrey Hudson



MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Acute Caffeine Supplementation in Regular Caffeine Consumers Increases Relative Strength in Knee Flexors

There is strong evidence supporting the ergogenic properties of caffeine with aerobic exercise, but potential ergogenic benefits to anaerobic activities remain in question. These studies of anaerobic exercise have varied designs and equivocal results. The impact of acute caffeine ingestion in habitual caffeine consumers is also unclear.

PURPOSE

To study the effects of acute caffeine ingestion on peak torque (PT), average power, perceived exertion (RPE) and perceived pain index (PPI) during exercise with an isokinetic dynamometer in habitual caffeine consumers.

METHODS

Physically active, habitual caffeine consumers (n=33; 30 female, 3 male; age: 21±1; mass: 60.25±6.79 kg) participated in a placebo-controlled intervention. Subjects were matched and added to a caffeine or placebo group. All subjects abstained from caffeine for 4 days, supplemented with 5mg·kg of caffeine for 3 days and on the final testing day consumed 6mg·kg of caffeine or placebo (insoluble fiber) one hour before testing. Isokinetic PT and average power were tested in the subjects' dominant leg at 60°·s^{-1}, 180°·s^{-1}, and 300°·s^{-1}. Short duration endurance was assessed in 30 repetitions at 180°·s^{-1}. Isometric PT was measured at 30° and 90° flexion of the non-dominant leg. Data were analyzed with either independent t-tests or repeated measures ANOVA with an alpha of 0.05. PT values were divided by the participant's body mass and presented as means (caffeine vs. placebo) ± SD.

RESULTS

No significant differences between caffeine and placebo groups were observed for any knee extension variables. Knee flexion peak torque at 60°·s^{-1} (0.85±0.23 vs. 0.66±0.18 N-m/kg; p=0.03) and 300°·s^{-1} (0.61±0.11 vs. 0.58±0.22 N-m/kg; p=0.02) were statistically significantly higher in caffeine group compared with placebo. No significant differences observed in average power. No between group differences in RPE or PPI were observed in response to the exercises.

CONCLUSION

The current study demonstrates that acute caffeine ingestion slightly increases isokinetic peak torque in subjects regularly ingesting moderate amounts of caffeine, but many other anaerobic performance markers remain unaffected by caffeine ingestion.

STATUS

Faculty

AUTHORS

Geoffrey Hudson

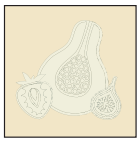
T. Hannings

A.J. Visek

L. DiPietro

RESEARCH MENTOR/ DEPARTMENT CHAIR

Loretta DiPietro



MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Consumption of Low-calorie Sweeteners in the United States 2009-12

We have previously demonstrated that low-calorie sweetener (LCS) consumption increased in the United States (US) between 1999 and 2008 (from 9% to 15 % in kids and from 27% to 32% in adults), but little is known about current consumption. We therefore analyzed National Health and Nutrition Examination Survey (NHANES) data collected in 2011-12 and compared LCS consumption patterns across socio-demographic subgroups. Dietary sources of LCS were identified using NHANES food descriptions. Prevalence of consumption nationally and by age, race, gender, socio-economic status, educational attainment, were estimated using two 24-hour dietary recalls. F-tests were used to evaluate differences in consumption across socio-demographic subgroups. Forty-two percent of the adults and 26% percent of children reported consuming an LCS-containing food or beverage in 2009-12. Thirty-one percent of adults consumed beverages and 11% consumed foods sweetened with LCS. In addition, 14% reported addition of LCS from packets to their foods or beverages. Similar findings were observed among children, with 19% and 8% consuming LCS-containing beverages and foods, respectively. Less than 1% of children reported consuming LCS packets. LCS consumption was highest among non-Hispanic white (47%) compared to non-Hispanic black (29%), and Hispanic (32%) adults ($p<0.001$). More women (46%) than men (37%) consumed LCS ($p<0.001$). LCS consumption also increased with age (51% of adults aged 55-74 years vs. 30% of adults 18-34 years, $p<0.001$), socio-economic status (49% of adults in the highest vs. 29% in the lowest income tertile, $p<0.001$), and educational attainment (34% of adults with less than high school degree vs. 50% of those with college degrees or higher, $p<0.001$). Our results demonstrate that LCS consumption has continued to increase markedly in the US, with more striking increases in consumption among children. Consistent with prior data (12 % beverages with LCS vs. 4% foods and packets with LCS in kids and 25% beverages with LCS vs. 15% foods and packets with LCS in adults, in 2007-08) LCS-containing beverage consumption continued to comprise the majority of reported LCS intake, among both children and adults.

STATUS

Staff

AUTHORS

Yichen Jin

Allison C. Sylvetsky

Jean A. Welsh

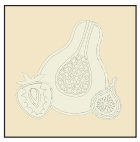
Kristina I. Rother

Sameera A. Talegawkar

RESEARCH MENTOR/ DEPARTMENT CHAIR

Allison C. Sylvetsky Meni

EXERCISE & NUTRITION SCIENCES



MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Comparison of healthy food incentive redemption rates: A systematic review

INTRODUCTION

Healthy food incentive (HFI) programs may increase food access for low-income individuals. In many HFI programs, participants must spend part of their nutrition assistance benefits at a farmers' market in order to receive a matching incentive. Conversely, the Produce Plus program offered by the District of Columbia Department of Health provides low-income residents with a flat $10 voucher/family/market/day to purchase produce from farmers' markets. We conducted a systematic review to determine whether Produce Plus redemption rates differ from other HFI programs.

METHODS

A systematic search of scientific and grey literature databases was performed to identify potentially eligible articles. Inclusion criteria included: US-based program, participants were federal nutrition assistance recipients, incentive vouchers were redeemable at farmers' markets, and redemption rates or effect on other federal assistance redemption were reported. Program administration data and redemption rates were abstracted from eligible articles.

RESULTS

After inclusion criteria were applied to the 257 articles identified in the database search, 14 studies remained for analysis. Redemption rates ranged from 45%-93%, with highest rates in the Health Bucks program (93%), a WIC intervention study (91%) and Produce Plus (90.4%)– all at least partially flat benefit programs. Programs that distributed benefits at the farmers' market also tended to have higher redemption rates. Monetary value of the benefits offered by each program varied considerably, but tended to be higher in flat benefit programs ($20-160/season).

DISCUSSION

Flat benefit programs may have higher redemption rates because of lower burden and higher monetary benefit. On-site distribution may also improve redemption rates.

STATUS

Graduate Student

AUTHORS

Meghan McGonigle

Anna Bost

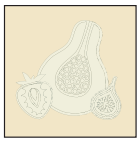
Sara Pellegrino

Lillie Rosen

Kim Robien

RESEARCH MENTOR/ DEPARTMENT CHAIR

Kim Robien



MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Evaluating fruit and vegetable intake among farmers' market incentive participants in DC

INTRODUCTION

The Produce Plus program offered by the District of Columbia (DC) Department of Health provides $10 per family/market/week to participants of federal financial and nutrition assistance programs to spend on fresh fruit and vegetables (F&V) at farmers' markets. The objective of this study was to determine whether F&V intake among Produce Plus participants differs from that of the average DC population.

METHODS

Using a cross-sectional survey, program participants were interviewed at markets across DC between June and September 2015. Questions included the Behavioral Risk Factor Surveillance System (BRFSS) F&V module which assesses F&V intake over the previous month. Participants' F&V intake was compared to 2013 DC BRFSS F&V data.

RESULTS

A total of 288 Produce Plus participants were surveyed; results are presented here as median (interquartile range). Compared to 2013 DC BRFSS data for individuals reporting annual household incomes of <$35,000, Produce Plus participants reported higher fruit (2.0(1.0-3.0) vs. 1.0(0.4-2.0) times/day) and vegetable (2.0(1.3-3.5) vs. 1.4(0.8-2.3) times/day) intake compared to BRFSS respondents with similar household incomes. Produce Plus participants reported higher fruit intake as the season progressed and they were more likely to have previously received program benefits (June: 1.4(1.0-2.4) vs. August/September: 2.0(1.0-3.0) times/day). Vegetable intake stayed constant throughout the season (June: 2.1(1.5-3.2) vs. August/September: 2.1(1.3-3.8) times/day).

DISCUSSION

Participants in the Produce Plus program reported higher F&V intake compared to DC BRFSS respondents with similar incomes, but still below recommended levels. A prospective study is planned to more fully assess whether the Produce Plus program increases participants' F&V intake.

STATUS

Graduate Student

AUTHORS

Sara Pellegrino

Anna Bost

Meghan McGonigle

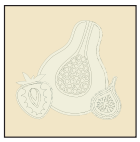
Kim Robien

Lillie Rosen

Uriyoan Colon-Ramos

RESEARCH MENTOR/ DEPARTMENT CHAIR

Kim Robien



MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Plasma concentrations of sucralose following ingestion of sucralose containing beverages in children and adults

OBJECTIVE/BACKGROUND

Sucralose is partially absorbed after oral ingestion, with the majority excreted in the feces. Interestingly, high doses of oral sucralose are associated with relatively lower plasma concentrations than low doses, which may be due to activation of a gut efflux transporter. Few data are available on circulating concentrations of sucralose, particularly after ingestion of doses found in commercially available products. The objective of this study was therefore to determine the amount of sucralose absorbed following ingestion at doses typically consumed in 'real life,' and to compare its absorption in children and adults.

METHODS

We conducted a same-subject cross-over study in healthy adults and children. Ten healthy adult volunteers (mean age 29.7 yr, BMI 25.8 kg/m^2) consumed 355mL water containing 0, 68, 170, or 250mg sucralose (equivalent to 1-4 diet sodas). A second group of adult volunteers (n=11, mean age 27.4 yr, BMI 26.3 kg/m^2) consumed 355mL Diet Rite Cola™ (68mg sucralose and 41mg acesulfame-potassium (ace-K)) or 68mg sucralose and 41mg ace-K mixed in seltzer in randomized order prior to a glucose load. Normal-weight children (n=10, mean age 9.1 yr) were randomized to consume 240 mL water containing 0 or 68mg sucralose in an identical study design. Blood was collected before beverage ingestion and serially for 120 min.

RESULTS TO DATE

At the relatively low sucralose doses provided, sucralose absorption was directly proportional to the amount ingested. Average plasma sucralose concentrations were 40% higher after the 250mg compared to 170mg (AUC 38,035 ± 9,007 vs. 27,423 ± 5,987 ng/mL/120 min). Similarly, sucralose AUC increased 3-fold after 170mg compared to 68mg (AUC 27,423 ± 5,987 vs. 9,206 ± 949 ng/mL/120 min). Sucralose AUCs were comparable whether administered in water, combined with ace-K, or in Diet Rite Cola™ (AUC 9,206 ± 949 vs. 9,320 ± 1,168 vs. 8,281 ± 1,168 ng/mL/120 min). Concentrations of sucralose were markedly higher in kids than adults (mean $AUC_{0\text{-}120}$ 20,911 ± 5,741 (kids) vs. 9,059 ± 3740 (adults), $p<0.0001$) after ingestion of the same 68 mg dose; however, plasma concentrations were similar in children and adults when doses were adjusted for weight.

CONCLUSIONS

We conclude that intestinal sucralose absorption is similar regardless of the vehicle of administration, and increases in a linear manner when provided within the range of reasonable human sucralose consumption. Furthermore, intestinal sucralose absorption at doses typically found in diet sodas led to markedly higher plasma concentrations in children compared to adults, which warrants further study.

STATUS

Faculty

AUTHORS

Allison Sylvetsky (Meni)

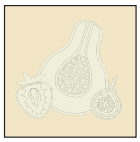
Viviana Bauman

Jenny Blau

Kristina Rother

RESEARCH MENTOR/ DEPARTMENT CHAIR

Loretta DiPietro



MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Relative Importance of the Fun Factors: Pattern Matched Perceptions among Players, Parents, and Coaches

BACKGROUND

The FUN MAPS are evidence-based blueprints for the fun integration theory, youth sport's first-ever stakeholder-derived, theoretical framework for promoting fun through structured skill development and competitive play (Visek et al., 2015). Developed from the direct input of players, parents, and coaches, the FUN MAPS identify and quantify the importance of 81 fun-determinants within 11 factors (i.e., *Positive team dynamics, Trying hard, Positive coaching, Learning and improving, Game time support, Games, Practices, Team friendships, Mental bonuses, Team rituals,* and *Swag*). However, the FUN MAPS are based on the combined input from players, parents, and coaches. Efforts to promote the most fun for children requires their priorities to be considered independent of adults and comparatively to one another within and across sex, age, and competition level. Additionally, to elucidate exact points of consensus/discordance between children and adults, players' priorities should be considered alongside parents and coaches' perceptions. Therefore, the purposes of this study were to use pattern matching displays, useful for determining within and between group differences, to identify the extent to which children's (n = 142) reported importance of the 11 factors evolves throughout their development and how their perceptions compares to adults (parents, n = 57; coaches, n = 35).

METHODS

The Concept Systems® Global MAX license was used to produce pattern match displays for consensus analysis (r). Mann-Whitney U tests were used to identify the fun-factors on which groups significantly differed; and, the Fisher r-to-z transformation was used to determine whether consensus between pattern matches were significantly different from one another.

RESULTS

Results indicate remarkably high degrees of consensus among children, regardless of sex, age, and competition level comparison (r's = .90-.97). Consensus was also high among children and parents (r = .93); however, it was significantly lower among children and coaches (r's = .68-.93). Pattern matches are displayed using sophisticated, illustrative ladder graphs.

DISCUSSION

Novel findings from this study provide a more complete context for understanding children's fun priorities across all 11 fun-factors. Overall, with respect to players, results support the gender similarities hypothesis, rather than the gender differences hypothesis and the other age and competition level assumptions that have long guided organized youth sport. The discordance observed between older players and coaches is of great concern to children's continued participation into adolescence and may account for the dramatic dropout that occurs around the age of 13. Best practices for optimizing children's fun sport experiences are forwarded.

STATUS

Faculty

AUTHORS

Amanda Visek

Ciera Jones

Heather M. Mannix

Avinash Chandran

Lauren Beckley

Sara Achrati

Karen McDonnell

Loretta DiPietro

RESEARCH MENTOR/ DEPARTMENT CHAIR

Loretta DiPietro

GLOBAL HEALTH

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Improving the Sustainability of the Ugandan Village Health Team Program

The population of Uganda is 37.6 million and the gross national income per capita is $1 per day. The average life expectancy is 59 years and 1 in 15 children die before in their 5th birthday. In 2001, the Ministry of Health established Village Health Teams in order to address this gap in healthcare delivery. Omni Med, an NGO operating in the Mukono district, partnered with the government to train select village members in the prevention of the most common fatal diseases, how to identify and refer sick individuals to local health centers, and to document these incidences. Omni Med trained over 1,100 VHTs, however, declining funding from the government and varying levels of supervision led to an attrition rate of 30%.

The purpose of this project was to investigate new approaches to improve the effectiveness and sustainability of the VHT program. Information was gathered about the government's current involvement in the program through meetings with Department of Health officials. Interviews with VHT members were conducted to assess reasons for continued involvement and challenges that they faced in their field work.

It was determined that the Ministry of Health was not well connected with VHT members and did not have an accurate understanding of the problems that VHTs face. Omni Med generated a proposal to bring VHT members to the local clinic each week to assist clinic staff with HIV screenings, antenatal care, and vaccinations. Omni Med proposed bringing volunteer VHTs each week to the health center to strengthen their connection with the department of health. This should allow for increased supervision, training, job satisfaction and long-term retention.

STATUS

Medical Student

AUTHOR

Mallette Asmuth

RESEARCH MENTOR/ DEPARTMENT CHAIR

Edward O'Neil Jr.

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Human resources in urban health systems: a retrospective assessment of the readiness in Nairobi to provide HIV-related services

BACKGROUND

Human resources are the cornerstones of well-functioning health systems. Despite higher concentrations of human resources for health in urban areas, urban populations experience higher mortality from communicable and non-communicable diseases. Urban health system dynamics with respect to human resources for health in low- and middle-income countries needs better elucidation.

METHODS

We conducted a retrospective cross-sectional analysis to evaluate the readiness of health providers to deliver HIV/AIDS services in Nairobi, Kenya. We used data from Nairobi County in the 2010 Kenya Service Provision Assessment from 261 providers on 51 aspects of HIV/AIDS services. Readiness was assessed in terms of the proportion of health workers at different facility levels who were trained in HIV prevention, diagnosis, and treatment according to Kenyan government HIV/AIDS guidelines and policies.

RESULTS

Less than 11% of health providers reported being trained in the full complement of essential HIV services (10.31% prevention, 10.69% diagnosis, and 8.78% treatment). Nurses were the most common recipients of HIV/AIDS training. Only 16% of clinical officers and physicians reported training in HIV care and treatment although they are expected to be the main providers. The lowest proportions of health workers trained was observed in HIV care and treatment (14.18%), youth-friendly services (19.16%), and PMTCT (25.29%), some of the more critical services for HIV control.

CONCLUSIONS

The Kenya Service Provision Assessment provides useful data to assess the human resources for health component of health systems. Health workers in Nairobi County are under-prepared to provide essential HIV/AIDS prevention, diagnosis, and treatment services prescribed by Kenyan government policies. Uneven training levels across cadres of health providers impede a team-based approach to HIV care and treatment. The low training levels we find point to the urgency of scaling up training for all health cadres who provide HIV-related services at all facility levels, even in Kenya's better health worker-resourced urban areas.

STATUS

Graduate Student

AUTHORS

Cudjoe Bennett

Adriana Alminana

Sangeeta Mookherji

RESEARCH MENTOR/ DEPARTMENT CHAIR

Sangeeta Mookherji

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

A dose-response relationship between exposure to an HIV prevention intervention and preventive behaviors in Mozambique: Findings from the Capable Partners Program (CAP)

BACKGROUND

Mozambique has seen improvements in condom use and in the uptake of voluntary HIV counseling and testing (VCT), yet the overall uptake of preventive behaviors (such as reduction of sexual partners) is limited. Continued investments have been made in HIV prevention programs, including community-based behavior change communications (BCC) efforts carried out by FHI360's Capable Partners Program (CAP). However, evidence from Mozambique is limited regarding the minimum dosage of intervention programming necessary to encourage behavior change.

METHODS

In 2014, we conducted a multi-phased household cluster survey in 12 districts in 4 provinces of Mozambique where CAP was implemented. We interviewed 923 individuals aged 15-64 (399 men, 524 women), 624 of whom were exposed to CAP BCC, and 299 who were not exposed to any HIV intervention. Participation was divided into three levels according to respondent involvement in eight CAP activities in the past 6-12 months: low (1-3 instances of participation), medium (4-6 instances) and high (more than 7 instances). Activities included one-on-one talks with a peer educator, participation in discussion groups, and watching theater performances or films about HIV/AIDS. The participation variable was regressed on five outcomes: intention to seek VCT in the next 6 months, ever sought counseling and testing for HIV/AIDS (individual VCT), ever gone for an HIV test with any of their sex partners (couples VCT), condom use at last sex, and current multiple concurrent partners.

RESULTS

Our results suggest a significant dose-response relationship between CAP participation and three outcomes: intention to test for HIV at low (AOR=2.67;95%CI:1.49-4.78), medium (AOR=4.29;95%CI:2.14-8.58), and high (AOR=5.71;95%CI:3.32-9.81) participation, individual VCT at low (AOR=2.66;95%CI:1.52-4.67), medium (AOR=3.60;95%CI:2.14-8.58) and high (AOR=5.71;95%CI:3.32-9.81) participation and couples VCT at low (AOR=3.73;95%CI:1.52-4.67), medium (AOR=4.31;95%CI:1.79-10.38) and high (AOR=9.41;95%CI:4.48-19.79) participation. For condom use, only a medium level of participation was positively associated with reporting condom use at last sex (AOR: 2.81;95%CI:1.49-4.78), while no association was found for current multiple concurrent partners.

CONCLUSION

Initial findings suggest higher levels of participation in CAP activities are significantly associated with increased intention to seek VCT, and reporting individual and couples VCT. Investing in greater dosages of intervention programming may be worthwhile for behavior change.

STATUS

Graduate Student

AUTHORS

Floriza Gennari

E. Oliveras

E. Marinda

H. Bryant

RESEARCH MENTOR/ DEPARTMENT CHAIR

Rajiv Rimal

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Analysis of Kigezi Healthcare Foundation HIV Clinic Patient Surveys

The Kigezi Healthcare Foundation (KIHEFO) is a dynamic organization dedicated to providing health related services to the people of Kabale, Uganda. The KIHEFO HIV Clinic in particular has blossomed over the last few years from a small office capable only of short counseling sessions for newly diagnosed HIV patients to a multi-faceted team of doctors and nurses rotating through both clinic and village. The focus of this study was to analyze the KIHEFO HIV Clinic's data collected through patient surveys between the years of 2011 and 2014. The intent of which was to examine the trends over time in a wide variety of aspects including age at diagnosis, possible mode of transmission, condom usage, etc. Results showed there is much work left for the clinic, as a lack of education and unsafe sexual behaviors continue to provide barriers to HIV prevention. The analysis will serve the clinic primarily as a tool for measuring their progress in the community and as a foundation for KIHEFO's recent efforts to lobby for increased funding and support from local officials.

STATUS

Medical Student

AUTHOR

Selem Ghebrendrias

RESEARCH MENTOR/ DEPARTMENT CHAIR

Jessica Evert

SCHOOL OF MEDICINE AND HEALTH SCIENCES

A medical system on the rise: Observing how Thai culture coexists with Western style pediatric medicine

BACKGROUND

The South East Asian Country of Thailand has made great strides in the development of a more affordable and effective medical system, centered around the ideals of western medicine. With its "30 Baht" policy, any citizen can get all aspects of their medical visit at a government hospital for the equivalence of 1 US Dollar. However, even with this rapid progress and adoption of certain protocols such as America's St. Jude pediatric cancer treatment schedules, there are still many cultural and accessibility boundaries standing in the way of delivering fast and efficient treatment to Thai children diagnosed with cancer. Understanding these boundaries can help the country make an even greater advancement in the delivery of medical care to the Thai children.

OBJECTIVE

To define barriers that prevent children of Thai and Laotian families from receiving early diagnoses, earlier treatment and time efficient treatment courses for cancers, most particularly Neuroblastomas, Osteosarcomas, and hematologic leukemias. By defining these barriers, we then can propose changes to reduce this delay in care. Of most concern is the lack of accessibility to nearby government hospitals and the uneducated cultural belief that cancer is only a disease of the old.

METHODS

Every day over a period of two months, I observed hundreds of patient's cases and the interactions and treatment strategies of the families with the physicians. Most of the physicians have spent a great time of training in America and implement the strategies of American pediatric medicine. I was able to speak to the physicians and the students, hearing from the source what they believe are still the obstacles to quality care for these Thai children. I was able to follow certain patients over this time and observe their treatment journeys after being diagnosed with cancer. Each story was documented.

RESULTS

I found that cost of medical care did not seem to hinder the chemotherapy treatment process. Most costly in the treatment turned out to be the distance traveled to the hospital and the time taken off from labor for the parents that seemed to prevent the families from coming in as scheduled. Also, many parents delayed bringing their children after noticing the growing masses because they felt that it was an illness that god would fix and they believed that children do not get cancer. This leads to later presentations to the doctor, later chemotherapy, and worse prognosis.

CONCLUSIONS

Although Thailand has made great strides as a country in the treatment of pediatric cancers, there are still quite a few large barriers to further success and more lives saved. Treatment hospitals must be made more accessible to those families not in large cities and citizens must be educated on the concept that children can indeed get cancer. With these two large changes, children will present earlier and will have a better prognosis.

STATUS

Medical Student

AUTHOR

Laurel Hansen

RESEARCH MENTOR/ DEPARTMENT CHAIR

Azure Samuels

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Exploring the link between handwashing proxy measures and child diarrhea in 25 countries in Sub-Saharan Africa

BACKGROUND

Handwashing with soap is considered the most cost-effective intervention for reducing the risk of child diarrhea, but reliable measurement of handwashing behaviors is difficult. This study aimed to examine the association between proxy handwashing measures and child diarrhea.

METHODS

We used the most recent Demographic and Health Survey (DHS) and the Multiple Indicator Cluster Survey (MICS) data from 25 countries in Sub-Saharan Africa, which included 254,546 households. The data were collected between 2010 and 2014, and nationally representative samples of children under five years of age were selected for the analysis. The main explanatory variable was the handwashing ladder, representing a varying level of availability of handwashing materials in the household. The outcome variable for the study was reported two-week prevalence of child diarrhea. We used a generalized linear model (GLM) with Poisson family and log link to estimate the prevalence ratio of child diarrhea between children with a basic handwashing station and without a handwashing place. Both country-specific and pooled analyses were conducted.

FINDINGS

Over 50% of children in 15 countries did not have access to a place for handwashing in or around the home. Availability of water and soap at a handwashing place was associated with both increased and decreased prevalence ratios: 0.89 (95% CI 0.79–0.99) in Chad, 0.82 (0.69–0.97) in Mauritania, 1.30 (1.02–1.66) in Burkina Faso, and 1.67 (1.20–2.33) in Ghana. In other countries, significant differences in the prevalence of child diarrhea were not found. After controlling for country-fixed effects, the prevalence ratio was 0.95 (0.92–0.99), suggesting a protective effect of having a handwashing station with water and soap.

INTERPRETATION

Presence of water and soap at a handwashing place is an important indicator to prevent child diarrhea, and handwashing promotion programs should be tailored to the unique context of each country.

STATUS

Graduate Student

AUTHORS

Mitsuaki Hirai

Amira Roess

Cheng Huang

Jay P. Graham

RESEARCH MENTOR/ DEPARTMENT CHAIR

Jay P. Graham

SCHOOL OF MEDICINE AND HEALTH SCIENCES

The Bhutanes Diet and Gastric Cancer

Bhutan is a small, landlocked country to the north of India in the Himalayas. One of Bhutan's greatest healthcare challenges is the extremely high prevalence of Helicobacter pylori and gastric cancer. A study[2] in 2013 reported the H. pylori prevalence in Bhutan to be 73.4%. Another study in 2008[1] reported the strain of H. pylori in Bhutan to have higher virulence in comparison to the H. pylori strains in surrounding southeastern Asian countries. Furthermore, a study[3] in 2015 found the prevalence of gastric cancer to be twice as high as the United States (367 cases per 5 years per 800,000 people). Researchers have suggested this prevalence and virulence of H. pylori to be correlated with the high rate of gastric cancer in Bhutan. However, several physicians in Bhutan have voiced their concern over an additional factor that may be contributing to the high rate of gastric cancer: the Bhutanese diet. In a series of interviews conducted in July of 2015, these physicians stated their concern for several items in the Bhutanese diet that may predispose the population to gastric cancer. The physicians' greatest concerns were: 1) Heavily salted fish (due to the necessary salting preservation required to transport fish to landlocked Bhutan), 2) Chili peppers, 3) Uncooked yak meat, 4) Pork, and 5) The high consumption rate of alcohol. A case-control study is currently being designed to study the correlation, if any, of diet and gastric cancer in Bhutan. A dietary survey will be conducted among a group of Bhutanese patients with gastric cancer. The same survey will be conducted among a control group without gastric cancer. Rapid H. pylori test kits will be used to test each participant in the study. A practicing oncosurgeon and gastroenterologist in Thimphu, Bhutan have agreed to work as co-investigators on this study.

REFERENCES

1 "Geographic Differences in Gastric Cancer Incidence Can be Explained by Differences between Helicobacter pylori Strains." Yoshio Yamaoka, Mototsugu Kato, and Masahiro Asaka. Intern Med. 2008; 47(12): 1077-1083.

2 "Extremely high prevalence of *Helicobacter pylori* infection in Bhutan." Ratha-korn Vilaichone, Varocha Mahachai, Seiji Shiota, Tomohisa Uchida, Thawee Ratanachu-ek, Lotay Tshering, Nguyen Lam Tung, Toshio Fujioka, Masatsugu Moriyama, and Yoshio Yamaoka. World J Gastroenterology. 2013 May 14; 19(18): 2806–2810. PMCID: PMC3653155

3 "Geographical distribution of the incidence of gastric cancer in Bhutan." Tashi Dendup, James M Richter, Yoshio Yamaoka, Kinley Wangchuk, and Hoda M Malaty. World J Gastroenterology. 2015 Oct 14; 21(38): 10883–10889. PMCID: PMC4600589

STATUS

Medical Student

AUTHOR

Trent Hope

RESEARCH MENTOR/ DEPARTMENT CHAIR

Bob Morrow

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Using Larger Volume Thick Smears for the Diagnosis of *Mansonella ozzardi* in the Peruvian Amazon

Although filariasis *Mansonella ozzardi*, a parasitic filarial nematode transmitted by an arthropod vector (a blackfly or biting midge), is very common in some regions of the Peruvian Amazon, little is known about its clinical presentations, its actual distribution in the Amazon Basin, or its role in aggravation of other diseases.

Due to its distribution, presentation, and lack of information regarding co-infections (as seen in P. vivax malaria), *M. ozzardi* is considered a neglected disease worldwide. It presents with few symptoms and is often only discovered as an incidental finding when testing for other parasitic infections such as Malaria. Therefore, it is often difficult to establish the onset and duration of infection, vastly increasing the difficulty of diagnosis.

The Knott's test, the gold standard for the diagnosis of this disease, is difficult to perform, and not done routinely in a rural setting. As such, there is a need for appropriate alternative screening techniques in more remote regions such as Diamante Azul, Iquitos, Peru. For these reasons, we conducted a study to determine the sensitivity of blood smears, with varying blood volume in comparison to the Knott's test for the effective diagnosis of this disease.

STATUS

Medical Student

AUTHORS

Kurt Isaac-Elder

Salomon Durand

Dolores Rimarachin

Alejrandro Quiroz

Andres G. Lescano

Sowmya Sanapala

Kurt Isaac-Elder

Robert V. Gerbasi

RESEARCH MENTORS/ DEPARTMENT CHAIRS

Edward Smith

Salomon Durand

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

The experience and perceptions of sexual harassment against women in public transportation: The Case of Mexico City

BACKGROUND

A recent poll placed Mexico City as the second most unsafe city for female passengers. Evidence suggests that 65% of women in Mexico City experience gender-based violence (GBV) while traveling in the public transportation system.

METHODS

In December 2014, as part of a pilot evaluation of an intervention, "Hazme el Paro", seeking to promote safer environments and reduce the incidence of GBV for women traveling by bus, we surveyed 1,509 randomly selected women and men on two of the city's busiest bus routes.

RESULTS

Our findings indicate that, while traveling by bus, 58% of women have experienced GBV whereas 67% of men reported having witnessed GBV against women. Moreover, 18% of passengers reported believing that it is dangerous for women to travel alone. Among women, factors that significantly predicted perceived risk of traveling alone include personal experience with GBV (OR=1.92, 95% CI=1.12-3.31), having observed GBV against other women (OR=1.64, 95% CI=1.10-2.47) and the belief that women are personally responsible for their experience of GBV (victim blaming) (OR=1.80, 95% CI=1.15-2.84). For men, having observed GBV against women (OR=6.41, 95% CI=3.41-12.04) was the only predictor significantly associated with perceived risk for women traveling alone.

CONCLUSION

To improve the safety of women traveling in public transportation and reduce the incidence of GBV among female passengers in Mexico City, efforts should be targeted towards changing the social norms that sanction aggression towards women, specifically reducing victim blaming as this behavior inhibits reporting, encouraging effective nonviolent intervention by drivers and passengers, and improving the mechanisms for reporting perpetrators.

STATUS

Graduate Student

AUTHORS

Tahilin Karver

Rajiv N. Rimal

Bianca Bianchi Alves

Karla Dominguez Gonzalez

Floriza Gennari

Saúl Alveano

Abel Lopez Dodero

Marty Langelan

RESEARCH MENTOR/ DEPARTMENT CHAIR

Rajiv Rimal

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Microbial contamination in household water storage and diarrhea in developing countries

Annually it is estimated that there are 1.7 billion cases of diarrhea around the world every year, killing over 750,000 children under five. Diarrheal disease is most prevalent in developing countries as it is attributed to poor water quality. This review examines contamination levels at communal improved water sources and water stored at the household and their associations with diarrheal disease. Past studies have found a significant increase in contamination from the source to the household. However, there has been a global increase in improved water sources over the past decade. This study is the first to reflect the changes in global improved water infrastructure and its impact on household water contamination. The literature search was conducted using the PRISMA method. The study examined 20 articles that measured either total coliforms or *E. coli* in water at the source and household. Including studies that measure the prevalence of household diarrhea cases. A search of Scopus and PubMed provided a total of 503 citations. After reviewing abstracts for inclusion criteria, 21 studies remained. Of the remaining articles, 4 were discarded because the full text was not available for review. An additional 3 studies were added after looking through references of the included studies. Across the included studies there was a 64.5% and 39% increase in total coliforms and *E. coli* from source to household, respectively. Associations were found between microbiologic contamination of household storage and diarrheal diseases. The results show that increasing the access to improved water sources, alone, are not sufficient in lowering the prevalence of diarrheal disease. Household water use and storage technique greatly impact the quality of water. Interventions aimed to decrease the prevalence of diarrhea must impact the quality of water storage, hygiene in the household, and point of use treatment.

STATUS

Graduate Student

AUTHORS

Yonathan Kefelegn

Jay Graham

RESEARCH MENTOR/ DEPARTMENT CHAIR

Melissa Perry

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Predictors of Malnutrition in Different Geographic Regions of Peru

Malnutrition is responsible for over 3 million childhood deaths each year. Those who survive early nutritional deficiencies and the subsequent growth failure face life-long consequences, including long-term deficits in cognitive development, decreased academic achievement, and reduced economic opportunities later in life. Low height for age, or stunting, indicates chronic malnutrition, while low weight for height (wasting) indicates acute malnutrition. Caloric deficiencies, micronutrient deficiencies, intestinal parasites, and diarrheal diseases all directly contribute to acute and chronic undernutrition.

Peru is an ethnically and geographically diverse country that has experienced great economic growth and dramatic health improvements in the last decade. Nationally, stunting in children under five dropped from 31.6% in 2000 to 19.6% in 2011. Despite this overall improvement, a growing disparity has emerged: Urban and coastal areas have seen the greatest drop in stunting, but the prevalence of stunting remains high in rural and mountainous Andean areas. Research to-date has examined predictors of malnutrition for the country as a whole, but has not looked at specific geographic differences. Using the 2012 Demographic and Health Survey (DHS) dataset for Peru, this study aims to 1) describe the prevalence of stunting and wasting in different geographic regions of Peru, and 2) determine which factors predict undernutrition in each region.

STATUS

Graduate Student

AUTHOR

Elizabeth LaCroix

RESEARCH MENTOR/ DEPARTMENT CHAIR

Karen McDonnell

GLOBAL HEALTH

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Improving access to Primary and Emergency Care in Pont Morel, Leogane, Haiti

The effectiveness of medical aid provided by foreign NGOs in Haiti is increasingly questioned both internationally and by Haitians themselves. Many skeptics claim that current models used by foreign NGOs in Haiti fail to appropriately address the objective needs of the people they serve or to provide care that is culturally relevant and respects local systems and leadership. This research, based on three years of fieldwork completed with the non-profit YourStory International sought to both qualitatively and quantitatively measure the need for medical services in the village of Pont Morel, Leogane, Haiti in order to guide the creation of a long-term investment in medical infrastructure that meets the needs of the people of Pont Morel in a manner that is effective at challenging the structural dynamics that limit access to medical resources. This presentation will outline these dynamics as they were measured and outline current efforts that have been implemented and proposed to ensure that they addressed appropriately.

STATUS

Medical Student

AUTHORS

Kevin Lombardi

Tony Bistine

Alyssa Krebs

RESEARCH MENTOR/ DEPARTMENT CHAIR

Tony Bistine

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Pursuing meaningful support of Uganda's Village Health Teams: priorities, barriers, and opportunities

Uganda's Ministry of Health leads a community health worker program in which Village Health Teams (VHTs) volunteer to deliver basic health services and education to their communities. VHTs have a positive impact on health outcomes, but they are not optimally supported and there has been notable VHT attrition. This study evaluates the experience and perspective of VHTs and key VHT stakeholders in an effort to expand understanding of existing challenges facing VHTs and potential opportunities for meaningful support. A mixed-methods approach was employed through a self-administered survey of 134 VHTs across the Mukono and Wakiso districts in central Uganda. A key outcome is "predicted longevity," which is determined by whether the subject is confident that he or she can continue working as a VHT for ≥10 years if their existing support remains unchanged. In-depth interviews were held with 6 key informants, including civil servants and non-governmental organization (NGO) program managers. VHTs' greatest challenges include insufficient supplies and transportation. 89% receive "none" or "a little" transportation tools (e.g. bicycles), while 70% receive "enough" or "almost enough" distributable health supplies (e.g. deworming tablets). The majority of respondents receive at least some ongoing training, supervision, and meetings. In terms of desired additional support, key themes were money (e.g. transportation allowance), material supplies (e.g. rubber boots), and enhancing status and respect as health workers. Regarding predicted longevity, 57% felt able to continue working as VHTs for ≥10 years if existing support remains unchanged. Bivariate analysis found that predicted longevity was positively correlated with working in the Wakiso district (P=0.043). Across both districts, predicted longevity is positively correlated with experiencing less difficulty in home visiting (P=0.003), receiving more partnership with local health center staff (P=0.001), and cleaning the health center (P=0.003). Key informants view VHTs as having an important impact on health in Uganda and facing a number of systems-level challenges, predominantly stemming from lack of domestic resources and governance authority along with dependence on outside implementing partner NGOs. Despite facing significant challenges, most VHTs are motivated to fulfill their role as health workers. Opportunities for meaningful support include practical interventions and systems-level changes, all of which could significantly improve the sustainability and impact of Uganda's VHT program.

STATUS

Medical Student

AUTHORS

Daniel Mays

Edward O'Neil

Edison Mworozi

Benjamin Lough

Edward Mutimba

Zachary Tabb

Ashlyn Whitlock

William S. Schroth

RESEARCH MENTOR/ DEPARTMENT CHAIR

Edward O'Neil

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Identifying How the HIV Testing and Counseling Service Environment Impacts Adult HIV Testing Behaviors in East Africa

BACKGROUND

HIV testing and counseling (HTC) services are critical because early identification of people living with HIV facilitates enrollment in life-long HIV prevention, care and treatment services, which can lead to significant reductions in morbidity and mortality. Yet only 51% of people living with HIV in sub-Saharan Africa know their status. We examined the extent to which the regional HTC service environment was associated with whether adults received an HIV test in the previous 12 months using population-based data from three East African countries.

METHODS

We analyzed cross-sectional, nationally representative data from the Demographic and Health Survey (DHS) and Service Provision Assessments (SPA) in Kenya, Tanzania and Uganda from 2004-2010. Applying definitions from the World Health Organization (WHO), we generated two composite scores for each facility: HTC readiness, comprised of six indicators measuring a facilities' ability to offer standard HTC services, and HTC standard precautions, which measured facilities' adherence to quality control. We generated the regional average of these scores. We linked the DHS and SPA datasets regionally, pooled them (N=32,903) and applied a multilevel, mixed effects logistic regression model to identify facility- and individual-level factors that were associated with having received an HIV test within 12 months prior.

RESULTS

We found that an increased regional HTC standard precautions score was associated with an increased odds of being tested for HIV (OR=1.46; p<0.001) and that high-risk individuals (OR=1.09; p=0.199) and people living in rural areas (OR=1.13; p=0.035) were also at an increased odds. Compared with individuals aged 15-19 years, all older age increments were associated with a decreased odds of having been tested in the previous year; these results were statistically significant. Compared with no education, groups with higher levels of education were more likely to have been tested, although these results were not statistically significant. An increased regional HTC service readiness score was associated with a decreased odds of having been tested for HIV, although it was not statistically significant (OR=0.93; p=0.573).

CONCLUSIONS

These analyses describe for the first time the degree and extent of HTC program implementation in facilities and the relationship with individual testing behavior on a population level in East Africa. Our findings could inform possible interventions to deliver HTC more effectively, and potentially fill a critical knowledge gap in HTC implementation research.

STATUS

Graduate Student

AUTHORS

Catherine Nichols

John Sandberg

Laura Guay

Amira Roess

RESEARCH MENTOR/ DEPARTMENT CHAIR

Amira Roess

GLOBAL HEALTH

SCHOOL OF MEDICINE AND HEALTH SCIENCES

An international study of race and ethnicity in clinical guidelines

Clinical guidelines are published statements that distill current scientific evidence into recommendations for clinical decision-making. Some guidelines suggest using patient race and ethnicity in determining clinical management. These race specific guidelines (RSGs) have an implied counterstatement about the management of patients who are not in the ethnic group specified. This emphasis on ethnicity rather than other disease factors could lead to decreased quality of care. This study aims to provide a comprehensive review of the prevalence and evidence for race and ethnicity in guidelines internationally. We created a library of approximately 3500 guidelines published by medical and public health organizations in 12 English-speaking and non-English speaking nations. From these, a keyword search was used to identify those guidelines that referenced race and ethnicity. Selection criteria were then applied to determine if each guideline was an RSG. Our findings include 26 RSGs from Europe, New Zealand, Scotland, United Kingdom and the USA. We classified these guidelines based on the context in which race and ethnicity were referenced: treatment (type A, 10 RSGs), screening (type B, 12 RSGs), diagnosis (type C 1 RSG), and patient education (type D, 1 RSG). Level of evidence (CEBM classification) varied between these guidelines. Although race and ethnicity are used in only a small fraction of clinical guidelines, their use is not uniformly evidence based. Further work is needed to delineate their role in clinical practice. The relationship between ethnicity and disease is epidemiologically important, but should be applied clinically with caution.

STATUS

Medical Student

AUTHORS

David Samuel

Andrew Nguyen

Perry Payne

RESEARCH MENTOR/ DEPARTMENT CHAIR

Perry Payne

SCHOOL OF MEDICINE AND HEALTH SCIENCES

A Lack of Motivation and Guidance During High School Years Contributes to the High Teen Pregnancy Rates in Cordoba, Argentina

The purpose of this study was to investigate the factors contributing the high teen pregnancy rates in Cordoba, Argentina. According to UNICEF, Latin America has the highest percentage of live births to adolescent mothers (18%) compared to the world's average (13%) and the rate has continued to increase in Argentina in recent years (11.9% to 12.4%) (UNICEF, 2007) . A unique element to Argentina is that all education, including graduate school, and health care is free. Thus, the study aimed to address the following question: if education and health care is free, what resources did these women lack that contributed to such high teen pregnancy rates? Ninety-eight women older than 18 years old at Hospital Maternidad in Cordoba, Argentina were interviewed using a 7-minute questionnaire to analyze the high teen pregnancy rates. While a majority of the women came from low socioeconomics, did not complete high school, and had difficulty getting to the hospital with transportation, another contributing component involved the lack of guidance in school during their teenage years. Meaning, that when asked "What are your dreams?" and "What are your hobbies?" a majority of the women could not provide an answer, said "I don't have one", or said "To clean the house." After further discussion, they shared that no one asked them what their dreams were when they were in high school and that they were never pushed to think of future plans and ambitions. Another finding was that many women received sexual health education during high school, such as birth control, sexually transmitted infections, and safe sex, further suggesting that simply discussing sexual health will not lower teen pregnancy rates, but rather a multidisciplinary approach must be implemented to help guide women in planning their futures. As health care providers, this study highlights the importance of not only educating young women about sexual health, but also broadening one's approach during health visits to directly address the patient's future career goals and plans so that they may be inspired, motivated, and supported to pursue a higher education.

REFERENCES

UNICEF. "Teenage motherhood in Latin America and the Caribbean: trends, problems, and challenges." no. 4. January 2007.

STATUS

Medical Student

AUTHOR

Yasamin Soltanianzadeh

RESEARCH MENTOR/ DEPARTMENT CHAIR

Huda Ayas

HEALTH POLICY

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Youth has its disadvantages—Younger consumers are less likely to understand their health insurance

INTRODUCTION

Approximately 23 million people acquired health insurance as a result of Affordable Care Act. While access to insurance may have increased, applicants have been faced with a wide variety of choices of insurance products, in some cases more than they would have had with employer-based plans. Consumers faced with acronyms such as HMO, PPO, HDHPs, and POS are asked to choose coverage while they may have little understanding of what these terms mean and how they differ. Young people typically have had little exposure to insurance plans in the past and may be at a greater disadvantage in choosing a policy. This study examined understanding of one's health insurance plan as a function of age.

METHODS

Individuals attending a Washington, DC health exposition sponsored by the Rodham Institute completed an anonymous survey in August 2015. The exposition was hosted in an urban, medically underserved setting where the population has historically been predominantly African American; currently 92% of residents identify as such. The survey included questions on demographic information, insurance status, as well as questions related to obtaining insurance. Responses were excluded if questions regarding age or insurance knowledge were unanswered. The university institutional review board approved the study. Statistical analysis was performed using Fisher's exact test, with significance set at $p<0.05$.

RESULTS

There were 96 responses analyzed. Twenty eight (29.2%) individuals were over the age of 50 and 68 (70.8%) were younger. Twenty (29.4%) of the younger respondents reported understanding how their insurance worked. In the older age group, 26 (92.8%) understood their health insurance. Those over the age of 50 were more likely to have a firm understanding of their medical insurance plan compared to those under the age of 50 ($p=0.0001$). Among 28 college educated respondents, 23 (82.1%) understood their insurance. Fifty one (76.1%) of 67 respondents with less education had such an understanding. There was no difference with respect to education level ($p=0.5973$).

DISCUSSION

Our study revealed that younger customers are three times less likely to endorse an understanding of how their health insurance works. While the Affordable Care Act has expanded access to health insurance, many face a wider variety of options than they may have had prior to the passage of reforms. Because younger people have had less experience (or no experience) with health insurance in the past, they would benefit from educational resources to inform their choices. A disadvantageous selection of plan, deductible, and coinsurance may make financial concerns a greater component of medical decision making.

STATUS

Medical Student

AUTHORS

Kamal Baig

Gregory Piech

Matthew Caldis

Shreya Chablaney

Timothy Dougherty

Marie L. Borum

RESEARCH MENTOR/ DEPARTMENT CHAIR

Marie L. Borum

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Improved Access and Coverage Under The ACA: Are Immigrants at the Table?

RESEARCH OBJECTIVE

Noncitizen immigrants historically had low rates of insurance coverage and access to health care. Prior research has shown substantial improvements in coverage and access among adults ages 18 to 64 subsequent to Medicaid expansion and the establishment of Marketplace coverage in 2014 under the Affordable Care Act. Racial and ethnic minority populations and low-income families have seen substantial gains. However, many immigrants face legal, language, and financial barriers to enrolling in insurance and accessing care. Our study examines differences in improvements in access and coverage between immigrants and non-immigrants.

METHODS

Using National Health Interview Survey files, we compared improvements in coverage and access from 2013 to 2014 among a nationally representative sample of adults ages 18 to 64. We focus on uninsurance, usual source of care and having at least one visit to a doctor or other healthcare professional. We examined changes related to immigration status, adjusting for race/ethnicity and low-income (defined as <200%FPL) versus relatively higher-income (≥200% FPL) level.

PRINCIPAL FINDINGS

Uninsurance rates among noncitizens fell from 2013 to 2014 (51% to 44%), but remained dramatically higher than uninsurance among U.S. born and naturalized citizens. Among racial and ethnic groups, uninsurance rates were highest among Hispanics in both years (58% in 2014). In absolute terms, uninsurance rates fell more for noncitizens from 2013 to 2014 (7.2 percentage points) than U.S. born citizens (3.8%). But this represents a smaller relative improvement: the share of noncitizens who were uninsured fell less (14%) from 2013 to 2014 than the share of U.S. citizens (26%).

Among U.S. born and naturalized citizens, uninsurance rates fell primarily among those with incomes below 200% FPL. Among noncitizens, however, reductions in uninsurance were higher for those with incomes above 200% FPL (8.7%) compared with those below 200% FPL (6.0%). For noncitizen Hispanics, improvements in uninsurance were much higher for those above 200% FPL (13%) than below 200% FPL (6.0%), while changes were similar for noncitizen non-Hispanic whites, Asians and blacks with incomes above and below 200% FPL.

There were significant increases for noncitizens from 2013 to 2014 in having a usual source of care (5.1%) and having at least one visit to a doctor (5.5%). U.S. born citizens experienced a smaller improvement in usual source of care (1.5%) and the change in any visit to a doctor was not significant. Visits to doctors increased among naturalized citizens (3.4%), although the increase in having a usual source of care was not significant.

CONCLUSIONS

Because noncitizen immigrants had high rates of uninsurance before ACA expansions, they had greater absolute gains in insurance coverage and access to care than citizens. But the continuing barriers faced by immigrants, particularly low-income immigrants, meant that the relative gains in coverage were smaller than for citizens. Relative improvements in access were still strong for noncitizens, probably reflecting high unmet needs prior to the ACA. Policymakers should consider policies to relax barriers for noncitizen immigrants, such as the 5 year Medicaid waiting period or improving language services for those with limited English.

STATUS

Graduate Student

AUTHORS

Erin Brantley

Leighton Ku

RESEARCH MENTOR/ DEPARTMENT CHAIR

Leighton Ku

HEALTH POLICY

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Public insurance is not a barrier to colorectal cancer screening

INTRODUCTION

The Affordable Care Act (ACA) provided states and Washington D.C. the option to expand Medicaid coverage to beneficiaries with incomes up to 138% of the Federal Poverty Line. Expanded coverage went into effect in Washington D.C. on January 1, 2014. Insurance coverage, however, does not necessarily equate to access. This holds especially true for low-income, public insurance such as Medicaid as fewer providers accept this insurance. Colorectal cancer (CRC) screening is important for detecting precancerous colonic lesions and preventing progression to future disease. This study compares the rate of CRC screening in appropriately aged individuals on public insurance and in their privately insured counterparts.

METHODS

Individuals attending an August 2015 health exposition sponsored by the Rodham Institute completed an anonymous health survey. The exposition was hosted at a community center in an urban location with a historically African American predominant population. The survey included questions on demographic information, insurance information, access to primary care, and CRC screening. Data from the survey was analyzed in a Microsoft Excel database. Insurance types were classified as public insurance (Medicaid and other District government sponsored programs) or private insurance (Blue Cross, Aetna, etc.). Surveys were excluded if specific questions of interest were left unanswered. Statistical analysis was performed using Fisher's exact test, with significance set at $P<0.05$. The study was approved by the university's institutional review board.

RESULTS

There were 102 participants with an average age of 42.4. Ninety-three (91.2%) identified as African American. Fifty-six (54.9%) respondents had public insurance and 28 (27.4%) had private insurance. Twenty-nine (51.8%) of those with public insurance enrolled within the past 18 months, 25 (44.6%) enrolled earlier, and 2 participants did not respond. Given the predominantly African American population and the recent CRC screening recommendations advising this population to begin screening at age 45, a subgroup analysis was conducted in survey participants 45 years and older. Of the thirty-nine participants 45 years-old and above, 22 (56.4%) had public insurance and 17 (43.6%) had private insurance. Thirteen (59%) publically insured responders received CRC screening while 12 (70.5%) responders on private insurance had received CRC screening ($p=0.518$).

CONCLUSIONS

This study showed that public insurance was not associated with significantly decreased rates of CRC screening when compared with respondents with private insurance. In this study at a Washington, D.C. health expo, a majority of respondents with public insurance had acquired it in the previous 18 months, correlating temporally with ACA Medicaid expansion. While there has been concern that, despite having insurance, public insureds may have difficulty accessing health care, this did not appear to be a barrier to CRC screening in this population. Limitations of our study include a small sample size and a predominantly African American population. Additionally, the District of Columbia had, prior to Medicaid expansion, a greater-than-typical safety net insurance program, so referral patterns and provider acceptance may already have been established.

STATUS

Medical Student

AUTHORS

Matthew Caldis

Kamal Baig

Shreya Chablaney

Dan Gaballa

Gregory Piech

Timothy Dougherty

Marie L. Borum

RESEARCH MENTOR/ DEPARTMENT CHAIR

Marie L. Borum

HEALTH POLICY

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Virtual Community Can Improve Staffing, Retention, and Job Satisfaction

The approximate cost for training one new nurse is about $65,000. The price it takes to replace a nurse is 1.5 times the rate of the original price. The average duration to train one new staff nurse ranges about four months to a year. In addition, the turnover ratio among nurses across the country is about sixty percent. Ironically, the average duration of new staff nurses within that sixty percent is about six months.

With these facts, I believe that there is a retention issue among nurses within the nursing field. The work I will be presenting in my research poster will discuss how the virtual community can improve staffing, retention, and job satisfaction among nurses across the country. The educational program iCohere can be used to help improve these categories if used correctly and used consistently. Within the research poster, I will be discussing how the program iCohere can be used through my own personal use of the program and through real time surveys that were conducted within the Clinical Center at the National Institutes of Health.

STATUS

Graduate Student

AUTHOR

Brian Danner

RESEARCH MENTOR/ DEPARTMENT CHAIR

Paul Wong

HEALTH POLICY

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

A Systematic Review of Coal Fired Power Plant Proximity and Local Socioeconomic Status Trends and Outcomes

Among the significant sources of energy, coal based energy bears the largest share (42%) of the electricity produced in the United States. Already existing coal fired power plants are the largest emitter of carbon dioxide emissions in the United States. Among the cumulative emissions contributed by the industrial sector, significant portions are from coal fired power plants. Coal-fired power plants emit 66% of sulfur oxides, 40% of carbon dioxide, 33% of mercury and 22% of nitrogen oxides in the U.S. and are linked as risk factors to respiratory diseases, cardiovascular diseases and other ailments shown to impact environmental and human health. Along with the pervasive and injurious health effects that come with the presence of hazardous waste sites (i.e, toxic waste sites, landfills, congested highways), there are broader socioeconomic trends and outcomes related to their siting, especially affecting those who live near these facilities. This literature review research study surveyed the relationship between the location of coal fired power plants and the socioeconomic conditions and trends of proximate communities and the cumulative evidence suggested there to be direct link. The four studies used recent U.S. Census data to examine housing values and rents in relation to the location of coal fired power plants during the 1990s and found that there were statistically significant decreases in mean household income, decreases in housing values and proportion declines in educational attainment (declines in high school and college completion rates), and increases in the populations of black and hispanic residents.

STATUS

Graduate Student

AUTHOR

Oshane Mcrae

RESEARCH MENTOR/ DEPARTMENT CHAIR

Peter LaPuma

HEALTH POLICY

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Influence of Pharmaceutical Marketing on Prescribing for Medicare patients in the District of Columbia

IMPORTANCE

Pharmaceutical marketing efforts may complicate the decision-making process for prescribers by influencing them to prefer newer, more expensive drugs that may have limited information on efficacy and adverse effects.

OBJECTIVE

Analyze the potential impact of pharmaceutical marketing on prescribing for Medicare patients in DC.

DESIGN

Analysis of correlation between pharmaceutical marketing gifts and Medicare Part D claims data in DC in 2013.

SETTING

Data accessed from: DC AccessRx database (gifts annually reported to the DC Department of Health, January-July); Open Payments database (gifts reported to Centers for Medicare and Medicaid Services (CMS), August-December); and CMS database of Medicare Part D claims (January-December).

PARTICIPANTS

Inclusion criteria were licensed healthcare providers in DC, who are Medicare Part D prescribers listed in CMS. Healthcare providers in specialties with five or less subjects were excluded. Of 2873 subjects, 1750 (60.9%) did not receive pharmaceutical marketing gifts reported in AccessRx or Open Payments (control), and 1123 (39.1%) did receive gifts reported in AccessRx or Open Payments (exposed). Main outcome(s) and measure(s): Two sample t-tests were run on average cost per Medicare Part D claim, number of total claims, number of claims per beneficiary, and frequency of branded claims for the control and exposed groups.

RESULTS

Compared to non-gift recipients, gift recipients spent an average of $56 more per claim (P=1.8E-9). Gift recipients also made an average of 503 more total claims (P=1.4E-17), 2.2 more claims per beneficiary (P=4.2E-12), and 8.4% more branded claims (P=1.4E-27).

CONCLUSION AND RELEVANCE

Results suggest that pharmaceutical marketing efforts in DC in 2013 influenced Medicare Part D prescribing by increasing average cost per claim, number of total claims, number of claims per beneficiary, and frequency of branded claims. Although this study does not establish causation, it is the first to analyze these datasets and provide unique insight into the potential impact of pharmaceutical marketing efforts on prescribing for Medicare patients in DC. We recommend: further research on the influence of pharmaceutical marketing on prescribing; continuous and robust pharmaceutical marketing requirements; and expanded public access to improve transparency of conflicts of interest in healthcare.

STATUS

Medical Student

AUTHORS

Janani Raveendran

J.P. Podrasky

M.A. McMonagle

A. Fugh-Berman

A. Hogenmiller

S.F. Wood

RESEARCH MENTOR/ DEPARTMENT CHAIR

Susan F. Wood

HEALTH POLICY

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Are Children on Medicaid Disproportionately Prescribed Psychotropic Medication? The Role of Clinical and Access to Care Factors

Policymakers have expressed ongoing interest in reducing inappropriate psychotropic medication use among children, given evidence of high rates of psychotropic medication prescription for children on Medicaid relative to children with private insurance. We analyzed 2011-2013 NHIS data to examine the effect of insurance status on psychotropic medication prescription across primary and specialty care providers. We found that children with Medicaid and the Children's Health Insurance Program coverage are more than twice as likely to be prescribed psychotropic medication as children with private health coverage. However, that difference became statistically insignificant in nearly all circumstances when we controlled for demographic, clinical, and access to care characteristics. We suggest these findings highlight the nuanced nature of this issue, and note the need for policymakers to consider these complex factors when considering options to reduce potentially inappropriate psychotropic medication prescriptions among vulnerable children.

STATUS

Graduate Student

AUTHORS

Karen Spencer

Zachary Laris

Brian Bruen

RESEARCH MENTOR/ DEPARTMENT CHAIR

Brian Bruen

HEALTH POLICY

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Income-Related Inequalities in Utilization of Health Services Among Private Health Insurance Beneficiaries in Brazil

Brazil's 1988 health reform created the Unified Health System (SUS). SUS is a universal health system that emulates British National Health Service, featuring an open-ended benefit package and a major goal of health equity. An unforeseen consequence of the reform was that former beneficiaries of the social health insurance sought to sustain their privileged access to health services through private health insurance. Despite achievements in expanding healthcare access and improved health outcomes, recurring opinion polls suggest that Brazilians are skeptical about SUS' capacity to delivery timely and quality health services, making private insurance a priority to most households. The literature that focuses on health equity in Brazil strongly suggests that inequalities in utilization of health services exist between private insured and uninsured (SUS-dependent) individuals. No research exists, however, on whether inequalities in utilization of health services remain among privately insured individuals. In this study, therefore, we ask whether private coverage actually improves healthcare access, regardless of beneficiaries' income?

The study uses Andersen's behavioral model as a theoretical framework to analyze data from two rounds (1998 and 2008) of a national household survey. We assess fourteen dependent measures that reflect utilization across income quintiles. We then calculate concentration indexes as summary measures of inequality. Concentration curves compare the evolution of inequality over time. Decomposition analysis identifies the most relevant contributors to inequality. Physician services are analyzed as the probability of having a physician visit and the number of physician visits. Hospital services are analyzed as the probability of having a hospitalization, the number of hospital days during the last hospitalization, and the number of hospital admissions. The former two variables are broken down according to their financing source, either public (SUS) or private insurance.

We find very little inequality in levels of physician services utilization, although a statistically significant positive gradient persists in both survey rounds. SUS financed hospitalizations are rare among privately insured individual, but strongly concentrated among the poor. Most hospitalizations among the study group are funded thought private insurance, and they are highly concentrated among the rich. Premium rates and income are the most relevant contributors to inequality.

We find that private health insurance increases utilization levels of physician services, providing comparable access across income groups. However, we also find that private coverage does not guarantee that poor beneficiaries will have access to hospital services. Private insurance with low premiums that serve the poor should focus solely on ambulatory care.

STATUS

Graduate Student

AUTHOR

Heitor Werneck

RESEARCH MENTOR/ DEPARTMENT CHAIR

Patricia Pittman

SCHOOL OF MEDICINE AND HEALTH SCIENCES

National trends in Incidence and Outcomes of Acute and Chronic Pancreatitis

BACKGROUND

Acute and chronic pancreatitis have been associated with significant burden of disease. Recent studies have shown a rise in acute pancreatitis (AP) incidence in western countries. We report population based trends over a 20-year period in the incidence, survival, and costs in acute pancreatitis and chronic pancreatitis (CP) in the United States.

METHODS

We used data from the National Inpatient Sample and the Nationwide Inpatient Sample (NIS), Healthcare Cost and Utilization Project (HCUP), Agency for Healthcare Research and Quality to identify patient discharges between 1993 and 2013. Appropriate International Classification of Diseases, 9th Revision (ICD-9) diagnosis codes were used to isolate AP and CP cases.

RESULTS

In 1993, the number of acute pancreatitis admissions registered was 144,350. In 2013, this number rose to 274,775 representing an increase of 90.3%. Over this 20-year time period, CP admissions declined from 19,275 in 1993 to 13,385 in 2013 (30.6% decrease). Within the same time period, median charges per person increased for AP from $7,213 to $21,540 (198.6% increase). Similarly, median charges per person for CP increased from $6,654 to $21,083. In-patient mortality decreased from 2.34% in 1993 to .76% in 2013 for AP and from .96% in 1993 to .59% in 2010 for CP.

CONCLUSIONS

Over the past two decades, there have been considerable increases in AP admissions in the US and a simultaneous slight decrease in CP admissions. This trend is likely to continue in the near future and suggest a need for a better understanding of pancreatitis pathogenesis and risk factors.

STATUS

Medical Student

AUTHORS

Maryam Boumezrag

Lorna Richards

Andrew C. Meltzer

RESEARCH MENTOR/ DEPARTMENT CHAIR

Andrew C. Meltzer

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Impact of Nondiabetic End Stage Renal Disease on Brain Parenchyma

PURPOSE

The effects of diabetes mellitus (DM) on the cerebrovascular physiology have been well established. DM accelerates atherosclerotic disease, which in turn results in various insults to the brain. While many patients with DM suffer from chronic renal disease (CRD), end stage renal disease (ESRD) is not always caused by DM. The effect of ESRD in nonDM patients on the brain has not been elucidated. We tested the hypothesis that the brains of patients with nonDM-ESRD are affected differently as compared to those with DM-ESRD.

METHOD AND MATERIALS

We screened about 1500 patients with CRD. 53 patients with ESRD had a brain MRI at our center. Age, gender, blood pressure, HbA1c and BMI were recorded. Also brain MRI of these patients were reviewed for cerebral volume loss graded subjectively as mild, moderate and severe; 3rd ventricle diameter; white matter changes based on Fazekas scale and the presence or absence of lacunar and territorial infarcts.

RESULTS

29 patients have DM and 24 do not. There is no significant difference in the mean age, gender, mean blood pressures in the two groups. The mean BMI for DM and nonDM groups were 31 and 26 respectively (p=0.07). 83% of the DM patients had periventricular white matter lesions with Fazekas grade 2 or above compared to 50% in the nonDM group(p=0.03). 62% patients in the DM group had moderate cerebral volume loss with mean 3rd ventricle size of 7mm versus 50% in the nonDM group with mean 3rd ventricle size of 6mm (p=0.36). 62% of patients had lacunar infarcts and 34% had territorial infarcts in the DM group versus 46% with lacunar infarcts and 25% with territorial infarcts in the nonDM group (p>0.2).

CONCLUSION

The degree of periventricular white matter (PVWM) changes was statistically more severe in patients with DM. Although the lacunar and territorial infarcts and the mean cerebral volume loss were lower in the nonDM group, this difference was not statistically significant. This study supports the prior observations that PVWM changes are likely related to chronic microvascular ischemia. This type of pathology appears more prevalent in patients with ESRD secondary to DM than those with nonDM ESRD.

CLINICAL RELEVANCE/APPLICATION

This study suggests that the mechanism by which the brain parenchyma is affected in nonDM-ESRD group is different than those with DM. Studies are being undertaken to further characterize the causes of brain injury in this patient population in the hopes of finding ways to slow the disease progression.

STATUS

Postdoctoral Student

AUTHORS

Shivang Desai

D. Brown

S. Patel

D. Davidson

M.R. Taheri

RESEARCH MENTOR/ DEPARTMENT CHAIR

M. Reza Taheri

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Utilizing the NO-cMP Pathway

The nitric oxide-3′, 5′-cyclic guanosine monophosphate signaling pathway is a well-known signal transduction pathway which elicits several physiological and pathological processes. In this pathway, NO binds to the ferrous heme of histidine-105 on the prosthetic heme of the β1 subunit of soluble guanylyl cyclase, resulting in an increase of soluble guanylyl cyclase and cGMP synthesis. In cancers, however, a mechanism affecting the transcription and translation of soluble guanylyl cyclase inhibits the anti-oncogenic effects of the pathway.

I hypothesize that pharmacologically manipulating cGMP in lung carcinoma via timosaponin A-III and/or genetically restoring sGC expression will inhibit the proliferation of lung carcinoma cells.

As experimental approach, the H460 human large lung cell carcinoma cell line was cultured in 2D culture. MTT assay, PCR, qPCR, and time course were utilized to assess cell proliferation, to detect and quantify of genes and proteins expression, and to quantify the concentration of α1-sGC and β1-sGC, respectively.

Through my study, I found that pharmacologically manipulating cGMP in lung carcinoma via timosaponin A-III increased the expression of α1-sGC and β1-sGC and inhibited the proliferation of lung carcinoma cells. Moreover, timosaponin A-III affects gene expression in a concentration-dependent manner. The NO-cGMP pathway may facilitate development of new protocols involving activation of sGC to treat human malignant tumors by influencing NO and cGMP signaling.

STATUS

Lab Intern

AUTHOR

Armond Dorsey

RESEARCH MENTOR/ DEPARTMENT CHAIR

Ka Bian

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Outcome measurements in chronic neuropathic pain patients receiving multiple rounds of ketamine infusions

BACKGROUND

Chronic neuropathic pain is known to impact many aspects of quality of life (QOL). Ketamine, a phenycyclidine derivative with both anesthetic and analgesic properties, has been previously shown to provide relief in patients receiving outpatient infusions of the drug.

OBJECTIVE

To assess the effect of outpatient ketamine infusions on QOL outcome measurements in patients with chronic neuropathic pain who have received several rounds of ketamine infusions.

METHODS

Patients with chronic neuropathic pain were asked to complete the brief pain inventory (BPI) concerning the impact of their chronic pain on aspects of their QOL (overall daily pain score, general activity, walking, work, relationship with others, sleep, and enjoyment of life) before receiving ketamine infusion and two to four weeks after the ketamine infusions at the follow up clinic visit. The patients ranked the impact of pain on QOL, from a scale of zero (no impact) to ten (severely impacts). Overall change in QOL both prior to treatment with ketamine infusion and after administration were evaluated. Four predictors (age, sex, race, and BMI) were also used in order to evaluate any change on QOL due to demographics. Only patients who received more than one infusion were included in the study.

RESULTS

There were 34 patients in the sample, with mean age 43.0 (SD 12.8), mean BMI 26.0 (SD 8.2), 68% female, 74% white, 18% black, and 9% other or unknown race. 11 patients had 2 episodes of ketamine infusion, 6 had 3 episodes, and the remaining 17 patients had between 4 and 19 episodes (median number of episodes = 3.5). The model predicting mean BPI score pre-infusion (using each subject's first episode of ketamine infusion only), was significant (p=.036), indicating a significant effect with moderate effect size. The only predictor with a significant independent association with mean BPI pre-infusion was pain (p=.0042). The model predicting post-infusion mean BPI score was not significant (p=.59). In the model predicting change from pre to post-infusion in mean BPI score at episode 1, the only significant predictor was BMI (p=.041). In the mixed model predicting pre-infusion mean BPI across repeated episodes of ketamine infusion, there was a significant episode effect (p=.029). After adjusting for covariates, the mean pre-infusion BPI scores at episodes 2 through 15 are not significantly different from episode 1, but starting with episode 16, all later episodes have significantly lower pre-infusion BPI scores than episode 1. In the model predicting the pattern of pre-infusion BPI scores across episodes, there was a significant interaction by age (p=.016), with older patients have reduced pre-infusion BPI scores at episodes 5 & 12, compared with younger patients.

CONCLUSION

Expanding upon our previous study, we examined QOL outcomes for returning ketamine infusion patients with chronic neuropathic pain based on their BPI scores. Ketamine infusions were found to continuously improve patient's pain scores over multiple rounds of infusion. Ketamine infusions were also found to have greater affect in older patients as well as patients with a greater BMI. However, other predictors or QOL were not found to be significantly different.

STATUS

Medical Student

AUTHORS

Karthik Dwarki

Brendan Keen

May Chin

Richard Amdur

RESEARCH MENTOR/ DEPARTMENT CHAIR

May Chin

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Identifying factors associated with unnecessary emergency department transfers in the California trauma system

"Secondary overtriage" (SO) is a term currently used in the trauma literature to describe when a patient is discharged home from the receiving hospital shortly after being transferred from another hospital. Within the population of adult trauma patients, the rate of secondary overtriage ranges from 4.21-24% of patients who are transferred (1-5). In addition to the costs, patients and their families are left with the burden of returning to their communities post-discharge (6). SO also diverts resources to patients with minor injuries and places unnecessary burdens on tertiary care centers (5, 7), and therefore represents a potentially unexplored area of cost savings to an overburdened healthcare system. We propose a retrospective analysis to study the issue of SO using patient and hospital-level databases from the California Office of Statewide Health Planning and Development (OSHPD) and the US Department of Agriculture continuum codes. Specifically, we aim to assess the rate of SO in California; characterize the demographic, clinical, and structural characteristics associated with SO; and determine the diagnoses for which transfers could be potentially avoided. We hope this research will help providers and policymakers develop targeted interventions, such as the establishment of telehealth partnerships and transfer protocols, which will ultimately improve the quality of patient care and reduce unnecessary healthcare spending.

REFERENCES

1 Con J, Long D, Sasala E, Khan U, Knight J, Schaefer G, et al. Secondary overtriage in a statewide rural trauma system. J Surg Res. 2015.

2 Sorensen MJ, von Recklinghausen FM, Fulton G, Burchard KW. Secondary overtriage: the burden of unnecessary interfacility transfers in a rural trauma system. JAMA Surg. 2013;148(8):763-8.

3 Tang A, Hashmi A, Pandit V, Joseph B, Kulvatunyou N, Vercruysse G, et al. A critical analysis of secondary overtriage to a Level I trauma center. J Trauma Acute Care Surg. 2014;77(6):969-73.

4 Osen HB, Bass RR, Abdullah F, Chang DC. Rapid discharge after transfer: risk factors, incidence, and implications for trauma systems. J Trauma. 2010;69(3):602-6.

5 Ciesla DJ, Sava JA, Street JH, 3rd, Jordan MH. Secondary overtriage: a consequence of an immature trauma system. J Am Coll Surg. 2008;206(1):131-7.

6 Kindermann DR, Mutter RL, Houchens RL, Barrett ML, Pines JM. Emergency department transfers and transfer relationships in United States hospitals. Acad Emerg Med. 2015;22(2):157-65.

7 Xiang H, Wheeler KK, Groner JI, Shi J, Haley KJ. Undertriage of major trauma patients in the US emergency departments. Am J Emerg Med. 2014;32(9):997-1004.

STATUS

Medical Student

AUTHORS

Renee Hsia

Jennifer Liao

RESEARCH MENTOR/ DEPARTMENT CHAIR

Renee Hsia

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Bridge to Care: How a Medical School can Partner with a Public Health Department

On the border of DC, Prince George's County, Maryland has a substantially low per capita number of primary care physicians (83 per 100,000 residents), lacking a primary care safety net for residents[1]. Approximately 80,000 residents are uninsured, with high rates of chronic disease (asthma, obesity, HIV/AIDS) and low rates of preventative care[1]. To address these disparities, The GW University School of Medicine and Health Sciences Healing Clinic, a student-run free clinic, created a unique partnership with the Prince George's County Health Department to form the "Bridge to Care" Clinic. The partnership has two objectives: 1. to link those with insurance to a primary care physician within the county and 2. to be the only primary care access point for the uninsured within the Health Department. Student directed projects were undertaken to address each of the following obstacles: 1. limited no-cost or affordable care delivery options within the health department, and the county for referrals, 2. recognition of the spectrum of volunteer clinical experience and clinic capacity, 3. complex patient population with multiple chronic comorbidities, limited resources, and frequent language barriers. First, an assessment of the community health system sought to identify community partners where patients could be referred at no cost for services unattainable through the health department, such as: specialty care, legal services, or HIV support services. Second, a volunteer resource manual was developed to assist students through language barriers, simple protocols in clinic, history and physical exam, differential diagnoses, EMR documentation, and screening tools at the point of care. Lastly, a patient navigator program was created to address patients' complex needs through adequate education, referrals, and follow up. Future work of the GW Healing Clinic must evaluate the impact of the student-directed initiatives on the partnership and primary care delivery to those underserved in the DC metro area.

REFERENCES

1 Lurie N, Harris K, Shih R, et al. *Assessing Health and Health Care in Prince George's County.* Arlington, VA; 2009. Available at: http://www.rand.org/pubs/technical_reports/TR655.html.

STATUS

Medical Student

AUTHORS

Bridget Huysman

Madeline Taskier

Kent Aje

Priyanka Joshi

Kate Denny

David Popiel

Lisa Alexander

RESEARCH MENTOR/ DEPARTMENT CHAIR

David Popiel

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Diminished Smell in a Teenage Girl

Disorders of smell are rare, particularly in pediatric patients. The most common cause of transient anosmia is nasal obstruction associated with upper respiratory infections. Moreover, nasal polyps, nasal and nasopharyngeal tumors, and enlarged adenoids can cause obstruction of the nasal air circulation and thereby diminish the sense of smell. Anosmia can often be difficult to confirm, particularly if a pediatric patient has true anosmia. Many children with olfactory dysfunction may not recognize their deficits, or often pretend to smell to please their parents, or prevaricate to attract attention. Moreover, long, complex olfactory tests are impractical owing to the short attention span of some young children, and are further limited because odor concepts require experience with odors that some children have yet to come across.

STATUS

Medical Student

AUTHOR

Aria Jamshidi

RESEARCH MENTOR/ DEPARTMENT CHAIR

Brian Reilly

SCHOOL OF MEDICINE AND HEALTH SCIENCES

G-Protein Coupled Receptor GPR37L1 Regulates Sodium Reabsorption in Renal Proximal Tubule Cells

GPR37L1 is expressed mainly in brain glial cells and muscle-myenteric nerve layers in the gastrointestinal tract. GPR37L1 transgenic mice have decreased systolic blood pressure (SBP), whereas GPR37L1 KO mice have increased SBP. The kidney is critical in the regulation of BP but there are no studies reporting the kidney expression and renal function of GPR37L1. Immunostaining and immunoblotting showed that GPR37L1 is expressed in the apical membrane of proximal tubules of the mouse kidney; RT-PCR of renal proximal tubule and collecting duct cells obtained by laser capture micro-dissection of mouse kidney sections, confirmed these findings. In addition, chronic high salt diet increased the renal expression of prosaposin, a precursor for saposin C, a natural ligand for GPR37L1. Infusion of prosaptide, a synthetic ligand for GPR37L1, decreased SBP in mice by 10 ± 2.8 mm Hg. To determine the roles of GPR37L1 in renal sodium transport, we over-expressed the protein in human renal proximal tubule (RPT) cells (n=3). Intracellular sodium was increased in GPR37L1-transfected RPT cells (3.2 ± 0.6 fold , $P<0.001$) compared with mock-transfected cells. Immunoblot analyses showed increased phosphorylation of Erk1/2 (1.52 ± 0.06 fold, $P<0.05$), and ribosomal S6 protein (1.39 ± 0.08 fold, $P<0.01$) in RPT cells over-expressing GPR37L1. Na^+,K^+-ATPase expression was decreased by 29% ± 3.5 ($P<0.05$) in GPR37L1-transfected RPT cells. Taken together, these results show that GPR37L1 is expressed in RPT cells and signal via the Erk1/2 pathway. GPR37L1 increases intracellular sodium in RPT cells by decreasing the exit of sodium due to a decrease in Na^+,K^+-ATPase expression and activity at the basolateral membrane. These results indicate that GPR37L1 may play a role in sodium transport in RPT cells and may be novel targets to designing drugs to treat patients with hypertension.

STATUS

Faculty

AUTHORS

Prasad Konkalmatt

Xiaoxu Zheng

Pedro A. Jose

Ines Armando

RESEARCH MENTOR/ DEPARTMENT CHAIR

Alan G. Wasserman

SCHOOL OF MEDICINE AND HEALTH SCIENCES

66 year old woman with hemoptysis: A case report/review of literature discussing scleroderma, vasculitis, & malignancy

A 66 year-old Hispanic Caucasian lady with a 14 year history of diffuse scleroderma and bilateral stage II-B invasive breast cancer presented for evaluation of a vasculitic rash and hemoptysis. On examination vital signs were stable and cardiovascular exam was normal. Pulmonary exam revealed coarse crackles to the mid-lung fields bilaterally with bronchial breath sounds at the left apex. Abdominal exam was benign with no hepatosplenomegaly. Musculoskeletal exam revealed bilateral sclerodactyly with modified Rodnan Skin Score of 14 and contractures of the digits. There was a large punched-out ulceration over the right third metacarpophalangeal joint measuring 1x0.7x0.2 cm with desiccated tendon in the base. Multiple similar ulcers were noted over other joints, and on the legs she had a petechial rash consistent with leukocytoclastic vasculitis.

CT thorax revealed multiple lung nodules and masses, bilateral lower lobe honeycombing, bibasilar reticular changes with traction bronchiectasis, ground glass opacities in bilateral upper lobes with multiple calcified granulomata with cavitation.

Laboratory evaluation revealed normocytic anemia, ESR 23 mm/hr, CRP 14 mg/dL, c-ANCA titer of 1:640, with proteinase-3 antibody of 39.9 U/mL. Anti-nuclear antibody was positive at a titer of 1:160 homogenous pattern and additional serologic testing revealed positive RNA polymerase III antibody at 33.4 units.

Differential diagnosis included infections causing cavitating pneumonias, granulomatosis with polyangiitis and other ANCA-associated vasculitides, and primary or secondary malignant lung lesions.

The patient underwent left thoracoscopic wedge resection of the left lower lobe. Gram stain, acid fast and fungal stains with cultures were all negative. Histopathology demonstrated background fibrosis, cyst formation, and bronchial metaplasia consistent with scleroderma-associated lung disease. Additionally, areas of necrotizing granulomatous inflammation and vasculitis were seen consistent with focal vasculitis. Subjacent to the pleura atypical epithelial proliferation was seen and these cells stained diffusely positive for MAK-6, GATA-3, estrogen receptor and mammoglobulin. Taken together the findings were consistent with RNAP III-positive diffuse scleroderma with associated breast cancer, presenting with lung metastases and ANCA-associated vasculitis consistent with limited GPA.

The patient was treated with pulse-dose glucocorticoids for 3 days followed by prednisone 60 mg daily along with Rituximab for her ANCA-associated vasculitis. The breast cancer was treated with anastrazole 1 mg daily. She is currently doing well. This case emphasizes the now well-recognized co-temporal relationship between scleroderma and malignancy, and the emerging pathophysiologic understanding of the relationship between autoantigen mutations in malignant tissues and autoimmune triggering.

STATUS

Rheumatology Fellow

AUTHORS

Jonathan Miller

Falin B. Patel

Kara Couch

Sean McNish

Robert Seigel

Samantha Easley

Victoria Shanmugam

RESEARCH MENTOR/ DEPARTMENT CHAIR

Victoria Shanmugam

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Does Pain catastrophizing predict functioning?

INTRODUCTION

Pain catastrophizing is an exaggerated negative response to an actual or anticipated painful experience. Sullivan et al. created the pain catastrophizing scale (PCS) to help better quantify the level a patient catastrophizes. Recent studies focus on pain catastrophizing as a predictor of pain severity, distress, and quality of life. Evaluation of pain catastrophizing and its association with baseline characteristics could help identify patients who are at high-risk of catastrophizing. Furthermore, determining if pain catastrophizing is a predictor of daily functioning may help target therapy for high-risk patients.

MATERIALS AND METHODS

With IRB approval, the Pain Catastrophizing Scale (PCS) and an additional questionnaire were randomly administered to 65 chronic pain patients at GW pain clinic between January 2015 and June 2015. Data included age, gender, duration, cause of pain, and opioid use. The additional questionnaire assessed the impact of pain on the following aspects of daily functioning: activity, mood, walking, relations, sleep, enjoyment of life, and work. Each was scored on a 1 to 10 scale, where 1 indicated least amount of interference to functioning and 10 indicated greatest amount of interference. For each subject these scores were averaged to determine an overall functioning score (OF). Pearson's Correlation Coefficient (r) was used to assess relationship between PCS score and OF.

RESULTS

There were no significant associations between patient baseline variables and the PCS score including: age, opioid use, gender, and cause of pain. The association between PCS and OF resulted in a Pearson r of 0.53 ($p<.0001$), indicating a strong positive linear association. After adjusting for possible confounding effects of age, gender, known cause of pain, and other-cause, PCS remained significantly associated with overall functioning ($p=.0004$). In the adjusted model, each 10-point increase in PCS was associated with a 0.8-point increase in OF.

CONCLUSION

There was no significant association between PCS score and baseline variables including age, gender, opioid use, or cause of pain. Based on this patient population, the mechanism of pain catastrophizing is not related to etiology, treatment modality, or patient demographics. However, PCS score was significantly associated with the overall functioning score ($p = 0.0004$). Patients with a higher PCS score, had greater interference with daily functioning. These results suggest PCS score can be used as a predictor of daily functioning.

STATUS

Medical Student

AUTHORS

Amit Singal

Mohit Bansal

May Chin

RESEARCH MENTOR/ DEPARTMENT CHAIR

May Chin

SCHOOL OF NURSING

Contributing Variables of 30-day readmission and ER utilization

BACKGROUND

Patients in the United States, especially the elderly and frail, are vulnerable to poor outcomes from our current health care system. Fragmentation in delivery of care such as miscommunication and lack of follow-up can lead to oversight in diagnosis and disease management. Appropriate Transition of Care (TOC) services to address these issues reduce unnecessary readmission and frequent visits to the Emergency Department. These activities also improve the quality of care and are expected to reduce healthcare cost.

OBJECTIVES

The purpose of this descriptive study was to identify if certain characteristics place patients at higher risk for 30-day readmission and ER Utilization. The aim of the study was to identify the impact of specific variables (age, gender, diagnosis, marital status, social support, and TOC nurse phone call follow up) on 30-day readmission and ER utilization in adults over 65 years old. Additional data was used to compare the cost of care for this patient population and whether there is any benefit to offering TOC follow-up to this patient cohort.

METHODS

A secondary data analysis analyzed clinical data collected over an 18-month time frame by a TOC nurse using a descriptive-correlational design. The subjects for this study are patients embedded in an Internal Medicine practice in Upstate New York over the age of 65 and admitted to the target hospital in the community. Statistical correlation with SPSS software using logistic regression was used to report the variables and determine their relationship to 30-day readmission and ER utilization.

RESULTS

A tracking tool collected 1,376 patients in the inpatient arm and 1,575 in the ER visit group. After applying the inclusion and exclusion criteria from the study, 367 patients were included in the 30-day readmission group and 525 patients were included in the ER Utilization data set. Readmission rate was 28.6% for the inpatient admission. Among all variables, TOC nurse phone calls made to patient within 48 hours of discharge was the only significant variable at the 5% level (p value = 0.03). In the ER Utilization group, 21.7% of the patients experienced frequent ER Utilization over a 30-day period. Among this group, married individuals and younger age significantly impacted frequent ER utilization (p values = 0.003 and 0.000, respectively).

CONCLUSIONS

Follow up care can improve the quality of care and decrease cost through a reduction in 30-day readmission. While this service does not impact frequent ER utilization based on the available data, identifying patients who are vulnerable to frequent ER visits (unmarried and elderly) will direct further studies to this susceptible population. Additional studies should be conducted in a variety of patient populations to further identify the variables that impact care and decrease healthcare cost.

STATUS

Graduate Student

AUTHORS

Carol Braungart

Pearl Zhou

Cindy Chan

RESEARCH MENTOR/ DEPARTMENT CHAIR

Pearl Zhou

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Bridging the gap: caring for the injured worker abroad

As corporations expand and establish themselves on foreign soil, the number of U.S. employees traveling abroad has grown exponentially. Traveling is inherently risky. Illness and injury abroad pose a significant threat to the productivity of an enterprise, as well as continuity of care for the employee. In this project, the status quo of corporate travel medicine was reviewed and novel solutions to current challenges were addressed.

To gain insight into this largely secretive industry several strategies were utilized. Due to the scarcity of academic articles published on this subject matter, information was gathered from insurance company websites, articles published in insurance magazines, travel assistance company resources and various newspaper articles. The most significant contribution came from conversations with Dr. Christopher Lang, a board certified emergency physician with more than 15 years experience in the travel medicine industry.

Based on the research findings, we conclude that the current paradigm for caring for the injured worker abroad is contingent upon dozens of factors including, but not limited to, the insurance provider, the nature of the injury and the geographic location. We also identified several areas of this industry that could be improved upon.

Corporate travel medicine is a largely unexplored topic within academic circles. Our research provides insight into this industry and provides medically oriented travel suggestions for employers and employees. It is our hope that these conclusions will contribute to the quality and continuity of care for those traveling abroad.

STATUS

Medical Student

AUTHOR

Kelsey Dorwart

RESEARCH MENTOR/ DEPARTMENT CHAIR

Christopher Lang

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Evaluation of a Domestic Violence Chat Helpline

BACKGROUND

Domestic violence (DV) is a serious and prevalent public health issue in the United States. Victims and survivors of DV can suffer from negative physical, mental, sexual, and reproductive health problems, and have negative social and economic complications. Although DV is a known problem, there are many gaps in knowledge, research, and program evaluation. This cross-sectional research project seeks to evaluate the effectiveness of The National Domestic Violence Hotline (NDVH) and its younger counterpart Love is Respect (LIR). NDVH and LIR provide crisis intervention, resources, referrals, and healthy and abusive relationship information nationwide. These services have traditionally been offered via phone lines, but as the technology improves these services are being utilized more via chat based modes.

METHODS

This study incorporates peer reviewed observational listening techniques used by other hotlines to examine 217 chats from a single day of the chatline. Each chat is analyzed using a conceptual framework to assess the provision of quality and responsive services by the advocate to the chatter. Variables to assess our evaluation are both qualitative and quantitative in format.

RESULTS

This study is ongoing and our presentation will provide quantitative metrics on performance towards providing information and resources to chatters and will assess how often expressed needs by the chatter are met within the chat session. Qualitative data will be presented to provide the context of the situation and to illustrate the quantitative data presented.

CONCLUSION

This evaluation is the first of its kind and will provide helplines working with youth and adults a better understanding of the needs of their client population in addition to their advocate and program effectiveness.

STATUS

Graduate Student

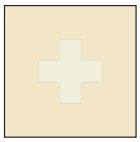
AUTHORS

Carrie Downing-Larick

Karen McDonnell

RESEARCH MENTOR/ DEPARTMENT CHAIR

Karen McDonnell



MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Preliminary Results from the Assessment of the National Domestic Violence Hotline and National Teen Dating Abuse Helpline

Domestic violence is a well-documented public health issue with many implications for a range of health outcomes that has recently received renewed attention, in part due to several high profile cases reported on in the media. With the burgeoning of new technologies through which to offer victims and survivors of domestic violence with crisis intervention and other support and referral services, it has become increasingly important to investigate how people access and use those technologies. This type of investigation is an important step in ensuring that these services are catered and prepared for the needs of the people using them. Additionally, this type of investigation also highlights the ability of federal policies to keep up with key trends in how victims and survivors access the support they need, or the lack thereof. The object of this study has been to employ STATA-based quantitative analysis to investigate how hotline visitors are using the online chat services, their expressed needs during the chats, and how those needs are met by the chat sessions. Preliminary results have indicated that regardless of how the service user contacts the hotline (through phone, text, or online chat), they initially learn about the hotline and how to access its services through the internet. Continued analysis of survey results may present informative findings regarding the demographic characteristics of those who contact the hotline and their preferences for different modes of support delivery in terms of ease of use, privacy, safety, and other primary concerns. The implications of this study and further research may reveal additional patterns in usage and modes of access to the National Domestic Violence and Dating Abuse Helpline, guiding future targeted efforts to increase and expand access among various demographics as well as to refine national level policies that seek to respond to the needs of victims and survivors of domestic violence.

STATUS

Graduate Student

AUTHOR

Rosalind Fennell

RESEARCH MENTOR/ DEPARTMENT CHAIR

Karen McDonnell

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Effect of Imputation of Missing Data in HCUP NIS on Perioperative Pulmonary Outcomes Research in Patients with Sleep Apnea

BACKGROUND

Patients with sleep apnea (SA) are considered at increased risk for perioperative complications. We sought to study perioperative outcomes of patients with SA after orthopedic surgeries, using data from HCUP National Inpatient Sample (NIS), the largest all-payer database in the US. However, as with any large-scale data collection effort, NIS has a moderate amount of missing data in several patient-level variables such as patient race, admission source, admission type, etc. As a result, researchers often conduct inappropriate analysis based on complete cases, leading to invalid inferences. In this study, we assessed the effect of imputation of missing data on the analysis of perioperative outcomes in patients with SA.

METHODS

Our study sample consisted of all data in the 2010 NIS. Entries indicating the performance of a lower extremity joint arthroplasty (hereafter referred to as orthopedic surgeries) were identified and included in the sample. Discharges with a diagnosis code for SA were further identified. Primary outcomes included aspiration pneumonia (AP), adult respiratory distress syndrome (ARDS), and pulmonary embolism (PE). Multiple imputation was performed to impute missingness on patient race, admission source, admission type, etc. Patients with the diagnosis of SA were matched to those without the disease based on demographic variables using the propensity scoring method. Odds ratio (OR) with 95% confidence intervals (CI) for comparisons of primary outcomes between the matched groups were reported. Results based on complete case analysis and multiple imputation were compared.

RESULTS

We identified 238,674 entries for orthopedic procedures performed in 2010. Of those, 10.7% (n=25,438) carried a diagnosis of SA. Each SA patient was matched to three non-SA patients based on propensity scores. Using complete case analysis, none of the outcomes was significantly different between SA and non-SA patients (AP: OR=0.67, 95% CI= [0.34, 1.33]; ARDS: 2.01, [0.95, 4.29]; PE: 0.45, [0.20, 1.05]). In contrast, using data from multiple imputation, all outcomes were significantly different between SA and non-SA patients (AP: 1.36, [1.11, 1.67]; ARDS: 1.74, [1.35, 2.25]; PE: 0.63, [0.47, 0.84]).

CONCLUSION

Imputation of missing data had a significant impact on the analysis the perioperative outcomes in patients with SA after orthopedic surgeries. Complete case analysis was associated with reduced sample size and statistical power, leading to biased estimation and invalid inferences. Multiple imputation is a principled and practical approach to missing data problems.

STATUS

Graduate Student

AUTHORS

Yihe Huang

Yan Ma

RESEARCH MENTOR/ DEPARTMENT CHAIR

Yan Ma

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Characterizing the Unmet Mental Health Needs of Urban Adolescents

BACKGROUND

Untreated mental illness among adolescents is a major public health concern. Nationwide, 80% of youth with mental illness are not receiving mental health services.

METHODS

Medical records (546 total) were abstracted for patients 16-22 years old with a diagnosis of serious mental illness/serious emotional disturbance (SMI/SED) seen between May 2014 and July 2015. A retrospective review of randomized (n=100) eligible charts was performed to abstract demographics, psychotropic medication use, history of mental health referrals, past hospitalization(s), and resource utilization. Based on the criteria outlined by the 1992 Alcohol, Drug Abuse and Mental Health Services Administration Reorganization Act, patients were categorized into mild, moderate, and severe categories. They were considered "mild" if they had a diagnosis of ADHD, ADD, anxiety, dysthymia, or substance use disorder only; "moderate" if they had a SMI/SED (e.g. bipolar affective disorder, major depression), or a "mild" diagnosis with a comorbid intellectual disability, and/or a previous psychiatric hospitalization; "severe" if they had multiple SMI/SEDs or a hospitalization within the past year. Descriptive statistics were performed.

RESULTS

Our patient sample had a median age of 18.9 years (SD ±1.87) with the majority self-identifying as African American (94%) and publically insured (86%). Thirty-four percent were found to have "mild" mental illness, 55% "moderate", and 11% "severe". Forty-two percent of the patients sampled had two or more mental illness comorbidities. Forty-eight percent were currently on psychotropic medication ("mild" 41%, "moderate" 51%, "severe" 55%, respectively) and 30% had a reported Individualized Education Program (IEP) or 504 plan (38%, 25%, 27%, respectively). Fourteen percent had been previously hospitalized for mental illness (0%,15%, 55%, respectively). While 83% of patients were offered referrals (82%, 85%, 73%, respectively), only 40% were being followed by a certified mental health provider (35%, 42%, 46%, respectively).

CONCLUSION

In our population of largely minority, publicly insured youth, a large proportion of patients are not receiving needed mental health services. Studies have shown that untreated SMI/SED in adolescence leads to more intensive and costly treatment, and increases morbidity in adulthood. Our research demonstrates that despite primary care providers' documented referrals, many adolescents with SMI/SED are not connected to ongoing mental healthcare. There are many barriers to accessing mental health services, including stigma and difficulty navigating a complex health system. Future efforts should focus on care coordination between primary care and mental health services to encourage adolescents with SMI/SED to meet their healthcare needs.

STATUS

Medical Student

AUTHORS

Priyanka Joshi

Lisa Tuchman

RESEARCH MENTOR/ DEPARTMENT CHAIR

Lisa Tuchman

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Racial and Ethnic Disparities in Health Care: An Examination of State Inpatient Databases in the Utilization of and Outcomes following Total Knee Arthroplasty

BACKGROUND

The U.S. population is becoming more racially and ethnically diverse yet disparities in health care still exist. One area of medical care in which racial disparities have been identified is total knee arthroplasty (TKA)—an efficacious and cost-effective treatment option for individuals with advanced arthritis of the knee. Previous studies have documented that racial and ethnic minorities tend to have higher rates of adverse health outcomes and face more barriers utilizing the procedure. However, these studies predominantly focused on black and white disparities and were limited to Medicare patients or veterans. In this study, we sought to study racial disparities in TKA utilization and associated health outcomes using nationally representative data.

METHODS

We analyzed administrative data collected for the Hospital Cost and Utilization Project State Inpatient Databases (SID) from eight racially diverse states between 2001 and 2008. Patient race was categorized according to the SID: whites, blacks, Hispanics, Asians, Native Americans and mixed-race. Both crude and adjusted racial/ethnic disparities were evaluated. We also analyzed time trends in TKA utilization by race to assess whether access to TKA improved over time.

RESULTS

We identified a total of 547,380 admissions between 2001 and 2008 during which a TKA procedure was performed. In comparison with whites (4.65 per 1,000 population per year), blacks (3.90), Hispanics (3.71), Asians (3.89), Native Americans (4.40) and mixed-race (3.69) had lower rates of TKA utilization (P<0.0001). After risk adjustment, TKA utilization rates were significantly lower in blacks (OR=0.87, 95% CI: [0.85, 0.89], P<0.0001), Hispanics (OR=0.76 [0.68, 0.83], P<0.0001), Asians (OR=0.83 [0.78, 0.89], P<0.0001), Native Americans (OR=0.87 [0.81, 0.93], P<0.0001) and mixed-race (OR=0.84 [0.79, 0.90], P<0.0001) compared to whites. In general, disparities in TKA utilization rates worsened over 2002-2008 for minorities compared with whites. Minority patients were also less likely to undergo TKA in high-volume hospitals than whites. Moreover, blacks (OR=1.52 [1.17, 1.97], P=0.0017), Native Americans (OR=6.52 [4.63, 9.17], P<0.0001) and mixed-race (OR=4.35 [3.24, 5.84], p<0.0001) had significantly higher rates of mortality. In addition, blacks (OR=1.08 [1.01, 1.15], P=0.01) and mixed-race (OR=1.17 [1.001, 1.36], P=0.04) had higher rates of complications than whites.

CONCLUSION

Minorities had lower rates of TKA utilization but higher rates of adverse health outcomes associated with the procedure, even after adjusting for patient and health care system related characteristics. Future studies that consider specific patient-level information with psychosocial and behavioral factors are needed.

STATUS

Graduate Student

AUTHORS

Alexis Lan

Wei Zhang

Yan Ma

RESEARCH MENTOR/ DEPARTMENT CHAIR

Yan Ma

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Clinical Public Health in Practice: An Experience from a County Health Department

Much of a patient's health is affected by population level variables such as access to care, health literacy, living environment, and poverty. This essential integration of clinical practice and public health is termed Clinical Public Health. Part of Clinical Public Health is understanding local health policy, as created by departments of health. This enables physicians to advocate for change of existing policies to improve the health of their patients. The goal of this project was to identify and describe the practical applications of clinical public health in a busy county health department.

I worked on a variety of projects to develop a broad perspective of the issues the health department faced including analyzing tobacco and long term care policy. I recruited potential partners for tobacco-free advocacy, then analyzed the tobacco-free policy of the county schools, and made recommendations for future amendments. I also analyzed policies relating to state long-term care waivers and zoning laws for assisted living facilities. I saw how the charity care system functioned through the homeless action team, homeless health clinic, and community clinics. I observed the integration of Community Service Board and Health Department programs for the new integrated care program. Finally, I was able to observe the departmental response to a measles outbreak.

During my internship, I encountered many policies that effect patient access to care. For example, zoning requirements can positively affect the number of assisted living beds for low income individuals. Additionally, administrative separation of mental and physical health leads to barriers in serving patients who live with mental and physical health challenges. I observed that a lack of policies can lead to challenges in finding specialty care for charity cases. These issues are examples of opportunities for clinical public health partnership and advocacy that could lead to improved community health. These issues are currently being addressed by the department.

These experiences have helped to better define the health system and opportunities for clinical public health in the county. Observing the department dynamics and barriers first hand has clarified opportunities for clinical public health partnerships with county health departments that can ultimately lead to better health outcomes for patients.

STATUS

Medical Student

AUTHORS

Jamie Majdi

Sharon Arndt

Lawrence Deyton

RESEARCH MENTOR/ DEPARTMENT CHAIR

Lawrence Deyton

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Epidemiology of Alcohol-Related Visits to United States Emergency Departments, 2001-2011

BACKGROUND

Alcohol intoxication accounts for approximately 1.5% of all emergency department (ED) visits in the United States. In the context of a strained ED system, understanding the epidemiology of alcohol-related ED visits at a national level represents an important area of research.

OBJECTIVES

To characterize trends in alcohol-related visits to U.S. EDs from 2001 to 2011.

METHODS

A retrospective review of data on national ED visits among patients aged 18 years or older between 2001 and 2011 was conducted using the National Hospital Ambulatory Medical Care Survey (NHAMCS). Alcohol intoxication was defined by either a diagnosis of idiosyncratic alcohol intoxication, acute alcohol intoxication, alcohol abuse, or ethyl alcohol, or by a reason for visit coded in NHAMCS as alcohol-related problems, adverse effects of alcohol, alcoholism, or alcohol detoxification. Demographic characteristics were examined for trends in alcohol-related visits. Trends in resource use were examined. ED length of stay (LOS) was assessed for changes across the study period. We also assessed trends in the total hours spent on ED care for alcohol-related complaints at a national level. Data were grouped into two-year sets to improve statistical power. Proportions were compared using survey-weighted chi square tests, while tests for trend were assessed using survey-weighted logistic regression.

RESULTS

Between 2001-02 and 2010-11, alcohol-related visits increased from 2,459,748 to 3,856,346 ($p=0.049$). There was no notable increase in proportion of visits across all tested demographic and hospital-level categories. The use of advanced imaging increased 232.2% over the study period ($p<0.001$), while the mean number of medications provided increased from 1.41 to 1.75 ($p=0.016$). Overall LOS increased 16.1% ($p=0.028$), while LOS among admitted patients increased 24.9% ($p=0.076$). Total alcohol-related hours spent in EDs nationwide increased from 5.6 million in 2001 to 11.6 million in 2010, an increase of 108.5% ($p<0.001$) compared with an increase in overall ED hours of 54.0% ($p<0.001$).

CONCLUSION

Alcohol-related ED visits are increasing at a greater rate than overall ED visits and represent a growing burden in length of stay and resource use.

STATUS

Medical Student

AUTHORS

Peter Mullins

Maryann Amirshahi

Jesse Pines

RESEARCH MENTOR/ DEPARTMENT CHAIR

Jesse Pines

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Identifying Venous Thromboembolism in Cancer Patients Using Veterans Affairs Administrative Data

IMPORTANCE

The validity of administrative data in identifying diagnoses within the Veterans Affairs (VA) database, including viral hepatitis, cirrhosis, H. pylori, and cancer metastasis has been reported. International Classification of Diseases-9 (ICD-9) validity for venous thromboembolism (VTE) in cancer patients within the VA database is unknown.

OBJECTIVES

Determine the validity of ICD-9 codes for VTE in cancer patients in a local VA database.

DESIGN

We conducted a retrospective study utilizing data from the Washington, DC VA Cancer Registry and the Electronic Health Records (EHR). VTE diagnosis was identified using the ICD-9 codes for Pulmonary Embolism and Thrombosis, with subsequent confirmation via comprehensive chart reviews.

SETTING

Veterans Affairs Medical Center, Washington, DC.

PARTICIPANTS

6,678 patients with cancer were identified from 1999-2015 using the cancer registry. We applied the algorithms above and identified subjects with VTE in the database.

EXPOSURES

N/A

MAIN OUTCOME(S) AND MEASURE(S)

The primary outcome study measurement was the validity of ICD-9 for VTE in cancer patients. Positive (PPV), negative predictive (NPV) values, sensitivity, specificity, and likelihood ratios were calculated. Our hypothesis, that ICD-9 codes alone are not predicative of VTE diagnosis in our cancer registry, was formulated during data collection after initial chart reviews yielded false positives.

RESULTS

Initial application of ICD-9 codes for VTE among 6,678 subjects yielded 616 VTE. Chart reviews confirmed the presence of VTE among 403/616. The ICD-9 codes had a 65% PPV, 95% NPV, 57% sensitivity and 96.4% specificity. Estimated prevalence of VTE in 6,678 subjects is 10.6%. Positive and negative likelihood ratios were 15.8 and 0.45, respectively.

CONCLUSIONS AND RELEVANCE

Within our local VA database, ICD-9 codes for VTE are not sensitive for identifying patients with VTE. Accurate ICD coding by physicians is paramount for patient care and research purposes. There is a lack of data on physician coding education. A systematic literature review revealed variable ICD-9 code validity based on the population of interest making larger studies challenging with added need for manual abstraction for validation. Provider education on proper use of ICD code is important for health outcomes research perspective and would allow for more accurate retrospective research.

REGISTRATION

N/A

STATUS

Medical Student

AUTHORS

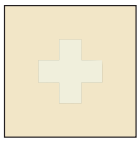
Noah Ravenborg

Najeebah A. Bad

Dalia Abdelaziz Mobarek

RESEARCH MENTOR/ DEPARTMENT CHAIR

Dalia A. Mobarek



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Job Satisfaction Among British Physician Associates

PURPOSE

To assess the level of satisfaction of British Physician Associates (PAs) with their jobs and to determine which specific factors affect PA job satisfaction.

METHODS

All British PAs were invited to participate in the annual census of the United Kingdom Association of Physician Associates (UKAPA) in May 2014. Of the 191 PAs living and working in the UK, 135 completed the survey (70.6%). The annual census collects data regarding specialty, location and scope of practice. In 2014, a job satisfaction survey was imbedded in the annual census. Respondents were asked to complete the Cooper 10-item job satisfaction scale, which has been validated in physician populations world-wide[1,2]. In addition, PAs were asked several PA-specific job satisfaction questions which have not been validated. Of the 135 respondents to the census, 124 completed the entire job satisfaction portion of the survey. Results were analyzed using SPSS version 22.0.

RESULTS

PAs were found to be satisfied with their work. No factor assessed by the survey had lower than 70.2% satisfaction rates. Only 8.0% of respondents reported being dissatisfied with their work overall. Most (87.1%) of PAs reported being "moderately satisfied" or "very satisfied" with their work. Of the satisfaction factors assessed, PAs were most satisfied with their colleagues, with 95.2% reporting satisfaction with their teams. PAs were least satisfied with their ability to use their training and abilities, with only 70.2% of participants reporting satisfaction with this aspect of their work. PAs were most satisfied with their hours of work, variety of their work, and physical working conditions and least satisfied with the pay and recognition they receive for their work.

DISCUSSION

Like their American colleagues[3], British PAs are generally satisfied with their work. They are least satisfied with their ability to fully use their training, which is likely due to the youth of the profession in Britain and lack of understanding of the PA role.

REFERENCES

1 Cooper CL, Rout U, Faragher B. Mental health, job satisfaction, and job stress among general practitioners. *BMJ*. 1989;298(6670):366–70.

2 Hills D, Joyce C, Humphreys J. Validation of a job satisfaction scale in the Australian clinical medical workforce. *Eval Health Prof.* 2012;35(1):47–76.

3 LaBarbera DM. Gender differences in the vocational satisfaction of physician assistants. *JAAPA*. 2010;23(10):33–4, 36–9.

STATUS

Faculty

AUTHORS

Tamara Ritsema

Karen A. Roberts

RESEARCH MENTOR/ DEPARTMENT CHAIR

Karen Wright

HEALTH SERVICES

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Assessing the Effectiveness of Partners in Quitting, a Text Message-Based Smoking Cessation Program

This presentation will discuss the implementation of Partners in Quitting, a new text message-based smoking cessation program. It will also provide preliminary data on client engagement rates, program effectiveness, and program challenges. Partners in Quitting is an outreach program that has been implemented at Bread for the City, a large DC hub for free health and social services. Partners in Quitting provides an evidence-based, easily accessible, and comprehensive smoking cessation program to the clients of Bread for the City.

STATUS

Medical Student

AUTHOR

Rachel Schoenbrun

RESEARCH MENTOR/ DEPARTMENT CHAIR

Karla S. Bartholomew

SCHOOL OF MEDICINE AND HEALTH SCIENCES

The Barry Farms Health Festival: Transforming Medical Education Through Community Partnerships

The George Washington University School of Medicine and Health Sciences Healing Clinic and the Rodham Institute collaborated in partnership with community organizations from the DC Community Hub to organize the Barry Farms Health Festival for the underserved residents of Wards 7 and 8 in Washington, DC. Barry Farms, located in Ward 8 is one of the oldest African American communities in DC with approximately 33% of families below the poverty line[1]. Additionally, the region has one of the lowest per capita rates of physicians significantly reducing access to healthcare for residents[2]. The Health Festival was designed to meet the health education needs of the community, based on a community assessment conducted by the Community Hub focusing on diabetes, mental health, access to primary care and social services. Students were assigned to specific health content areas from the assessment results such as diabetes, heart disease, car safety, etc., partnered with participating faculty to design education content, and worked with community residents one-on-one at the festival. Over 24 community-based organizations provided screenings and information about local services exposing both residents and students to the network of services that exist in the district. This study assesses student perceptions and experiences from the Health Festival to inform future programming and to understand medical students' desire for community-based service learning. In a post-festival survey, 99% (n = 76) of students replied that they would be willing to participate in another community-based event and 76% of students strongly agreed or agreed that they would like to enter a specialty that serves underserved patients. Integrating community health partnership into medical education through programs like the Barry Farms Health Festival and the GW Healing Clinic cultivates the next generation of physicians that will become advocates for health equity, practicing in underserved communities.

REFERENCES

1 Census Profile 2010 Ward 8, Office of Planning, DC.gov, http://planning.dc.gov/sites/default/files/dc/sites/op/publication/attachments/DCOP_SDC_Profile November, 2010.

2 Bureau of Clinician Recruitment and Service, Health Resources and Services Administration (HRSA), U.S. Department of Health & Human Services, http://datawarehouse.hrsa.gov/tools/hdwreports/Reports.aspx April 2014.

STATUS

Medical Student

AUTHORS

Madeline Taskier

Bridget Huysman

Emmeline Ha

Jehan El-Bayoumi

Aileen Chang

Monique Duwell

RESEARCH MENTOR/ DEPARTMENT CHAIR

Jehan El-Bayoumi

HIV/AIDS

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Using Biofeedback in HIV+ Patients

BACKGROUND

The prevalence of HIV in Washington, DC is estimated to be at least 3%, triple what the World Health Organization defines as an epidemic. Even at that conservative estimate, the number of people living with HIV in the District of Columbia is the highest in the nation. Individuals living with HIV face stigma, anxiety, stress and depression, among a host of other physical and mental effects. Stress has a significant impact on the immune system and a biofeedback program can be of benefit to patients undergoing any stress. Biofeedback is a technique that trains people to improve their health by controlling certain bodily processes that normally happen involuntarily, such as heart rate, blood pressure, muscle tension, and skin temperature, usually with deep breathing and relaxation techniques.

OBJECTIVE

The objective of this project is to work with a small group of HIV+ patients to examine the effects of biofeedback on stress and anxiety levels and heart rate variability, as well as to equip them with a new tool to cope with stress. Additionally, this project serves as a small pilot program to determine how best to implement a similar program on a larger scale.

METHODS

For this project, I worked with 3 HIV+ patients at Bread for the City under the supervision of Dr. Randi Abramson (Medical Director of Bread for the City). Five 30-minute biofeedback sessions were conducted with each patient using the HeartMath iPad application. Additionally, two surveys (the Perceived Stress Scale and the PROMIS-29) were administered at the first and last session to assess emotional parameters such as stress, depression, and pain. One patient did not complete the final session or survey.

RESULTS

While some survey parameters remained unchanged or worsened, some parameters improved after the program. Additionally, all patients provided anecdotal evidence of the benefits they received from the program. Lastly, much was learned about how to implement a program like this on a larger scale, as well as in populations that may be marginalized, oppressed, or disadvantaged.

CONCLUSIONS

Important takeaways from this project are the implications of a large-scale program of this nature. Many challenges were revealed throughout the study, especially as it pertains to implementing a program like this in marginalized or oppressed populations. However, biofeedback is a simple technique that can be easily incorporated into a patient's treatment regimen and can have significant benefits for interested patients.

STATUS

Medical Student

AUTHORS

Domenique Escobar

Mikhail Kogan

Randi Abramson

RESEARCH MENTOR/ DEPARTMENT CHAIR

Mikhail Kogan

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Impact of chronic sexual abuse and/or depression on systemic immune biomarkers in HIV negative and HIV positive women

INTRODUCTION

Understanding the complex immunologic factors involved in HIV infection and these roles in the context of chronic sexual violence and depression are critical when considering the prevention, transmission, and treatment of HIV-1. Biological mechanisms linking non-consensual sex and psychosocial stress are poorly understood, may impact the immune system independently and/or in concert, and could affect clinical recommendations for those at risk of HIV-1.

We investigated an array of biomarkers in plasma samples from a cohort of women from the Women's Interagency HIV Study (WIHS) repository. We hypothesized that depression and/or chronic sexual violence in women lead to an altered immune response, and that these markers are more dysregulated in HIV + women compared to HIV – women.

METHODS

Using commercially available enzyme-linked immunosorbent assays (ELISA), we analyzed cytokines (TNF-α, IL-6, IL-1α, IL-1ß, TSP-1, TGF-ß), chemokines (IL-8, IP-10, MCP-1, MIP-3α), defensins (HBD-2 and HNP1-3), and anti-inflammatory anti-HIV molecules (SLPI and Elafin) in 8 groups of women (n=7-10). Within both of the HIV – and HIV + groups, there was a Control group (no lifetime abuse or depression), an Abuse group (lifetime sexual abuse but no depressive symptoms), a Depression group (with CES-D score ≥ 16 but no history of sexual abuse) and an Abuse + Depression group (with both sexual abuse history and depression). Linear regression modeled levels of biomarkers using sexual abuse and depression as predictors, and the interaction between abuse and depression was included. Viral load and CD4 counts were included as covariates (SAS 9.4).

RESULTS

The greatest differences were found in biomarkers MIP-3α, IL-6, and IL-1ß. Among HIV – women, MIP-3α levels were found to be significantly higher in the Abuse and Abuse + Depression groups, whereas IL-1ß levels were significantly lower in Abuse + Depression compared to Control and Depression-only groups. MIP-3α and IL-6 followed opposite patterns in HIV + women, with significantly lower and higher levels, respectively, in Abuse and Abuse + Depression groups compared to Control or Depression only.

CONCLUSIONS

Our data suggest that distinct systemic biomarkers are altered by sexual abuse chronicity, depression, and this pattern can be altered by HIV status. Additional studies with larger sample sizes are necessary to evaluate the biological mechanisms of HIV acquisition and transmission in correlation with sexual abuse and depression.

STATUS

Graduate Student

AUTHORS

Monika Juzumaite

Maria Pyra

Jason Daniels

Kathy Weber

Mariel Jais

Mimi Ghosh

RESEARCH MENTOR/ DEPARTMENT CHAIR

Mimi Ghosh

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Are Patient Retention Efforts Cost-Effective?: A Cost Analysis of a Retention Intervention for HIV Patients at United Medical Center

BACKGROUND

Washington, District of Columbia (D.C.) boasts among the highest prevalence of HIV in the U.S., with an epidemic on par with some developing countries. The prevalence of HIV is highest (3.1%) within Ward 8 of D.C., which is the primary service area of the Infectious Disease Care Center (IDC) of United Medical Center (UMC). Linking the high prevalence rate to a low rate of patient retention, the IDC has over a 12-month period, invested $73,586 into operationalizing a HIV-patient retention protocol. The protocol serves as a framework by which the IDC may lower the cost of retention, increase the rate of retention, and ultimately make retention more cost-effective. Retention promotes antiretroviral therapy, sustains viral load suppression, and reduces the incidence of HIV transmission. The results of this retrospective, facility-based, costing study is intended to incentivize policy makers, with the ability to optimize the HIV treatment cascade, to facilitate an improvement in retention rates through structural reform.

METHODS

Micro-costing direct methods are applied to measure the impact of enhanced provider contact with patients across time. The methods account for all fixed and variable labor and non-labor costs, and require the units of analysis to be individualized in panel or time series. Sensitivity analysis was performed on each distinct baseline cost variable, to determine the association between cost and enhanced patient-provider contact. Expenditure and outcomes data inform multiple Return on Investment (ROI) analyses. ROI was calculated as the intervention benefit or deficit (the averted or incurred sum of fixed and variable costs associated with the intervention) divided by the intervention cost. In compliance with HAHSTA performance measures, retention is defined as at least one medical visit in each 6-month period of the 24-month measurement period with a minimum of 60 days between medical visits.

RESULTS

The intervention did not improve the visit constancy of the historically retained patients, however it did generate a positive ROI (1%) per additional patient retained in care. The 1% ROI was calculated by dividing the marginal benefit of additional patient retention ($48) by the marginal cost of an additional patient retained in care beyond the pre-intervention period ($4,906). Accounting only for patients that were historically retained, the rate of retention fell from 149 (78.8%) during the pre-intervention period, to 134 (70.9%) during the intervention period. However, of the 31 patients newly enrolled during the pre-intervention period, the intervention achieved an unprecedented 96.8% rate of visit constancy, and also lowered per patient cost of retention by over 50% from $4,954 to $2,374.

CONCLUSION

The model used to determine cost savings assumes that the units of analysis were individualized in panel or time series. It also assumes that because analyses occurred in a single fiscal year (FY2015) it was unnecessary to account for inflation or discount rates, respectively of previous or subsequent years. Analyses provided an estimated cost of a clinic-based retention in care intervention. The results reveal the intervention is cost-effective. The results also provide useful information for guiding decisions about planning or scaling-up HIV retention interventions.

KEY WORDS

HIV, retention in care, cost-effectiveness, micro-costing, costing study, COPC.

STATUS

Graduate Student

AUTHOR

Alfred Larbi

RESEARCH MENTOR/ DEPARTMENT CHAIR

Freya Spielberg

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Bacteroides are associated with GALT iNKT cell function and reduction of microbial translocation in HIV-1 infection

Invariant natural killer T (iNKT) cells are innate-like T cells that respond to lipid antigens presented by CD1d. These immunoregulatory cells have the capacity for rapid cytokine release after antigen recognition and are essential for the activation of multiple arms of the immune response. HIV-1 infection is associated with iNKT cell depletion in the peripheral blood; however, their role in the gastrointestinal-associated lymphoid tissue (GALT) is less well studied. Our results show that iNKT cells are found at a higher frequency in GALT compared to blood, particularly in HIV-1 elite controllers. The capacity of iNKT cells to produce IL-4 and IL-10 in the GALT was associated with less immune activation and lower markers of microbial translocation, while Treg frequency showed positive associations with immune activation. We hypothesized that the composition of the microbiota would influence iNKT cell frequency and function. We found positive associations between the abundance of several *Bacteroides* species and iNKT cell frequency and their capacity to produce IL-4 in the GALT but not in the blood. Overall, our results are consistent with the hypothesis that GALT iNKT cells, influenced by certain bacterial species, may play a key role in regulating immune activation in HIV-1 infection.

STATUS

Staff

AUTHORS

Dominic Paquin-Proulx

Christopher Ching

Ivan Vujkovic-Cvijin

Douglas Fadrosh

Liyen Loh

Susan Lynch

Peter Hunt

Douglas Nixon

Devi SenGupta

RESEARCH MENTOR/ DEPARTMENT CHAIR

Douglas Nixon

INSTITUTE OF BIOMEDICAL SCIENCES

HIV-specific T cells can be Expanded from Virus-naive Donors to Target a Range of Epitopes: Implications for a Cure Strategy

BACKGROUND

The Berlin patient remains the only case of functional HIV cure and long-term independence from anti-retroviral drugs, despite multiple attempts to eradicate infection with allogeneic hematopoietic stem cell transplant (HSCT). HIV+ individuals with hematologic malignancies who receive allogeneic HSCT may face viral rebound during the immune reconstitution period following transplant. One potential approach to prevent this is to administer virus-specific T cells, a strategy that has proven success in preventing other viral reactivation post-transplant, such as CMV and EBV.

OBJECTIVE

We have previously expanded broadly-HIV-specific T cells from HIV+ patients; however allogeneic transplants only contain virus-naïve T cells. We thus sought to develop a robust, reproducible platform that can expand HIV-specific cells from the naïve pool in the allogeneic setting. We hypothesize that HIV-specific T cells can also be primed *ex vivo* from seronegative individuals to effectively target and suppress HIV replication *in vitro*.

DESIGN/METHODS

Peripheral blood mononuclear cells isolated from virus-naïve donors are used to generate dendritic cells and T cells. T cells are stimulated three times with DCs pulsed with HIV-pepmix and a combination of cytokines that promote proliferation and differentiation. We tested T cells for (1) specificity against HIV antigens and individual peptides, (2) pro-inflammatory cytokine secretion in response to stimulation with HIV peptides, and (3) ability to suppress HIV replication.

RESULTS/DISCUSSION

We successfully expanded (75.705 mean fold expansion) HXTCs recognizing HIV antigens from virus naïve donors. IFNg ELISPOT showed HXTCs (n=8) were specific against Gag (mean=331.25 SFC/1e5 cells) and Nef (mean=242.63 SFC/1e5 cells) vs Irrelevant (mean=13 SFC/1e5 cells). HXTCs produced significantly pro-inflammatory responses ($p<0.05$) to stimulation by gag/nef, as determined by levels of TNF-alpha, IL-2, IL-6, IL-8, and perforin (n=3). Importantly, HXTCs (n=4) were able to suppress HIV replication more than non-specific CD8+ T cells when co-cultured with autologous CD4+ T cells infected with HIV SF162 (HXTC 78.62% viral suppression compared to CD8+ T cell 34.19% viral suppression). HXTCs showed both HLA Class I or II specificity for individual HIV epitopes, as determined by HLA blocking and IFNg ELISPOT. This is the first report demonstrating generation of functional, multi-HIV antigen specific T-cells from HIV-negative donors, which has implications for using allogeneic HSCT as a functional HIV cure. The low frequency of circulating HXTCs post-infusion suggests these HXTCs could have a significant effect on preventing viral rebound.

STATUS

Graduate Student

AUTHORS

Shabnum Patel

Sharon Lam

Conrad Russell Cruz

Kaylor Wright

Christina Cochran

Richard Ambinder

Catherine Bollard

RESEARCH MENTOR/ DEPARTMENT CHAIR

Catherine Bollard

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Investigating Sperm Sex Chromosome Disomy in HIV Positive Men on Highly Active Antiretroviral Therapy (HAART)

PURPOSE

Reproductive technologies have made it possible for HIV-positive individuals to conceive children free from HIV. Consequently, semen parameters have been studied in HIV positive men, as well as men on Highly Active Antiretroviral Therapy (HAART). Studies have reported inverse associations between semen parameters and both HIV and HAART status, however, reported results have been inconsistent. Rates of sperm abnormalities have not been well characterized in these men. With many HAART regimens consisting of drugs meant to suppress HIV DNA replication, attention to preserving DNA integrity is necessary, particularly among men interested in fathering a child. By investigating disomy rates, this exploratory study sought to evaluate the association between HIV, HAART, and the DNA quality of human sperm.

METHODS

Nine men from the Multicenter AIDS Cohort Study (MACS) provided samples that were divided into two separate aliquots. One contained semen only, while the other contained semen and a preservative (DMSO or Sorbitol). Date of sample collection ranged from the early 1980's to 2011 and differed by HIV status and HAART status. Multi-probe fluorescence in situ hybridization (FISH) was performed for each aliquot (n=18). The slides were imaged using confocal microscopy with spectral imaging and disomy rates were quantified using semi-automated scoring methods. Statistical analyses consisted of Wilcoxon Rank Sum, Kruskal Wallis, and Wilcoxon Signed Rank tests for comparison of means.

RESULTS

Qualitatively, HIV-positive men had higher rates of disomy and lower nuclei scored, irrespective of HAART status. Similar results were found for HAART positive men. There were also qualitative differences in mean nuclei count by preservation status. Differences between means did not reach statistical significance.

CONCLUSIONS

While additional analyses are ongoing, these results indicate that the FISH assay was viable for both preserved and non-preserved sperm and that sperm aneuploidy rates may be altered based on HIV and HAART status. However, the sample size was limited, and these findings need to be replicated in larger studies with more statistical power.

STATUS

Graduate Student

AUTHORS

Nicholas Porter

GiaLinh Nguyen

Heather Young

Melissa Perry

RESEARCH MENTOR/ DEPARTMENT CHAIR

Melissa Perry

COLUMBIAN COLLEGE OF ARTS AND SCIENCES

HIV-1 Latency: Models, Techniques and Quantification

It's estimated that over 36 million individuals worldwide are infected with HIV-1, a virus with no cure. HIV-1 viral load may be reduced to undetectable levels in the plasma of infected patients by antiretroviral therapy (ART), but treatment interruption leads to viral rebound. The primary barrier to eradicating HIV-1 is the ability of the virus to establish latency in reservoirs within infected individuals, even those receiving ART. HIV-1 establishes latency early after infection by a variety of molecular mechanisms and it becomes transcriptionally inactive in CD4+ T central memory cells. Current HIV-1 eradication strategies rely on the use of latency reversal agents to reactivate the virus from latent reservoirs. These "shock and kill" strategies have shown some promise in vivo. One primary means of reactivation focuses on inhibiting histone deacetylases (HDACs) because of their role in the post-translational regulation of HIV-1. Because latently infected cells in vivo are rare, in vitro cell models provide unique mechanistic tools to better understand the establishment and maintenance of HIV-1 latency.

Here, we reviewed the literature and provide a comprehensive list of the current available models of HIV-1 latency and experimental approaches to quantify the reservoir. We depict the experimental tools, reagents and protocols necessary for the establishment of these models in the laboratory.

Model 1 – "ACH-2 cells". These cells are descendants of a human T-cell line infected with acute lymphoblastic leukemia, contain only one integrated copy of HIV-1, and provide an excellent model of early infection and latency due to the low amounts of RNA expressed before activation. Model 2 – "The Sharon Lewin model". This highly cited model relies on chemokine receptor binding to primary CD4 T-cells, which allows for infection with wild type HIV-1 and establishment of latency in physiological conditions. Model 3 – "The Eric Verdin model". This model also relies on leukemic immortalized T-cells known as Jurkat cells with single site integration of HIV-1 and have incorporated green fluorescence protein (GFP) so expression can be measured accurately by flow cytometry.

To measure the size of the inducible reservoir two main methods are currently accepted. Both the quantitative viral outgrowth assay (QVOA) and the Tat/rev Induced Limiting Dilution Assay (TILDA) are reliable approaches to accurately determine the frequency of latently infected cells with inducible provirus.

Latency models and novel quantification techniques are essential to advancing the field towards an HIV-1 cure.

STATUS

Undergraduate Student

AUTHORS

Andre Raposo

Paul M. Zdinak

Miguel de Mulder Rougvie

Douglas F. Nixon

RESEARCH MENTOR/ DEPARTMENT CHAIR

Douglas F. Nixon

SCHOOL OF MEDICINE AND HEALTH SCIENCES

DNA-PK Inhibition Potently Represses HIV Transcription and Replication

DNA-dependent protein kinase (DNA-PK), a nuclear protein kinase that specifically requires association with DNA for its kinase activity, plays important roles in the regulation of different DNA transactions, including transcription, replication and DNA repair, as well as in the maintenance of telomeres. We reported DNA-PK facilitated HIV transcription by interacting with the RNA polymerase II (RNAP II) complex recruited to HIV LTR and identified potential DNA-PK targets within the carboxyl terminal domain (CTD) of RNAP II through kinase assays. In our current study, DNA-PK inhibition via highly specific small molecule inhibitors replicated the shRNA-mediated abrogation of both HIV transcription and replication in latently infected myeloid and lymphoid cell lines, the main cell types targeted by HIV. These inhibitors also impaired HIV replication in primary CD4+ T-cells. Pre-treatment of the HIV-infected cell lines with the DNA-PK inhibitors also resulted in severe impairment of the phosphorylation of the serine 2 and serine 5 of the RNAP II CTD upon stimulation. Chromatin immunoprecipitation (ChIP) analysis showed the inhibition of DNA-PK activity led to the establishment of transcriptionally repressive heterochromatin structures at the HIV LTR. These findings confirm the important role of DNA-PK in HIV transcription and replication and excitingly we have identified two strong inhibitors of DNA-PK that successfully limit the reactivation of latently HIV-infected cells. In light of the fact that these transcriptionally silent proviruses are well protected from both the immune system and HAART regimens, which prevents complete eradication of the virus, we present strong evidence for the inclusion of DNA-PK inhibitors as supplements to HAART regimens, to enhance their restriction of HIV replication.

STATUS

Postdoctoral Student

AUTHORS

Geetaram Sahu

Kalamo Farley

Alex Ochem

Larisa Dubrovsky

Michael Bukrinsky

Gary Simon

Mudit Tyagi

RESEARCH MENTOR/ DEPARTMENT CHAIR

Mudit Tyagi

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Co-infection with Hepatitis C Virus Enhances Premature Aging in HIV Patients

Premature aging in HIV patients has become a major concern that compromises the lifespan of HIV patients. Several factors play a role in accelerating aging in HIV patients. Enhanced inflammation has been proposed to be the main factor that augments aging. In developed world, HCV co-infection is quite common in HIV patients. HCV infection is known to upregulate the expression of various pro-inflammatory cytokines. Therefore, we hypothesized that co-infection with HCV could also be an important factor that augments aging in HIV patients. In order to examine the influence of HCV infection on aging in HIV co-infected patients, we analyzed 60 subjects aged from 45 to 60 belonged to four different groups--normal, HIV infected, HCV infected and HIV/HCV co-infected. The plasma samples from the four groups were used to assess the cytokine profile while PBMC samples were subjected to telomerase enzyme activity analysis. The cytokine profile showed increased levels of pro-inflammatory cytokines, such as IP10 and sCD163 in HCV-infected patients, who are infected either alone or co-infected with HIV. Interestingly, the HCV-infected and HIV/HCV co-infected groups exhibit less telomerase activity than the HIV-infected group. In summary, our preliminary results support our hypothesis and suggest that HCV co-infection accelerates aging process in HIV patients.

STATUS

Postdoctoral Student

AUTHORS

Lin Sun

Geetaram Sahu

Marc Siegel

Gary Simon

Mudit Tyagi

RESEARCH MENTOR/ DEPARTMENT CHAIR

Mudit Tyagi

HIV/AIDS

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

"You can't tell nobody": Fears surrounding HIV infection by Black Women

BACKGROUND

Limited attention and research has focused on prevention and reduction of HIV/AIDS infection among African American women. Studies of broader populations acknowledge to some extent the role that fears of infection and stigma play in delaying or preventing individuals from taking an HIV test or seeking care. However, few studies examine such fears exclusively among African American women.

PURPOSE

The purpose of this study is to understand fears surrounding HIV infection among African American women.

METHODOLOGY

This qualitative study uses an applied research approach in order to derive recommendations to improve current HIV testing programs in Washington, D.C. Semi-structured interviews with low-income African American women explored general care preferences, fears associated with HIV infection, feelings associated with clinic based HIV testing.

RESULTS

Twelve areas of fear emerged, including sharing one's positive HIV status, paying for care, feeling/being along, being blamed, being shamed, not having emotional support, being treated differently, taking care of responsibilities, being stigmatized, infecting others, becoming sick and having to change one's lifestyle. Topics that made participants feel most afraid elicited strong emotional and verbal reactions, indicating that the respondents had little to no control over the issue. These areas included being stigmatized, being treated differently, losing privacy and confidentiality, not being able to take care of one's responsibilities.

CONCLUSION

HIV prevention and treatment organizations should consider integrating programming to address fears of stigma, being treated differently, losing privacy and confidentiality, and not being able to take care of one's responsibilities. Inclusion of these concepts may reduce fears among African American women seeking HIV services.

STATUS

Graduate Student

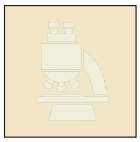
AUTHORS

Veronica Vela

RESEARCH MENTOR/ DEPARTMENT CHAIR

Holly Mead

IMMUNOLOGY/INFECTIOUS DISEASES



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Identification of Plasmodium Proteins from Children's ield Isolates Targeted by Immune Sera Using a Proteomics Approach

Malaria is a life-threatening parasitic infection caused by Plasmodium species. *Plasmodium falciparum* is the most deadly parasite species, and most deaths occur among children living in Africa where a child dies every minute from malaria. That is because children are more susceptible to severe malaria which occurs when infections are complicated by serious organ failures or abnormalities in the patient's blood or metabolism. However, as children grow older and experienced repeated attacks of malaria, they develop immunity that protects them from disease. This goal of project was to identify surface proteins from children's parasite isolates adapted to in-vitro culture that are recognized by children's immune sera. This was achieved by (1) identifying gene products recognized by adult's immune sera and by children's immune sera respectively, (2) comparing gene products from 2 field isolates collected from malaria infected children that are recognized by immune sera, and (3) determining the function of the identified proteins by Gene Ontology. After data analysis, 114 and 46 proteins were immune-precipitated by immune sera from children and adult respectively. Of those, 61 proteins were annotated as exported conserved membrane proteins of unknown function, which may be immunogenic. This research is still ongoing, mainly relating antibodies to the identified membrane proteins with protection from disease. In addition, the data will be analyzed by de novo sequencing to identify *Plasmodium falciparum* erythrocyte membrane protein 1 (PfEMP1) variants, because they are recognized as variable proteins that are very important to *Plasmodium falciparum* virulence.

STATUS

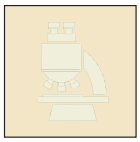
Medical Student

AUTHOR

Naissem Andemel

RESEARCH MENTOR/ DEPARTMENT CHAIR

Michal Fried



INSTITUTE OF BIOMEDICAL SCIENCES

Cellular backpacking as a method of enhanced tumor efficacy and modulating the immune environment

BACKGROUND

Through a technique known as "cellular backpacking" we have demonstrated conjugation of nanoparticles (Prussian blue nanoparticles – PBNP) onto the surface of immune cells. Cellular backpacking allows the use of cells as vehicles for nanoparticle transport and the combination of two treatment modalities. These PBNP can be targeted by a near infrared laser, which allows for tumor ablation and modification of the environment to increase susceptibility to immune attack. Furthermore, cellular backpacking may allow for additional immunomodulatory capabilities to the immune cell, which is an attractive avenue of research for hematological malignancies.

OBJECTIVE

We hypothesize that cellular backpacking will not only allow us to couple nanoparticles and immune cells for increased anti-tumor efficacy, but it will arm immune cells used for hematopoietic stem cell transplantation with additional immunomodulatory properties. It is our hope that by manipulating the release of specific cytokines involved in inflammatory processes we can shift the balance following cell transplant to encourage a more beneficial graft-versus-tumor (GVT) response rather than the detrimental graft-versus-host-disease (GVHD) outcome.

METHODS

T lymphocytes were isolated from healthy donors and cultured in vitro with cytokine support. Using NHS-ester crosslinking we have stably conjugated nanoparticles (PBNP) onto the surface of T lymphocytes. T cells were either non-specifically stimulated with PHA or fabricated to be specific for Epstein Barr Virus (EBV) and were stimulated with EBV-positive target cells.

RESULTS

We demonstrated maintenance of T cell phenotype and function following cellular backpacking, as well as improved anti-tumor effects in vitro with the combination of nanoparticle-mediated tumor ablation and T cell targeted toxicity. We were able to demonstrate a dose-dependent effect of nanoparticles backpacked to the surface of T cells to T cell production of pro-inflammatory cytokines such as IFNy (27 120 pg/ml vs. 8014 pg/ml vs. 1618 pg/ml with 10x, 1x, and 0.1x PBNP, respectively), and IL-2 (704 pg/ml vs. 302 pg/ml vs. 36 pg/ml with 10x, 1x, and 0.1x PBNP, respectively) and anti-inflammatory cytokines such as IL-10 (3053 pg/ml vs. 1243 pg/ml vs. 51 pg/ml with 10x, 1x, and 0.1x PBNP, respectively). These results serve as a springboard for future studies utilizing cellular backpacking as a means to enhance T cell repertoire and establish a favorable graft-versus-tumor environment in patients following transplantation.

STATUS

Graduate Student

AUTHORS

Rachel Burga

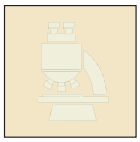
Catherine M. Bollard

C. Russell Cruz

Rohan Fernandes

RESEARCH MENTOR/ DEPARTMENT CHAIR

Rohan Fernandes



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Histone Deacetylase 11 (HDAC11) Plays As a Novel Transcriptional Regulator in Hematopoiesis under pathological conditions

During hematopoiesis, multilineage progenitor cells and the precursors are committed to individual hematopoietic lineages. In normal myelopoiesis, the immature myeloid cells (IMCs) differentiate into macrophages, neutrophils or dendritic cells. However, under tumor burden, these IMCs differentiate into myeloid derived suppressor cells (MDSCs) result in an upregulation of immune suppressive factors[1]. The development of normal or malignant is tightly controlled by endogenous signals such as transcription factors and epigenetic regulations. HDAC11 is the newest identified members of the histone deacetylase (HDAC) family. Previous study in our group had identified HDAC11 as a negative regulator of interleukin 10 (IL-10) production in antigen-presenting cells(APCs). However, the mechanisms of HDAC11 in normal and malignant hematopoiesis remains unclear.

We have uncovered for the first time that in the absence of HDAC11, upon LPS stimulation, neutrophils isolated form mice displays an overproduction of pro-inflammatory cytokines such as TNF-alpha and IL-6 using both mRNA and protein analysis. Strikingly, these HDAC11 KO neutrophils showed a significantly higher migratory and phagocytosis activity, resulting from an overexpression of the migratory receptor and cytokine CXCR/L2. We have performed Chromatin Immunoprecipitation (ChIP) analysis on the neutrophils and discovered that HDAC11 was recruited to the promoter regulatory region of these genes we have identified.

Not only does HDAC11 plays a crucial role in the neutrophil function, our group have also found out that lacking of HDAC11 increase the suppressive activity of Myeloid-drived Suppressor Cells (MDSCs). The previous publication of our group had shown that the tumor bearing mice experienced a much more aggressive growth pattern in the HDAC11 KO mice compare with C57BL/6 wild type control. We observed a markedly higher expression of the lineage-specific transcription factor C/EBP-β mRNA in the $CD11b^+/Ly6G^+$ granulocytic compartment the $CD11b^+/Ly6C^+$ monocytic compartments of HDAC11KO mice relative to control mice. C/EBP-β has been proved to play a crucial role in the MDSCs generation and function[2]. To explore the mechanism we found out that HDAC11 was recruited to the promoter region of C/EBP-β of the primary myeloid cells.

Taken together, we have uncovered a previously unknown role for HDAC11 as a transcriptional regulator in neutrophils and MDSCs function. In the absence of HDAC11, neutrophils function more pro-inflammatory upon infection. And interestingly, HDAC11 may function as an epigenetic checkpoint of C/EBP-β gene expression in the MDSCs under tumor condition. Our findings will lead to a better understanding of this novel role of HDAC11 in myeloid biology under different pathological conditions.

REFERENCES

1 Condamine T, Gabrilovich DI. Molecular mechanisms regulating myeloid-derived suppressor cell differentiation and function. *Trends Immunol* 2011; 32(1): 19-25.

2 Marigo I, Bosio E, Solito S, et al. Tumor-induced tolerance and immune suppression depend on the C/EBPbeta transcription factor. *Immunity* 2010; 32(6): 790-802.

STATUS

Staff

AUTHORS

Jie Chen

Eva Sahakian

John Powers

Fengdong Cheng

Hongwei Wang

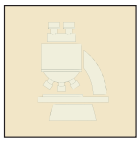
Alejandro Villagra

Javier Pinilla-Ibarz

Eduardo Sotomayor

RESEARCH MENTOR/ DEPARTMENT CHAIR

Eduardo Sotomayor



INSTITUTE OF BIOMEDICAL SCIENCES

Genome editing for functional genomics of schistosomes

The *Streptococcus pyogenes* Type II CRISPR system is the keystone of the CRISPR revolution. The system centers on a programmable endonuclease that catalyzes a double stranded break (DSB) in target DNA. The system has been shown to be active in many species including human, mouse, zebra fish, fruit fly, malarial parasite and yeast. It has revolutionized experimental genome editing, and portends hitherto unparalleled advances and positive prospects for gene therapy, biomedicine, and biological systems at large. Adaption of CRISPR technology for editing the genome of schistosomes and other parasitic platyhelminths would be desirable. Here we targeted the IPSE gene of *Schistosoma mansoni* for 'knockout'—deletion mutation in the coding region of the gene. First, using a double reporter plasmid system, NIH 3T3 fibroblasts were transfected with pX330-IPSE1 and pRGS-tgt-IPSE1. By FACS, ~9% cells were RFP+ve, GFP+ve, indicating cleavage of exon 1 of SmIPSE gene (within pRGS-tgt-IPSE1). Second, *in vitro* incubation of plasmid pRGS-tgt-SmIPSE1 that includes part of exon 1 of the IPSE gene, including a protospacer adjacent motif (PAM), with a macromolecular complex of guide RNA (gRNA) and recombinant Cas9 linearized the plasmid, presumably the consequence of a directed DSB catalyzed by Cas9. Third, cultured schistosomula were transfected using square wave electroporation with recombinant Cas9 of *S. pyogenes* complexed with gRNA matching residues 22 - 44 of exon 1 of the IPSE gene. Indels at the IPSE locus were evident by two hours later, detected by quantitative PCR, in ~13% of the cells of the parasites. The Type II Cas9 System is active in schistosomes.

STATUS

Graduate Student

AUTHORS

Christina Cochran

Victoria H. Mann

Arnon D. Jurberg

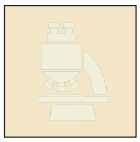
Wannaporn Ittiprasert

Gabriel Rinaldi

Paul J. Brindley

RESEARCH MENTOR/ DEPARTMENT CHAIR

Paul J. Brindley



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Oral Allergy Syndrome Disappearance in Pregnancy

PURPOSE

The purpose of this case study is to illustrate the unique disappearance of an IgE mediated oral allergy syndrome during pregnancy while making a theoretical immunologic connection to the improvement of Th1 mediated multiple sclerosis during pregnancy.

CASE REPORT

A 39 y.o. G1PO 20 week female with PMH of oral allergy syndrome(OAS), otherwise known as pollen food allergy syndrome, to apples, peaches, almonds, cherries, and avocado as well as Spring seasonal allergies presented for follow up to her allergist. This particular patient's seasonal allergies had been controlled with an antihistamine, Omnaris, and allegra. During the pregnancy, the patient had not taken any allergy medication. As noted, the patient had previously experienced pruritus of the mouth to apples and almonds. However, throughout the pregnancy, the patient had consumed these foods on a regular basis without symptoms. As she had presented in winter, her seasonal allergies had not begun to bother her, but on the basis of cross-reactivity that the oral allergy syndrome is founded on, it is likely that her seasonal allergies would improve as well during pregnancy. However, it should be mentioned that OAS does worsen during the pollen season due to the cross reactivity being more prevalent.

This interesting case report is similar immunologically to the ever-evolving study of the improvement of Th1 mediated multiple sclerosis in pregnancy. Recent studies have suggested that an estradiol receptor may play a role in a woman's immunology during her pregnancy. Multiple sclerosis pregnant patients exhibit remission in their last trimester of pregnancy when their estrogen levels have peaked. Postpartum, when estrogen levels have fallen, a relapse occurs in these patients. Such research supports the use of oral estriol to mediate the immune system in a multiple sclerosis patient to decrease the relapse rate.

CONCLUSION

This case study illustrates an important, still mysterious connection between the effects of pregnancy on a woman's immune system. As many patients continue to avoid foods that they attribute to their OAS symptoms, it is still unknown whether this case could be generalized. The evolving research in the estradiol receptor in remitting multiple sclerosis patients shows further importance of the need to distinguish this link and thus be able to use it to mediate these immunologically mediated syndromes and diseases.

KEYWORDS

Oral allergy syndrome; IgE; Multiple Sclerosis; Estradiol receptor; Oral estriol

STATUS

Medical Student

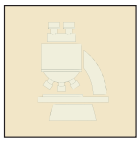
AUTHOR

Kerian Dodds

RESEARCH MENTORS/ DEPARTMENT CHAIRS

Robert H. Miller

Prashant Rohatgi



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Parkinsonian Symptoms with Fever

CASE DESCRIPTION

A 75-year-old man presented in August 2015 with sepsis and one day of confusion, fever of 104°F, a WBC of 19.80, and blood pressure of 204/91, in the setting of a recent admission for small bowel obstruction. On exam, he was only oriented to self with slurred speech, tongue and bilateral quadriceps fasciculations, cogwheel rigidity and tremor of bilateral upper arms, and dysmetria. He did not have skin changes, no meningeal signs, or visual problems. He was treated empirically for meningitis. Head CT, MRI, abdominal CT, CXR (Chest X-Ray) were negative. He remained febrile and hypertensive for four days, with worsening Parkinson's features. Blood and urine cultures were negative and antibiotics were stopped. Neurology started a Sinemet trial. LP revealed mild pleocytosis and no detectable WNV. On day six, his WBC resolved, blood pressures were under control, and defervesced—only with supportive care. All of his Parkinson's symptoms resolved. On day seven, serum WNV IgM was positively elevated > 5.00. One week later, he had seroconverted.

DISCUSSION

This case report reminds us of the necessity to heighten public health awareness for WNV. It also portends the need for WNV surveillance in order to control disease spread.

Our priorities need to shift toward early disease identification and implementation of control measures.

Frequently, WNV cannot be detected in serum because the viremia is short lived and peaks before clinical symptoms are present. Only one case report has documented that WNV can present as Parkinsonian symptoms including hypomimia, bradykinesia and postural instability. Persistent fever without a known source should initiate a search for the cause, and merits a thorough review of the patient's social history.

Treatment should be focused on supportive care while pending laboratory confirmation of WNV, and irrespective of imaging studies. Consistent with the literature, our patient did not have significant imaging findings. WNV can be a preventable disease if preventative measures are taken.

STATUS

Medical Student

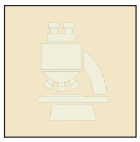
AUTHORS

Nikki Duong

Alita Mishra

RESEARCH MENTOR/ DEPARTMENT CHAIR

Alita Mishra



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Different Sequencing Platforms Give Distinct Measures of Alpha Diversity of the Pulmonary Microbiome Detected in Cystic Fibrosis

INTRODUCTION

Cystic fibrosis (CF) is an autosomal recessive disorder that causes abnormal salt and water transport across epithelia due to a mutation in the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR). Mutations in CFTR cause thick mucus to collect in airways, clogging them and making breathing difficult. Cilia cannot remove pathogens in the respiratory tract, resulting in recurrent and chronic bacterial infections. Currently, bacteria are identified by culturing on media. There are diverse species that grow in a patient's lung, so it can be hard to identify all pathogens. A noveler method of bacterial identification involves next generation sequencing (NGS) of the bacterial 16S rRNA gene. Prior studies using NGS have identified a large number of bacteria present in the CF lung, and that a loss of bacterial diversity is associated with disease progression. Two state-of-the-art platforms that can sequence the CF lung microbiome are MiSeq and PacBio RS II. Our goal was to determine whether MiSeq, with shorter reads, can still identify the dominant pathogen and a similar measure of alpha diversity compared to PacBio in CF sputum samples.

METHODS

The bacterial DNA from the sputum of 10 de-identified subjects with CF was extracted to make 16 samples. MiSeq was used to sequence V3/V4 with read lengths of 250 base pairs. Identification of bacteria was done using BaseSpace (Illumina). PacBio sequenced the full 16S rRNA gene (~ 1450 base pairs) using ≥16 passes via circular consensus sequencing. Software from the ChunLab was used for bacterial identification. The Shannon Index (SI) was used to calculate alpha diversity.

RESULTS

13 matched samples were sequenced on both platforms. 609 (±132) OTUs were identified with MiSeq, compared to 88 (±59) with PacBio ($p < 0.001$). The Shannon Index for MiSeq was calculated to be 1.916 (±0.517) and 2.005 (±0.656) for PacBio ($p = 0.018$). The agreement of the dominant pathogen was 92% between the two platforms

DISCUSSION/CONCLUSIONS

Although the dominant pathogen was identified by both platforms, MiSeq identified a larger number of operational taxonomic units (OTUs), which is observed in the measures of alpha diversity. Only 49.4% of the MiSeq OTUs were classified to the genus level, compared to 99.3% of PacBio OTUs. PacBio was able to more accurately identify the taxa of the OTUs, but MiSeq was able to find rare OTUs not identified by PacBio. Determining the strengths and weaknesses of each platform will help choose the correct platform for future studies.

STATUS

Medical Student

AUTHORS

Andrea Hahn

Amit Sanyal

Geovanny Perez

Anamaris M. Colberg-Poley

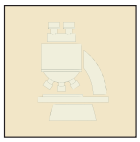
Joseph Campos

Mary C. Rose

RESEARCH MENTOR/ DEPARTMENT CHAIR

Andrea Hahn

IMMUNOLOGY/INFECTIOUS DISEASES



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Site-Specific Commensal Control of T Effector Function in Human and Non-Human Primate Skin

Skin is a large immunologically rich organ, containing more total T cells than in circulation. Yet the factors that control T effector function in human skin remain poorly understood. Our laboratory recently reported that specific commensals can uniquely and lastingly tune distinct subsets of T cells in mouse skin. We have developed novel techniques that have enabled us to investigate the relevance of the mouse model to humans and non-human primates (NHP). Notably, we have shown via flow cytometry and fluorescence microscopy that CD3+ T cells are enriched in areas of NHP skin with high density of appendages such as hair follicles, a primary site of commensal colonization. In order to investigate whether commensal bacteria could play a role in shaping human skin immunity we considered the topographical diversity of the skin microbiome, and sought to determine whether T cell populations also varied by site. We have shown that the proportion of T cells producing IL17 is enhanced in the scalp, while IL13 producing T cells are enriched in the face. Preliminary experiments also suggest that markers of tissue residence and chemokine receptor expression may differ between these two sites, and this may have functional ramifications. Many diseases, including pathologies thought to be T cell mediated such as psoriasis and vitiligo vulgaris, show skin site tropism so specific that it can be diagnostic. These findings open the door to greater understanding of the human skin immune system and may ultimately reveal potential targets for therapy of skin pathology.

STATUS

Medical Student

AUTHORS

Sarah Himmelfarb

Shruti Naik

Samira Tamoutounour

Heidi Kong

Kelly Stone

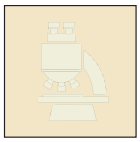
Joshua Milner

Jason Brenchley

Yasmine Belkaid

RESEARCH MENTOR/ DEPARTMENT CHAIR

Yasmine Belkaid



MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

The Influence of Specific Mucin Content on the Microbiome of Middle Ear Effusions from Children with Chronic Otitis Media

BACKGROUND

Otitis media (OM), an infection of the middle ear, occurs as a result of acute microbial pathogenesis and can progress to chronic OM (COM) following numerous episodes. The role of microbes in COM remains unclear. It has been reported that mucins are required for middle ear immune defense against pathogens. We aimed to characterize the microbiome of middle ear effusions (MEEs) from patients with COM in efforts to determine the relationship between varying microbial communities and the presence of secretory mucins MUC5B and MUC5AC. We hypothesized that MEEs with high mucin content would show a distinct microbiome largely devoid of typical acute OM pathogens.

METHODS

42 MEEs from children ages 3 to 146 months with COM undergoing myringotomy at Children's National Medical Center were recovered. Western blot analysis was performed using anti-MUC5B and anti-MUC5AC antibodies. DNA was extracted and sequenced using Illumina Nextseq500. Non-human sequences were classified using Kraken and Pathoscope, limiting classification to bacteria already identified within humans. Statistical analysis and comparison of the microbiome of MEEs to patient demographics, past medical history, and mucin content were performed using R.

RESULTS

39 MEEs were positive for MUC5B, 29 for MUC5AC, and 28 for both. On average, 12.1% of sequenced DNA was identified as non-human of which Kraken classified 4.9%. 66% were bacterial, 7.8% archaeal, and 26% viral. After excluding an outlying purulent sample almost exclusively containing *Pseudomonas*, the five most prevalent bacterial genera included *Mycoplasma, Methanococcus, Methanosarcina, Haemophilus,* and *Yersinia*. After limiting classification using Pathoscope, we found that *Actinobacillus, Cyanothece, Haemophilus, Achromobacter,* and *Stenotophomonas* were the five most abundant genera. The overall proportion of *Cyanothece* within the microbiome of samples containing both mucins when compared to those containing just one was significantly increased (p= .041). Mucoid samples, compared to serous samples, showed an increase in the proportion of *A. pleuropneumoniae* (p= .044). Samples from children who experienced significant hearing loss contained a higher proportion of H. influenzae (p=.033).

CONCLUSION

As one of the first to characterize the MEE microbiome, we saw a wide variety of bacteria, including some that have not yet been classified within humans. By limiting our sequences to those previously classified within the human body, we found significant variations in microbial communities between numerous variables including MUC5B and MUC5AC presence, hearing loss, and mucoid vs. serous effusions, suggesting an association between the MEE microbiome and COME pathogenesis.

STATUS

Graduate Student

AUTHORS

Anna Krueger

Stephanie Val

Karuna Panchapakesan

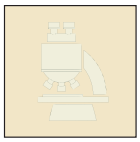
Marcos Perez-Losada

Joe Devaney

Diego Preciado

RESEARCH MENTOR/ DEPARTMENT CHAIR

Mimi Ghosh



MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Incidence of Dengue among U.S. Peace Corps Volunteers, 2000–2014

Dengue is a mosquito-borne viral disease that currently threatens as many as 3.97 billion people globally living in tropical and subtropical climates. Dengue infection can range from being asymptomatic to causing severe plasma leakage and even death. The incidence of dengue has continued to increase over the past 50 years, and the lack of a vaccine or specific treatment makes disease surveillance essential to reducing morbidity and mortality. United States Peace Corps Volunteers (PCVs) are a globally-distributed group of long-term travelers that often volunteer in dengue-endemic countries. This study aims to describe the patterns of dengue incidence among PCVs between 2000 and 2014. Laboratory-confirmed cases of dengue reported among PCVs from January 1, 2000 to December 31, 2014 were analyzed. The overall global incidence rate of dengue among PCVs was 1.12 cases per 1,000 Volunteer/Trainee (VT) months. The highest cumulative rate of dengue was reported among PCVs in the Caribbean region (5.51 cases per 1,000 VT months) followed by East and South Asia (3.34), Central America (2.55), and the Pacific Islands (2.30). The comparison of yearly dengue incidence rates among PCVs in the Dominican Republic, Nicaragua, and the Philippines to WHO reported incidence rates led to relative risk estimates ranging from 852.9 to 1.1. PCVs appear to have similar dengue incidence rates to other long-term travelers, but greater incidence rates than country-natives. The incidence rates of dengue among PCVs vary by year and region. Continued surveillance is critical for understanding the dynamic epidemiology of dengue and developing evidence-based intervention efforts.

STATUS

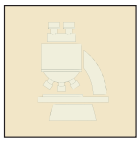
Staff

AUTHOR

Avery Lee

RESEARCH MENTOR/ DEPARTMENT CHAIR

Dante Verme



INSTITUTE OF BIOMEDICAL SCIENCES

Human herpesviruses HHV-6A and 6B accelerate clinical and radiological disease in a nonhuman primate model of multiple sclerosis

Viruses, particularly human herpesviruses, have long been suggested to be an environmental risk factor for the pathogenesis of Multiple Sclerosis (MS). Human herpesviruses HHV-6A and HHV-6B are associated with MS, in addition to several other inflammatory disorders of the central nervous system (CNS). To investigate this viral trigger hypothesis in a nonhuman primate, we asked whether marmosets previously inoculated with HHV6 exhibit an altered disease course of experimental autoimmune encephalomyelitis (EAE) compared to naïve animals. EAE is an well-accepted model of CNS inflammatory demyelination and reflects clinical and radiologic aspects of MS when induced in marmosets.

To mimic a physiologically relevant route of exposure, marmosets were inoculated intranasally with HHV-6A (n=6), HHV-6B (n=4) or uninfected control material (n=6) monthly for four months. Six months after the last viral inoculation, all animals were immunized with white matter homogenate to induce EAE. All animals underwent neurologic exams, *in vivo* brain MRIs, and peripheral blood (PB) and saliva collection bi-monthly until predetermined clinical endpoints. Upon necropsy, the CNS and other tissues were collected for viral distribution and immunohistochemistry studies.

A subset of marmosets inoculated with HHV6A or HHV6B (HHV6^{+}EAE) mounted antiviral antibody responses and had detectable viral DNA in saliva and PB. Following EAE induction, HHV6^{+}EAE marmosets exhibited accelerated and more aggressive clinical disease compared to controls, with significantly shorter survival times ($p=0.01$). HHV6^{+}EAE marmosets also had an earlier onset of brain lesions ($p=0.04$) and mounted earlier and more robust anti-myelin antibody responses.

Following HHV-6 inoculations, there was no detectable increase in serum anti-myelin antibodies, and no evidence of increased T cell responsiveness to myelin antigens, suggesting that a direct mechanism such as molecular mimicry was not underlying the observation of accelerated disease in the virus inoculated marmosets. However, we observed increased cellular immune responses in HHV-6-inoculated marmosets following the viral inoculations. These data suggest that EAE acceleration may have resulted from a more indirect mechanism of inflammatory-mediated blood brain barrier breakdown, possibly due to a viral 'priming' of peripheral immune cells.

This study provides an experimental counterpart to the fertile field hypothesis, which puts forth that autoimmune diseases may be induced and/or exacerbated by microbial infections, and provides mechanistic insights into the interplay of viral and autoimmune components, which are believed to be involved in the complex pathophysiology of MS.

STATUS

Graduate Student

AUTHORS

Emily Leibovitch

B. Caruso

P. Sati

J. Billioux

J. Guy

L. Xiaozhen

J. Lefeuvre

M. Schindler

A. Silva

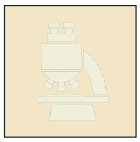
D. Reich

S. Jacobson

RESEARCH MENTORS/ DEPARTMENT CHAIRS

Steve Jacobson

David Leitenberg



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Micro-RNA and mRNA profiles associated with ectopic germinal center formation in thymus samples of patients with autoimmune myasthenia gravis

Myasthenia gravis (MG) is an autoimmune neuromuscular disorder caused by antibodies directed against proteins present at the post-synaptic surface of neuromuscular junction (NMJ). A characteristic pathology of patients with early onset MG is thymic hyperplasia with ectopic germinal centers (GC). However, mechanisms that trigger and maintain thymic hyperplasia are poorly characterized. Micro-RNAs (miRNA) are small, non-coding RNAs that are increasingly appreciated to be involved in the pathology of several autoimmune diseases. In order to determine the central mechanisms involved in the pathology, thymus samples from MG patients were assessed by histology and grouped based on appearance of GC compared to samples without them.

MiRNA and mRNA were evaluated using GeneChip® miRNA 4.0 Array and GeneChip® Human Transcriptome Array 2.0, respectively. Partek Genomic Suite 6.6 and Transcript Analysis Console 2.0 programs were used for further analysis. Thirty-four mature miRNA and forty eight annotated mRNA transcripts were identified that were differentially expressed between the two groups with greater than 1.5 fold difference in expression (ANOVA $p<0.05$). The cellular and molecular functions of the mRNAs involve cell death and cell survival, cellular proliferation, cytokine signaling and extra cellular matrix reorganization. The miRNAs identified are involved in cancer pathway. Reciprocal expression pairing of miRNA-mRNA was performed using Ingenuity Pathway Analysis (IPA) (QIAGEN). We identified 7 mi-RNA and mRNA pairs that are reciprocally regulated. One of the genes is Regulator of G protein Signaling 13 or RGS13 that is known to be expressed in GC B-cells and regulate responsiveness to chemokine signaling. Upregulation of RGS13 was found to be associated with specimens having GC and was paired with downregulation of miR-452-5p and miR-139-3p. We have identified other genes which may be important in the development of GC in MG thymus.

Our study shows that there is a distinct mRNA and miRNA expression pattern in the thymus and maintenance of autoimmunity is supported by regulatory pathways known to be involved in neoplasia.

STATUS

Postdoctoral Student

AUTHORS

Manjistha Sengupta

Bi-Dar Wang

Norman H. Lee

Gary Cutter

Linda L. Kusner

Henry J. Kaminski

RESEARCH MENTOR/ DEPARTMENT CHAIR

Henry J. Kaminski

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Acute Myopericarditis Due to Hepatitis E Virus Infection: The First Reported Case in the Western Hemisphere

INTRODUCTION

Hepatitis E is a single stranded RNA virus endemic to parts of Asia and Africa. Presentation ranges from asymptomatic to fulminant hepatic failure. Extrahepatic manifestations include acute pancreatitis, Guillain- Barre syndrome, neuralgic amyotrophy, hemolytic anemia, thrombocytopenia, glomerulonephritis, and mixed cryoglobulinemia [2]. Believed to be transmitted via the fecal-oral route, it has a short prodromal phase, and a self-limited symptomatic period lasting days to weeks [3] [4] Hepatitis E is a common cause of acute hepatitis in the world, but it is uncommon in the United States where it has typically been encountered in patients returning from developing countries or after consumption of undercooked pork.

Here we report a case of HEV-associated myopericarditis which we believe to be the first involving a patient who lives and travels in the western hemisphere. Our patient's disease was relatively mild. The other reported cases of HEV-myocarditis have occurred in India and in patients with severe illness [5].

CASE REPORT

A 50-year-old woman with history of Gilbert syndrome presented to our hospital with a two-day history of chest pain, palpitations, dyspnea on exertion, and a single syncopal episode. She had felt chilled but denied fever, abdominal pain, nausea, vomiting, icterus, jaundice, and any change in stool or urine color. She had returned from a two-week trip to Panama ten days earlier and noted a period of rhinorrhea and malaise while she was there. During the trip, she spent time in the rainforest, pastures, and cities. She denied any contact with live mammals. She had not used any medications, supplements, or herbal preparations. She denied alcohol and drug abuse. Physical exam was notable for mild, fluid-responsive hypotension and a pericardial friction rub. She was free of rashes, arthritis, and fever.

Laboratory studies included an elevated Troponin I at 1.32ng/mL (reference range 0 – 0.034) and creatinine phosphokinase MB of 5.4ng/mL (reference range 0-2.3). An electrocardiogram revealed generalized PR segment depression. Echocardiography demonstrated a small pericardial effusion. (Figure 1) Computed tomography ruled out pulmonary embolism. These findings support a diagnosis of myopericarditis. In addition, she was also noted to have elevated transaminases (serum AST 292 units/L, ALT 307 units/L) and bilirubin 1.7mg/dL (all unconjugated). Laboratory values are shown in table 1. A sonogram of the right upper abdomen showed a normal liver and gallbladder. Assays for hepatitis A, B, and C were negative as were those for cytomegalovirus and coxsackie A virus.

The patient was treated for myopericarditis with non-steroid anti-inflammatory drugs.. Her chest pain and dyspnea resolved and EKG changes normalized. Between her discharge and a follow up appointment two weeks later, positive results of an assay for immunoglobulin M directed against HEV were received. Her transaminase activity normalized and she was completely asymptomatic, so testing for HEV RNA was not obtained.

DISCUSSION

This is, to our knowledge, the only case of Hepatitis E myocarditis or pericarditis reported in the Western Hemisphere. Furthermore, it is the only reported case of myocarditis in the setting of a relatively minor HEV-related illness. While cardiac biopsy is the old standard, and cardiac MRI can be useful in the diagnosis, this patient had mild a mild course that did

continued on following page

STATUS

Medical Student

AUTHORS

Timothy Dougherty

Showkat Bashir

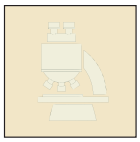
Mahmuda Khan

J. Adam

M.L. Borum

RESEARCH MENTOR/ DEPARTMENT CHAIR

Timothy Dougherty



continued from previous page

not justify invasive testing. Her cardiac troponin I was elevated, a finding that signifies myocarditis with 89% specificity [6].

The clinical presentation of myopericarditis is variable. While some cases are discovered incidentally, manifestations may range from pleuritic chest pain, decreased exercise tolerance, palpitations, and dyspnea to arrhythmia, dilated cardiomyopathy, and cardiogenic shock. Chest pain might be indistinguishable from ischemic pain; signs of myocarditis can mimic those of acute coronary syndrome. The development of concomitant pericarditis in the setting of myocardial inflammation is common [7].

Viral infection is the most common cause of myocarditis [7] [8] and viral hepatitides have been associated with myocarditis [9]. Theories of pathogenesis include viral cytopathic changes, activation of the innate immune system, TNF over-expression, dysregulation of helper and regulatory T lymphocyte populations, and molecular mimicry resulting in autoimmune cardiomyocyte damage [7] [10]. Hepatitis C virus in particular has shown evidence of cardiac tropism and has been shown to result in myocarditis and cardiomyopathies in patients with chronic hepatitis C [10]. A few cases of Hepatitis A-related carditis have also been reported [11] [12]. Three cases of Hepatitis E-associated myocarditis have been reported in India [5] [13]. All of those patients were male and were critically ill. It is not clear why this patient had such a mild course. One possibility is that different virus genotypes may produce milder disease. Although there is significant geographic overlap with respect to the genotype isolates, Genotype 3 is common in North America but not in India and is associated with milder disease [1]. Other potential explanations include variations in host immunity or environmental factors such as selenium deficiency or mercury exposures [7].

This case of a Western hemisphere traveler with Hepatitis E-associated myocarditis is unique and serves as a reminder that Hepatitis E should be considered in patients who present with elevated liver transaminases and that the virus, known to result in severe disease in South Asia, can have significant consequences in the West as well. It also reminds clinicians that myopericarditis and HEV infection may vary widely in terms of clinical severity; while the severe presentations of these illnesses may be life-threatening, establishing the diagnosis in a mild illness can be valuable and reassuring.

REFERENCES

1 Agarwal R and Naik S. Epidemiology of Hepatitis E: Current Status. *Journal of Gastroenterology and Hepatology* 2009;24:1484–1493.

2 Bazerbachi F, Haffar S, Garg SK, Lake JR. Extra-hepatic manifestations associated with hepatitis E virus infection: a comprehensive review of the literature. *Gastroenterology Reports* 2015: 1–15

3 Kamar N, Bendall R, Legrand-Abravanel F, Xia NS, Izopet J, Dalton HR. Hepatitis E. *Lancet* 2012;379: 2477-88.

4 Dalton HR, Stableforth W, Thurairajah P, Hazeldine S, Remnarace R, Usama W, Farington L, Hamad N Sieberhagen C, Ellis V, Mitchell J, Hussaini SH, Ijaz, S, Bendall RP. Autochthonous hepatitis E in Southwest England: natural history, complications and seasonal variation, and hepatitis E virus IgG seroprevalence in blood donors, the elderly and patients with chronic liver disease. *Eur J Gastroenterol Hepatol* 2008;20:784-90.

5 Premkumar M, Rangegowda D, Vashishtha C, Bhatia V, Khumuckham JS, Kumar B. Acute Viral Hepatitis E Is Associated with the Development of Myocarditis. *Case Reports Hepatol*. 2015; 2015: 458056.

6 Smith SC, Ladenson JH, Mason JW, Jaffe AS. Elevations of cardiac troponin I associated with myocarditis: experimental and clinical correlates. *Circulation* 1997;95:163-168

7 Cooper LT. Myocarditis. *N Engl J Med* 2009, 360:1526-1538

8 Pollack A, Kontorovich AR, Fuster V, Dec GW. Viral myocartitis-diagnosis, treatment option, and current controversies. *Nat Rev Cardiol*. 2015 Jul21.

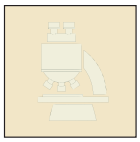
9 Omura T, Yoshiyama M, Hayashi T, Nishiguchi S, Kaito M, Horiike S, Fukuda K, Inamoto S, Kitaura Y, Nakamura Y, Teragaki M, Tokuhisa T, Iwao H, Takeuchi K, Yoshikawa J. Core protein of hepatitis C virus induces cardiomyopathy. *Circ Res* 2005 Feb 4;96(2):148-50.

10 Sanchez MJ, Bergasa NV. Hepatitis C associated cardiomyopathy: potential pathogenic mechanisms and clinical implications. *Med Sci Monit.* 2008;14:RA55–63.

11 Yazu T, Miyata Y, Matsuura H, Kimura H, Koga S. A case of hepatitis A accompanied with acute myocarditis. Nihon Shokakibyo Gakkai Zasshi. 1988 Jun;85(6):1304-7.

12 Jagtap R, Sethi R, Jeloka T. Hepatitis A leading to myocarditis. J Assoc Physicians India. 2008 May;56:391-2.

13 Goyal B. K., Mishra D. K., Kawar R., Kalmath B. C., Sharma A., Gautam S. Hepatitis E associated myocarditis: an unusual entity. *Bombay Hospital Journal*. 2009;51(3):361–362.



SCHOOL OF MEDICINE AND HEALTH SCIENCES

SPP1 gene polymorphisms and response to glucocorticoid treatment among myasthenia gravis patients

Oral glucocorticoids (GCs) are the primary therapy for patients with myasthenia gravis (MG). However, wide inter-individual variability exists in treatment response. A cohort of 250 MG subject treated with GCs were involved, and 12 polymorphisms in secreted phosphoprotein 1 (*SPP1*) gene were longitudinally evaluated for the contribution of response to the initial 3 months of GCs therapy. Improvement ≥ 3 units of Quantitative MG score (QMGS) change for patients with QMGS > 16, ≥ 2 units of QMGS change for patients with QMGS between 2 to 16 or QMGS after treatment becoming zero was judged as being sensitive to GC. The gene product of SPP1, osteopontin (OPN), plasma levels were assessed among MG subjects in relationship clinical parameters including *SPP1* genotype. No differences were observed for the allele distribution between GC sensitive/insensitive groups but the rs11728697 C/T + T/T genotypes were more frequent in the GC insensitive group compared to the GC sensitive group (100% versus 64.6%), indicating an association of rs11728697*T allele with GC insensitivity ($p_{dominant}$ = 0.018; OR = 1.065). One risk haplotype (AGTACT) was identified (p = 0.003, OR = 5.81) in the GC insensitive group compared with GC sensitive group. Mean OPN levels were higher among MG subjects (68.3 ± 43.0 ng/ml) compared to healthy controls (50.2 ± 38.7 ng/ml; p = 0.013). There was no association between OPN concentrations and the GC sensitive haplotypes. The genotypes and the haplotype with rs11728697*T allele in *SPP1* gene were identified to be associated with insensitivity to GCs treatment and elevations in OPN plasma levels were found in the population of MG subjects. OPN may contribute to MG pathogenesis and treatment response in a select population of MG patients.

STATUS

Staff

AUTHORS

Yanchen Xie

Hai-Feng Li

Liang Sun

Linda L. Kusner

Shuhui Wang

Yunxiao Meng

Xu Zhang

Henry J. Kaminski

RESEARCH MENTOR/ DEPARTMENT CHAIR

Henry J. Kaminski

NEUROSCIENCE

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Site-specific modulation of the glial scar following cortical stab wound

Reactive astrocytosis and the subsequent glial scar is ubiquitous to injuries of the central nervous system, and primarily serves to protect against further damage, but is also a prominent inhibitor of neuronal regeneration. Manipulating the glial scar following injury has been extensively studied as a means to enhance neuronal regeneration and promote recovery. Previous work has shown that immediate ablation of proliferating astrocytes following injury to the CNS results in leukocyte infiltration and neuronal degeneration. Our work builds on these results, by introducing both spatial and temporal control of astrocyte apoptosis using a mouse model of inducible caspase-9 activity under the mouse GFAP promotor (GFAP-iCP9). Using a cortical stab wound, we tested both immediate and delayed ablation of astrocytes in the vicinity of the injury using chemical inducer of dimerization (CID). Both treatments have resulted in localized ablation of astryctes, but contrary to previous work there was reduced microglial response in both treatment groups. However, only delayed ablation of astrocytes had a protective effect on hippocampal CA1 neurons. Taken together, our results show that an immediate astrocytic response is essential in protecting the injury site, but subsequently serves to limit neuronal survival, partly because of a heightened inflammatory response.

STATUS

Resident

AUTHORS

Mohammad Abu-Rub

Reshmi Tognatta

Molly T. Karl

Robert H. Miller

RESEARCH MENTOR/ DEPARTMENT CHAIR

Robert H. Miller

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Diffusion Tensor Imaging in Ornithine Transcarbamylase Deficiency

The Urea Cycle Disorders (UCDs) are a relatively common (1:8200) group of inborn errors of ammonia metabolism. They have been correlated with a wide range of neurological deficits ranging from mild, nonverbal learning disabilities in heterozygote carriers to coma and death in children with severe deficits in enzymatic function. While severe disease can cause changes visible with normal T1 and T2 MRI, nonverbal learning deficits correlate best with white matter (WM) changes and cannot be detected by T1 or T2 imaging. Diffusion Tensor Imaging (DTI) is an imaging modality used to study WM integrity by analyzing the anisotropic (nonrandom) diffusion of water in the brain.

In this study DTI was used to characterize and further investigate WM changes in patients with partial ornithine transcarbamylase (OTC) deficiency, the most common UCD. The latest edition of TORTOISE, a rigorous program for DTI analysis developed by the Basser/Pierpaoli Lab at the NICHD of the NIH, was used to compare these images with a control group. Preliminary results show qualitative WM differences in the region of the optic radiation. Further DTI characterization of the WM changes seen in UCDs may provide an additional metric for evaluating the efficacy of various treatments for these disorders.

STATUS

Medical Student

AUTHORS

Emil Barkovich

Andrea Gropman

RESEARCH MENTOR/ DEPARTMENT CHAIR

Andrea Gropman

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Effects of low-frequency stimulation of anterior piriform cortex on kainate-induced seizures in rats

RATIONALE

Recent evidence in animals and humans suggests that low-frequency stimulation (LFS) has significant antiseizure properties. The anterior piriform cortex (APC) has been demonstrated to be a highly susceptible seizure-trigger zone, and may be critical for the initiation and propagation of seizures originating from cortical and limbic foci. We studied the effect of LFS of the APC on seizure frequency, severity, and duration in the kainate seizure model in rats.

METHODS

Adult Sprague-Dawley rats (n=7; Hilltop Lab Animals Inc, Scottdale, PA) were implanted with tripolar electrodes in the left APC, and recording electrodes bilaterally in the hippocampal CA3 regions. Rats were monitored continuously with video-EEG for the emergence of spontaneous recurrent seizures after induction of status epilepticus by intraperitoneal kainic acid injections (KA). After emergence of spontaneous seizures, animals underwent 2 weeks of baseline recordings to determine seizure frequency and duration. Then, LFS of the APC was applied 60-min on, 15-min off, for two weeks with 1 Hz biphasic square waves, each 0.1 ms in duration, at 200 μA. Another period of 2 weeks of video-EEG monitoring was done after the cessation of LFS. Changes in total and severe seizure frequency, between baseline, LFS, and post-LFS were analyzed using random effects Poisson regression model with a random intercept. Also We analyzed changes in seizure duration by using a random effects model based on log.

RESULTS

During LFS, seizures decreased by 37% compared with the baseline, but this was not significant. Between post-LFS and baseline, where there was a 95% reduction in the rate of seizure frequency (p=0.003). Additionally, there was an absence of severe seizures during the post-LFS period in relation to baseline. There was a 17 second decrease in median total seizure duration during LFS compared to baseline with a p-value trending toward significance (p=0.065). During the post-LFS period, only one seizure was recorded.

CONCLUSIONS

Electrical stimulation for treatment of epilepsy has shown limited benefit when compared to remarkable benefits in other neurologic and psychiatric disorders. While LFS has been underutilized, our findings suggest that LFS of the APC significantly reduced the severity and frequency of seizures in a well studied animal model, and to have a lasting carry-over effect.

SOURCES OF FUNDING

The study was made possible by the startup funds from the George Washington University and pilot grant from Clinical and Translational Science Institute at Children's National. Both sources of funding are for MZK.

STATUS

Postdoctoral Student

AUTHORS

Arezou Bayat

M.D. Skopin

M. Siddu

K. Tsuchiya

S. Joshi

S. Jahan

P. Connell

M.Z. Koubeissi

RESEARCH MENTOR/ DEPARTMENT CHAIR

Henry Kaminski

NEUROSCIENCE

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Localized, Ubiquitous Cell Ablation as a Novel, Non-Traumatic Model for Brain Atrophy

The ability to selectively ablate cells in the central nervous system (CNS) based on their gene expression profile has been a useful tool in studying many forms of neurological disease. In previous studies, we have shown that we can locally or systemically ablate cells using a combination of a transgenic mouse line and a chemical inducer of dimerization (CID) to manipulate the caspase-9 mediated apoptotic pathway, thus producing cell death through activation of an inducible caspase-9 (iCP-9) signaling cascade. Our current study builds upon our previous model by making use of a site-specific transgene, the cytomegalovirus gene (CMV), as opposed to a random gene insertion, to allow for ubiquitous expression throughout the genome. By driving the CMV gene via a Cre-recombinase transgenic line and crossing it with our iCP-9 flox animal, we have engineered a transgenic mouse that globally expresses our transgene of interest on which to test the utility of chemically induced dimerization as an experimental model for controlling localized cell death.

In order to experimentally test the efficacy of our system for inducing cell ablation *in vitro*, we prepared primary brain cell cultures from individual CMVcre; iCP9 transgenic and wild type mice at P2 and P3. Our data shows that within 24 hours of CID treatment, significant cell loss is detectable in cmvcre-iCP9 transgenic cultures, but not in wild type cultures. We have also shown, *in vivo*, that with direct injection of CID into the cerebellum of both adult (4 months) and developing animals (2 weeks), we can drive a localized region of complete cell death at just 2 days post injection. Therefore, our data demonstrates that the caspase-9 mediated apoptotic pathway can be manipulated using a chemical inducer of dimerization to induce localized, ubiquitous cell ablation in CMVcre; iCP-9 transgenic mice. These preliminary data suggest that our unique transgenic approach to controlling cell death may serve as a useful non-traumatic and non-immune-mediated alternative model for studying traumatic brain injury.

STATUS

Staff

AUTHORS

Kathryn Burke

Molly Karl

Kristy Ortega

Robert H. Miller

RESEARCH MENTOR/ DEPARTMENT CHAIR

Robert H. Miller

NEUROSCIENCE

COLUMBIAN COLLEGE OF ARTS AND SCIENCES

LabNIRS: A Spectroscopic Window to the Brain

In the summer of 2015, a study (by Nichole Cubbage) was conducted by making a test subject tap their right finger off and on for about 30 seconds. After only LabNIRS and MRI measurements were taken, a fusion software was used to merge the two kinds of images. We then later measured the same activity on EEG and compared the results. When one of the right fingers were moving, images recorded activity taking place in the left hemisphere of the brain. Oxygen in the cerebral blood increased in addition to the amount of electrical signals recorded by EEG.

LabNIRS contributes to significant areas of research in the studies of things like Alzheimer's disease, Schizophrenia, and stroke rehabilitation. The brain-function imaging system utilizes near-infrared light lasers to penetrate the cranium and measure oxygenated and deoxygenated hemoglobin in addition to the rate of change between the two within the brain.

LabNIRS has 80 fiber optic cables (40 pairs, 142 channels), each cable contains a near-infrared laser and photomultiplier which converts the light scattering and absorbing measurements into electrical signals. Prior to this version of an fNIRS system, spatial and temporal resolution were not as clear as most machines only used about 20 pairs of cables at the very most. More fiber optic cables and near-infrared lasers means reception of a denser, higher resolution image that captures even the faintest signals, thanks to the photomultiplier. Not only does LabNIRS have a higher quality imaging system, but it is also faster than many other systems that have come before it, specifically when it comes to measuring blood flow. LabNIRS is capable of recognizing things more efficiently in nearly every respect!

I would simply like to present the research I did this summer to inform the public about this kind of imaging. While I will share my personal experiments (brain measurements on musicians with sight-reading versus rehearsed music, etc). I also intend to inform attendees of how EEG, MRI, and LabNIRS can work together to truly be a window to the brain.

STATUS

Undergraduate Student

AUTHOR

Nichole Cubbage

RESEARCH MENTOR/ DEPARTMENT CHAIR

Joe Barrera

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Endoscopic, Transnasal, Transclival Approach to Pontine Cavernomas: A Case Report and Review of the Literature

The authors report a case of a 21-year-old male who initially presented to the emergency department with right sided hemiparesis. Subsequent MRI showed hemorrhage from a venrally located pontine cavernoma and the patient underwent a retrosigmoid craniotomy. Post-op imaging revealed a large developmental venous anomaly (DVA) immediately adjacent to the resection cavity and appeared to reveal a gross total resection. Approximately ten months post-op the patient presented with acute severe right sided hemiparesis with MR imaging revealing re-hemorrhage within the prior resection cavity concerning for residual cavernoma with the DVA located immediately adjacent to the hemorrhage. Given the anterolateral location of the lesion and the need for visualization of the DVA on re-resection, an endoscopic, endonasal, transclival approach was taken. This approach provided direct visualization of the lesion and the DVA allowing for a gross total resection without injury to the DVA. This approach should be considered as an alternative to conventional neurosurgical approaches for these types of lesions in carefully selected patients.

STATUS

Medical Student

AUTHORS

Nick Erickson

Cristian Gragnaniello

Alan Siu

Zachary Litvack

Jonathan H. Sherman

RESEARCH MENTOR/ DEPARTMENT CHAIR

Jonathan H. Sherman

INSTITUTE OF BIOMEDICAL SCIENCES

Environmental Enrichment Promotes Generation of Oligodendrocytes and Attenuates Hypoxia-Induced Perinatal White Matter Injury

Hypoxic damage to the developing brain sustained as a consequence of preterm birth is associated with permanent neurodevelopmental disabilities. This oxygenation failure predisposes preterm infants to white matter (WM) injury and is associated with many anatomical changes, the most distinctive of which is damage to the periventricular WM. This diffuse WM injury results in the loss of glial cells and causes a significant disruption in myelination, which leads to cognitive and behavioral impairments throughout childhood. However, the mechanisms underlying glia susceptibility and altered WM development as well as the potential for functional recovery from hypoxic injury are not fully understood. Here, we focus on utilization of an enriched environment to attenuate the effects of perinatal hypoxia (HX) on WM development.

Environmental enrichment (EE) is a noninvasive combination of social and physical enhancement of surroundings that provides mammals with more complex social interactions, exposure to novel stimuli, and an opportunity for voluntary physical activity. Previous studies demonstrated that the environment affects both neural plasticity and functional recovery after brain injury. Furthermore, social, family, and environmental factors contribute to improved cognitive outcome of premature children. Therefore, the environment plays a crucial role in promoting functional recovery in the CNS, and may play a role in the repair of developing WM after HX injury.

Data obtained using an established rodent model demonstrate that EE ameliorates the effects of perinatal HX and enhances oligodendrocyte regeneration after injury. Further, EE improved performance on a WM-specific behavioral task. Interestingly, EE did not have a WM effect on mice maintained under normal physiological conditions, but did induce hippocampal neurogenesis in a set of normoxic control experiments. *This project will test the hypothesis that the resultant oligodendrogenesis and behavioral improvement seen following HX and subsequent EE will lead to enhanced myelination.* Control experiments will be performed to determine the relative individual contributions of locomotor activity and increased socialization. Also, we will investigate alternate paradigms of EE to determine whether critical periods of exposure and recovery exist.

While considerable progress has been made in identifying and modulating the mechanisms involved in premature brain injury, additional research is needed. The proposed study will not only shed light on the cellular and molecular mechanisms of WM injury, but will also aid in the development of new therapeutic approaches for enhancing recovery after early postnatal hypoxic injury during critical periods of neurodevelopment.

STATUS

Graduate Student

AUTHORS

Thomas Forbes

Beata Jablonska

Vittorio Gallo

RESEARCH MENTOR/ DEPARTMENT CHAIR

Vittorio Gallo

CHILDREN'S NATIONAL MEDICAL CENTER

Behavioral analysis of the effects of hyperammonemia in NAG-S knock-out mice

BACKGROUND

Hyperammonemia is the most serious metabolic disturbance resulting from defects in urea cycle enzymes because of central nervous system toxicity. Ammonia (NH3) readily crosses the blood brain barrier and saturates its removal pathway in astrocytes. High levels of ammonia impair the potassium buffering within the astrocytes and over activates the Na+-K+-2CL- cotransporter 1 in the neurons. High extracellular potassium impairs cortical inhibitory activity causing an overall hyperexcitability of cortical circuits.

OBJECTIVE

Hyperexcitability results in seizures which are one of features occurring as a result of hyperammonemia. A mouse model allows us to determine the possible mechanism of CNS damage and protection under these conditions. A previously developed mouse model created through the targeted deletion of the N-acetylglutamate synthase gene. This mouse develops hyperammonemia which can be prevented by dosing animal with N-Carbamoyl-L-glutamic acid in the drinking water. This withdrawal of Carbaglu from the drinking water results in death.

METHODS/DESIGN

Our study compared mice after Carbaglu withdrawal in the presence and absence of Memantine to determine its effectiveness in neuroprotection from hyperammonemia. We reviewed the video records from those two studies to quantify behavioral seizures in mice after medication withdrawal and subsequent demise of the animal. Then, we graded the seizure occurred.

RESULTS/DISCUSSION

Our result showed that 36% of the NAGS-/- mice (25% of the total number) had seizures with average grade of 4.6 on Racine scale. Average time interval between medication withdrawal to seizure of 17.2 hours. Death rate among the mice was 60.5% among NAGS-/- animals (40% of the total number). The interval between Carbaglu withdrawal and death was 17.7 hours. We showed no significant difference for the Memantine group in the activity decline over time before and after Carbaglu withdrawal. Actually, the non-Memantine group performed better. This observation may indicate that Memantine is not effective in CNS protection against hyperammonemia in urea cycle patients. Our next step will be exploring more target compounds to prevent hyperammonemia toxicity in the brain.

STATUS

Postdoctoral Student

AUTHORS

Saddiq Habiballah

Elena Pumbo

Yoon Jang

Judy Liu

Ljuba Caldovic

RESEARCH MENTOR/ DEPARTMENT CHAIR

Judy Liu

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Military Personnel Who Sustain a TBI Have Elevated Concentrations of Aβ40 and Lower Ratios of Aβ42/40 in Peripheral Blood

Blunt and blast traumatic brain injuries (TBI) are devastating medical conditions that are prevalent in civilian and military populations, respectively. While these injuries can be mild, moderate, or severe, long-term physical, cognitive, and psychiatric sequelae are suffered across all levels of severity and significantly impact quality of life. Extensive research has been conducted on biomarkers in peripheral blood after TBI, in an effort to identify and ultimately manage medical care by prophylactically treating patients at-risk for developing chronic deficits following TBI. We recently investigated another potential peripheral biomarker for TBI and found that chronic symptoms of TBI were linked to elevated concentrations of tau, one of the two hallmark proteins in Alzheimer's disease (AD). This similar pathology between TBI and AD led us to question the role of amyloid beta (Aβ), the other hallmark protein in AD, in the development of chronic symptoms following TBI.

This study assessed 71 U.S. military personnel, all of whom had been recently deployed. Blood samples were collected and analyzed for concentrations of Aβ40 and Aβ42 using Simoa, an ultrasensitive, single-molecule immunoassay. Symptomatology of depression, post-traumatic stress disorder (PTSD), and post-concussive disorder (PCD) were assessed by the Quick Inventory of Depressive Symptomatology, the PTSD Checklist Military Version, and the Neurobehavioral Symptom Inventory, respectively. Subjects with a history of TBI (TBI+) were compared to those without a history of TBI (TBI-). TBI+ subjects (n=53) were identified by either self-reporting a TBI on the Warrior Administered Retrospective Casualty Assessment Tool or by having a documented TBI in their medical record, while TBI- subjects (n=18) were classified as controls.

In TBI+ subjects as compared to controls, concentrations of Aβ40 were significantly higher ($F_{1,68}$=6.95, p=0.01), and concentrations of Aβ42 tended to be higher ($F_{1,64}$=2.98, p=0.09). Additionally, the ratio of Aβ42/40, a ratio that studies suggest better reflects the production of brain amyloid, was significantly different between the groups ($F_{1,62}$= 5.67, p=0.01), with the ratio significantly lower in the TBI+ group. The TBI+ group reported significantly more symptoms of depression, PTSD, and PCD, and when controlling for depression and PTSD, concentrations of Aβ40 ($F_{1,68}$=3.32, p=0.03) and the ratio of Aβ42/40 ($F_{1,62}$= 5.01, p=0.03) remained significantly different between the two groups. The elevated concentrations of Aβ40 and lower ratios of Aβ42/40, consistent with findings in patients with AD, suggest that alterations in Aβ may relate to the development of chronic sequelae after TBI and that Aβ may be a potentially useful biomarker.

STATUS

Medical Student

AUTHORS

Morgan Heinzelmann

Natasha Lejbman

Anlys Olivera

Rebekah Feng

Sijung Yun

Hyung-Suk Kim

Jessica Gill

RESEARCH MENTOR/ DEPARTMENT CHAIR

Jessica Gill

NEUROSCIENCE

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Allopregnanolone treatment for diffuse white matter injury in the preterm cerebellum

Diffuse white matter injury (DWMI) is observed in the majority of premature birth survivors who have neurological impairments. One factor in this injury may be the abrupt early loss of exposure to important placental hormones, especially when combined with hypoxia, inflammation and other insults. We used an animal model of preterm DWMI induced by postnatal chronic hypoxia to investigate the effects of allopregnanolone (ALLO), a neuroactive hormone made in the placenta and then the brain, on the cerebellar white matter. Specifically, we used ALLO to study the cellular mechanisms underlying DWMI and to test its potential in treating hypoxia-induced DWMI. ALLO did not recover cerebellum volume or white matter cerebellum volume, but ALLO-treated hypoxic animals demonstrated improved cerebellar function compared to hypoxic controls. ALLO remains as a potential therapeutic agent for preterm brain injury, but additional work is needed to fully understand its mechanistic actions and to optimize its course of treatment.

STATUS

Graduate Student

AUTHOR

Kyung-Min Lee

RESEARCH MENTOR/ DEPARTMENT CHAIR

Anna Penn

INSTITUTE OF BIOMEDICAL SCIENCES

Amygdala neural development mechanisms are linked to innate social and non-social behaviors during adulthood

Innate behaviors for fight, flight and reproduction are essential for species survival and propagation. As these innate behaviors manifest without prior training, there must be embryonic developmental mechanisms that specify these circuits. The medial amygdala (MeA), as a major target for olfactory inputs, has been implicated in the regulation of these innate behaviors. I aim to elucidate how embryonic transcription factors generate distinct neuronal subpopulations that regulate diverse social and non-social innate behaviors. During amygdala development there are at least two neuronal progenitor pools that contribute to MeA neuronal diversity. We focused on two embryonic progenitor populations that are marked by the expression of the transcription factors: *Dbx1* and the autism susceptibility gene *Foxp2*. We found that neuronal progenitors expressing the transcription factors *Dbx1* or *Foxp2* will become two distinct non-overlapping adult MeA neuronal subpopulations. These two populations express different molecular markers and possess distinct intrinsic electrophysiological properties. Furthermore, *Dbx1*-derived and Foxp2+ MeA neurons were activated during distinct innate behaviors involved in reproduction, aggression and predator avoidance. Therefore, activation of distinct neuronal subpopulations during key social and non-social behaviors are linked to transcription factor expression during development. Thus, future research should focus on how alterations in embryonic transcription factor expression can lead to social disorders characterized by amygdala based behavioral deficits, such as autism.

STATUS

Graduate Student

AUTHORS

Julieta Lischinsky

Katie Sokolowski

Peijun Li

Shigeyuki Esumi

Yasmin Kamal

Livio Oboti

Meredith Goodrich

Timmothy Hammond

Judy Liu

Joshua Corbin

RESEARCH MENTOR/ DEPARTMENT CHAIR

Joshua Corbin

NEUROSCIENCE

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Retinoic Acid Signaling in Embryonic Stem Cells

This project aims to improve our understanding of how embryonic stem cells (ESCs) are induced to form neurons, which is central for developing methods for using ESCs in repair and regeneration. It is known that retinoic acid (RA) signaling promotes neural differentiation of pluripotent stem cells; however, it is not clear when and where this occurs—does RA directly induce neurons from the ESCs themselves, or does it promote the proliferation or differentiation of an intermediate subtype of neural-specific stem cell. To assess this question, DNA constructs were made using destabilized green fluourescent proten (dGFP) that will allow us to observe the differentiation of embryonic stem cells (ESC) into neurons in real time. We made three constructs to allow for labeling of ESC as they mature into neurons. The first and second constructs express GFP and destabilized GFP respectively, and include a neomycin cassette for cell selection. The third uses a conditional variant of Cre (CreERT) that was transfected in combination with a reporter (floxed tdTomato) and a hygromycin cassette for selection. When Tamoxifen is added, the activated Cre will activate the tdTomato reporter, labeling RA activated cells and their progeny. These experiments have been initiated and results from these transfections are forthcoming. If successful, we can define the lineage relationship between RA-activated cells and mature neurons. Understanding how pluripotent stem cells become neurons also has implications for tumorogeneisis, specifically the uncontrolled proliferation in glioblastoma, which is critical for developing new treatments and to guide neurosurgical intervention.

STATUS

Medical Student

AUTHORS

Erin McCormack

Thomas M. Maynard

Beverly A. Karpinski-Oakley

Anthony LaMantia

RESEARCH MENTOR/ DEPARTMENT CHAIR

Anthony LaMantia

NEUROSCIENCE

COLUMBIAN COLLEGE OF ARTS AND SCIENCES

Effects of Essential Oil on Fear Memory and the Immune Response; A Potential Alternative Therapy for Post-Traumatic Stress Disorder (PTSD)

Stress and anxiety-related mental health disorders such as post-traumatic stress disorder (PTSD) are on the rise. Stress is known to modify the immune system and the balance of the autonomic nervous system. Despite the growing literature on immune system changes associated with direct stressors, the relationship between fear memory and the immune system has not been well characterized. Moreover, there are only two FDA-approved medications for PTSD. Orange essential plant oil (OEPO) has been previously found to have CNS depressant-like effects in mice. Therefore we examined the effects of OEPO on fear memory and immune cell activation in a mouse model of PTSD (Pavlovian Fear Conditioning). The treatment group (n=8) was administered 25% OEPO via olfactory exposure prior to and after fear conditioning. Mice exposed to 25% OEPO showed no difference in percent freezing during fear acquisition compared to controls. However, when tested for extinction retention 48 hours later the treatment group experienced a 17.21 ± 1.58 % ($p < 0.01$) significant decrease in freezing behavior versus control (3.67 ± 2.13%), suggesting that OEPO affects extinction of fear memory in mice. This appears to be independent of a shift in immune cell activation as treatment and control mice showed similar levels of splenocyte derived naïve / effector lymphocytes and antigen presenting cells. Both groups however showed increased levels of naïve T cells $CD62^{hi}CD44^{lo}$ 56.9(± 0.83)% relative to non-fear conditioned mice 46.3 (± 3.16)% ($p < 0.01$). These data suggest that OEPO enhances extinction of fear memory while its affects on the immune system remain unclear.

STATUS

Undergraduate Student

AUTHORS

Cassandra Moshfegh

Lauren Hopkins

Adam Swiercz

Hurr Chansol

Colin Young

Paul Marvar

RESEARCH MENTOR/ DEPARTMENT CHAIR

Paul Marvar

SCHOOL OF MEDICINE AND HEALTH SCIENCES

A Rare Disease, But a Costly One: The Case of Myasthenia Gravis

Myasthenia gravis (MG) is a chronic, autoimmune neuromuscular disorder affecting fewer than 200,000 individuals in the United States. Disease management is primarily outpatient, but disease exacerbations leading to hospital admission occur in upwards of a third of patients. We sought to determine the inpatient cost of care and assess changes over a 10 year epoch.

Our cohort was identified from the Nationwide Inpatient Sample database for the years 2003 through 2013 using the ICD-9-CM codes. We compared MG to a more common chronic neurological disorder, multiple sclerosis (MS), in which patients also require episodic hospitalizations and to the total US discharges.

Total costs of MG inpatient care costs rose by 13 fold during the study period to $546,834,101. In contrast, MS and all inpatient costs doubled. The increase was largely accounted for by an increase in patient discharges for MG from 870 to 5,353, while MS discharges were close to flat and total discharges dropped. Per discharge costs rose from $48,024 to $98,795 for MG, $16,989 to $32,767 for MS, and $19,666 to 39,462 for all discharges. Length of stay for MG patients increased from 7.4 to 8.0 days while staying flat in the other groups. More discharges were appreciate in the 0-17 year and 85+ year age groups for MG patients in 2013. For MG patients, the percentage with private insurance decreased and number of uninsured MG patients increased in 2013 compared to 2003. Regional variations in cost were appreciated with greater rises in mean charges in the Midwest and South for MG out of proportion to MS and all hospital discharges.

A dramatic rise in hospital discharges for MG has occurred with considerable increase in cost to the health care system. This was largely driven by growth in patient discharges. Our data set does not allow us to identify reasons for this but may reflect an increase in the prevalence of MG, improved identification of patients, or an underlying change in practice patterns.

STATUS

Medical Student

AUTHORS

Jacklyn Omorodion

Jesse Pines

Henry J. Kaminski

RESEARCH MENTOR/ DEPARTMENT CHAIR

Henry J. Kaminski

NEUROSCIENCE

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Ablating oligodendrocytes in the optic nerve as a model to study demyelination

Multiple sclerosis (MS) is a neurodegenerative disease that affects the central nervous system (CNS) resulting in permanent neurological deficits. MS is characterized by inflammation and infiltration of the immune cells into the CNS and loss of oligodendrocytes (OLs) and myelination of axons resulting in the creation of multiple plaques in the white matter tracts. One of the first and most common clinical manifestations in MS patients is optic neuritis characterized by inflammation and demyelination of the optic nerve. The pathology of MS and optic neuritis is complex. It is unclear whether inflammation is a primary cause or a consequence of OL and myelin loss and whether the loss of axonal communication is due to inflammation or demyelination. Furthermore, the effects of demyelination on neuronal viability are unknown. To address these issues, a transgenic mouse line (MBP-iCP9) was created, in which apoptosis can be experimentally triggered using Chemical Inducer of Dimerization (CID)in mature OLs expressing myelin basic protein (MBP) without directly affecting other CNS cell types. In this study, intravitreal injection was utilized to deliver CID to the vitreous of MBP-iCP9 transgenic mice 2 weeks after birth. Our data shows that CID injection results in OL apoptosis and myelin disruption that is absent in wildtype littermates. Future studies will determine whether OL apoptosis and myelin loss would lead to inflammation, axonal damage, and retinal ganglion cell loss.

STATUS

Faculty

AUTHORS

Ahdeah Pajoohesh-Ganji

Molly Karl

Kathryn Burke

Robert H. Miller

RESEARCH MENTOR/ DEPARTMENT CHAIR

Robert Hawley

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Hypoxia Results in White Matter Immaturity in a Piglet Model of Congenital Heart Disease

Congenital heart disease (CHD) is the leading birth defect, affecting almost 1% of births each year. Full-term infants with CHD display subnormal brain development, underlying impairments in fine/gross motor skills, language, and memory. CHD infants have a high incidence of brain injury; partly due to insufficiencies in cerebral oxygen delivery in utero. Diffusion tensor imaging (DTI) studies have revealed that white matter (WM) immaturity is common in infants with CHD. Due to technical and ethical difficulties, the effects of CHD-induced brain injury on the cellular level remain elusive. To emulate insufficient cerebral oxygenation in CHD, we developed a porcine chronic hypoxia model and analyzed the microstructural and cellular effects of CHD on/in the corpus callosum (CC) with DTI and immunohistochemistry, respectively. Fixed porcine brains were imaged with a 3T-magnet at Johns Hopkins University. The cerebrum was isolated from DTI images using ROI Editor and fiber tracking was performed using DTI Studio. The primary antibodies used were PDGFR-α to label oligodendrocyte (OL) progenitors, CC1 to label mature OLs, Casp3 to label apoptotic cells, and Ki67 to label proliferating cells. To ensure an unbiased assessment, cell counts were performed using Stereology. DTI analysis demonstrated that hypoxia leads to a global reduction in the number and length of WM fiber tracts along with a decrease in fractional anisotropy-a metric of WM integrity and maturity. Immunohistochemical analyses revealed a 75% decrease in the density of apoptotic mature OLs and an 85% decrease in the density of proliferating OL progenitors in the CC following hypoxia ($p<0.05$). Together, these findings indicate an OL lineage-specific vulnerability to hypoxic exposure where OL progenitors fail to generate new OLs at a rate necessary for normal brain development. Hence, therapies aimed at restoring the regenerative capacity of resident OL progenitors within the CC offer promising avenues to improving neurological outcomes in the growing CHD population.

STATUS

Medical Student

AUTHORS

Angeline Pham

Paul D. Morton

Ludmila Korotcova

Jiangyang Zhang

Richard A. Jonas

Vittorio Gallo

Nobuyuki Ishibashi

RESEARCH MENTOR/ DEPARTMENT CHAIR

Nobuyuki Ishibashi

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Defining Brain Chemical Changes and Areas of the Brain Most Affected by High Ammonia Levels in Children with Urea Cycle Disorders

BACKGROUND

Urea cycle disorders are amongst the most common of the inborn errors of metabolism. These disorders affect up to 1/25,000 live births in the United States and the number of children affected by partial defects may be much higher[1]. Urea cycle disorders can lead to high rates of disability if not treated early. The urea cycle converts nitrogenous waste, a toxic byproduct of protein metabolism, into urea, a safe compound, which is excreted in the urine. Children with urea cycle disorders are unable to fully metabolize nitrogenous waste in the liver, resulting in high levels of ammonia in the blood. Hyperammonemia has well known neurologic sequelae. However, the structural and chemical consequences of high ammonia in the brain of a developing child have not been well defined. Furthermore, due to compartmentalization, ammonia levels in the blood do not correlate well with levels of ammonia in the brain. Additionally, patients that experience high brain ammonia levels are not always symptomatic.

OBJECTIVE

To define with magnetic resonance spectroscopy (MRS) how the chemical levels of N-acetylaspartic acid, glutamine, glutamate, creatine, choline, myoinositol, lactate, and lipids vary from the norm in a child experiencing hyperammonemia. An additional objective is to evaluate the brain magnetic resonance images (MRI) of these same patients to identify parts of the brain most affected by high ammonia levels.

METHODS

This was a retrospective study in which 8 patients with various genetic defects in the urea cycle were identified. A neuro-radiologist read the MRI and MRS data and the data were analyzed for similarities.

RESULTS

MRS data showed that brain levels of myoinositol are decreased in patients with hyperammonemia. Levels of lactate, glutamate, glutamine, and choline are increased. N-acetylaspartic acid may be either decreased or normal. Creatine and lipid levels remain normal. MRI data showed that areas of the brain affected by high ammonia are the peri-insular region, the globus pallidus, and the frontal, temporal, and parietal lobes. The thalamus, occipital lobe, corpus callosum, and brainstem were unaffected in these patients.

CONCLUSION

The findings in this small retrospective study indicate that there may be a distinct chemical footprint of changes that occur in the brain when ammonia levels are high. This suggests that MRS could be a better tool to evaluate the biochemical consequences of high levels of ammonia in the brain rather than a blood ammonia level. Furthermore, MRI data suggest that there are distinct regions of the brain that are more sensitive to the effects of hyperammonemia than others.

REFERENCES

1 Summar, Marshall L., Dries Dobbelaere, Saul Brusilow, and Brendan Lee. "Diagnosis, Symptoms, Frequency and Mortality of 260 Patients with Urea Cycle Disorders from a 21-Year, Multicentre Study of Acute Hyperammonaemic Episodes." *Acta Paediatrica (Oslo, Norway* : 1992). U.S. National Library of Medicine, n.d. Web. 25 Feb. 2016.

STATUS

Medical Student

AUTHOR

Chelsea Robinson

RESEARCH MENTOR/ DEPARTMENT CHAIR

Andrea Gropman

NEUROSCIENCE

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Concordance of Language Lateralization Between Task Paradigms in Wernicke's Area and Inferior Frontal Gyrus—an fMRI study

Studies have shown that when compared to more invasive methods, fMRI is an accurate predictor of language laterality by using blood flow changes in the brain as a surrogate indicator of brain activation. The determination of language dominance by fMRI is made possible by the use of language paradigms or tasks, which elicit signal changes in specific regions of the brain. Despite the aforementioned advancements in non-invasive language determination, what are lacking in the literature are studies aimed at identifying agreement between the various types of language tasks and language regions. In this study we compared four language tasks across two neuroanatomical regions of interest to analyze the concordance of language laterality between tasks in each region, as well as between regions during each task. Twenty-two right-handed healthy adult volunteers and seventy adult patients with partial epilepsy were scanned with a 3.0T General Electric between 2003 and 2015. Images were processed in SPM8. All subjects completed an auditory decision task (ADT), an auditory categorization task, a listening task and a reading task. Activation data were collected in the Inferior Frontal Gyrus (IFG) and Wernicke's Area (WA), each selected based on their essential roles in language and the high levels of lateralization they have exhibited in previous fMRI studies. Language laterality was characterized in terms of a calculated laterality index (LI), as well as the categorical label left, right, or bilateral. As expected, patients showed the highest levels of atypical language dominance. However, for both controls and patients, the LI and categorical laterality data showed a strong tendency toward left-lateralization, with ADT proving to be the most lateralizing in both regions. For both groups, ADT was also the task with the most IFG-WA concordance (95% of controls and 80% of patients). WA was the most lateralized and most concordant region across all task pairs for both groups. Highest levels of IFG-WA concordance were observed across the Listen/Read task-pair in controls (100%) and the ADT/AUDCAT task-pair in patients (64%). Control subjects had significantly higher levels of complete agreement across all four tasks in WA than patients (68% vs. 33%). Control subjects also had significantly higher levels of complete agreement across all four tasks in IFG than patients (59% vs. 31%). Going forward, assessing concordance of lateralization of these language tasks in other brain regions will benefit our understanding of the greater language network and how its individual components drive language processes.

STATUS

Medical Student

AUTHORS

Eric Strong

Xiaozhen You

William D. Gaillard

RESEARCH MENTOR/ DEPARTMENT CHAIR

William D. Gaillard

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Astrocytes are crucial for developmental myelination but contribute to pathology early in myelin repair

Astrocytes have been implicated in multiple aspects of oligodendrocyte development and myelination although their functions in modulating myelination and myelin repair *in vivo* remain controversial. Here we show that GFAP+ astrocyte ablation during early postnatal spinal cord development inhibited oligodendrocyte development and myelination, demonstrating a critical role for astrocytes in promoting CNS developmental myelination. By contrast, in the adult CNS, localized ablation of GFAP+ astrocytes two days after a demyelinating insult enhanced the numbers of spared myelinating cells in both the spinal cord and corpus callosum, demonstrating a critical role for astrocytes in contributing to CNS demyelinating pathogenesis. Microarray analysis reveals astrocytic NF-kB signaling pathway as a major contributor to the pathological events compromising myelin repair in the adult brain. Together these studies demonstrate functional heterogeneity in GFAP+ astrocytes that is temporally and regionally specific.

STATUS

Postdoctoral Student

AUTHORS

Reshmi Tognatta

Molly T. Karl

Robert H. Miller

RESEARCH MENTOR/ DEPARTMENT CHAIR

Robert H. Miller

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Non-invasive Blood Tests Predict Steatohepatitis But Not Liver Fibrosis in Patients with Morbid Obesity

More than 90% of patients with Morbid Obesity (MO) have Non-Alcoholic Fatty Liver Disease, complicated by Non-Alcoholic Steatohepatitis (NASH) in 10-15% with progression to fibrosis-cirrhosis in approximately 15%. Liver biopsy is the gold standard, but several non-invasive tests have shown an ability to predict severe liver fibrosis and NASH. The noninvasive blood tests have not been tested in patients with MO.

METHODS

Sixteen liver biopsies from MO patients undergoing gastric bypass surgery were studied retrospectively, identified from those previously assigned in random sequence to one of 5 stages of fibrosis (0- no fibrosis to 4- cirrhosis, based on histologic assessment). Inclusion criteria after EMR review were diagnosis of MO (BMI ≥ 40 kg/m^2) and availability of data concerning sex, age, BMI, Diabetes status, platelet count, AST, ALT and albumin within 3 months preceding surgery; exclusion criteria were no other potential causes of liver pathology. Diagnosis of NASH was by pattern of pathology and association with a NASH score of ≥4, based on content of fat (0-3), lobular inflammation (0-3) and balloon hepatocytes (0-2). Tissue sections were stained with Sirius red (SR), scanned as whole slide images from which 10-20 grid fields were randomly selected to measure collagen proportionate area (CPA) using Image J software. Noninvasive blood tests for significant fibrosis (stages ≥ 2) included NAFLD fibrosis, BARD, APRI and Fib4 scores, based on combinations of age, BMI, Diabetes, AST, ALT, platelets and albumin.

RESULTS

Sixteen liver biopsies from patients with MO met the study criteria, 11 had fatty liver. Patients were on average 50.3 yrs, BMI 47.5 and 56% female. Quantitation of fibrosis by SR image analysis showed significant fibrosis (stages ≥ 2-4) in 7/16 biopsies (43.7%) and 6 of these had steatohepatitis (37.5%), all with significant fibrosis. There was poor correlation between the non-invasive test results and stage of liver fibrosis: NAFLD and BARD scores correctly assigned fibrosis scores in only 8/16 and 9/16 cases, respectively; APRI and Fib4 predicted 0 cases with stage 3-4 fibrosis. Elevations of AST and ALT were, however, strongly predictive of steatohepatitis: one or both were elevated in 6/7 with steatohepatitis, only one other case had minimally elevated ALT.

CONCLUSIONS

Non-invasive markers for significant liver fibrosis (stage ≥ 2) are not able to predict the stage of liver fibrosis in patients with MO; however, elevation of liver enzymes is strongly correlated with the presence of steatohepatitis.

STATUS

Research Fellow

AUTHORS

Erum Alhumood

Anne Chen

Ahmed Alrajjal

Lakshmi Kammili

Patricia S. Latham

RESEARCH MENTOR/ DEPARTMENT CHAIR

Patricia S. Latham

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Use of modified human adipose tissue-derived mesenchymal stem cells as a new therapeutic strategy for obesity and diabetes treatment

Mesenchymal stem cells (MSCs) are multipotent cells with trans-differentiation capacity. High glucose (HG-25mM) promotes adipogenesis, accumulation of intracellular reactive oxygen species, upregulation of inflammatory genes, and decrease oxygen consumption rate (OCR) in MSCs. In this study, we investigated whether upregulation of antioxidant enzyme systems prevents those effects promoted by hyperglycemia condition (HG) in MSCs. To address this question we used GFP-tagged adenovirus constructs to upregulate superoxide dismutase (SOD1 and SOD2; mitochondrial and cytosolic, respectively) in human adipose tissue-derived MSCs. AdGFP viral construct was used as a control. After viral transduction, MSCs were exposed to HG up to 14 days or delivered intraperitoneally into diet-induced obese (DIO - 45% or 60% high fat diet) C57BL/6J mice presenting fasting blood glucose levels above 200 mg/dL. *In vitro* results showed that both SOD1 and SOD2 upregulation reduced intracellular superoxide anion presence and improved OCR, but SOD2 was the most efficient. In addition, the upregulation of IL-6 and TNFa was abrogated. The presence of mitochondrial complex I and II were also investigated and they both seemed to be reduced in presence of HG. However, SOD1 and SOD2 upregulation prevented that. *In vivo* results confirmed homing-in of eGFP labeled MSC to different inflamed fat pockets, particularly pericardial and omental fat by direct imaging. After 4 to 6 weeks, mice which received SOD2-MSCs presented a better response to glucose tolerance compared to SOD1 and GFP in both DIO models. PCR and histological analysis of fat depots as well as serum analysis are in progress to confirm reduction of local and systemic inflammation. In conclusion, adipogenesis, fat inflammation, and lower respiration observed in MSC exposed to hyperglycemia (HG) can be minimized by upregulation of superoxide dismutase, particularly mitochondrial. Besides, SOD2 upregulation improves glucose tolerance in DIO mice subjected to both 45% and 60% high fat diet. We believe that delivery of SOD2 using MSCs to the inflamed adipocyte depots may be a novel yet safe therapeutic tool to combat obesity associated diabetes and impaired glucose tolerance.

STATUS

Staff

AUTHORS

Cleyton Domingues

Nabanita Kundu

Neeki Ahmadi

Sen Sabyasachi

RESEARCH MENTOR/ DEPARTMENT CHAIR

Sen Sabyasachi

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Adipocyte-Derived Exosomal microRNA Changes Correlated to Insulin Signaling Improvements Following Bariatric Surgery

INTRODUCTION

More than one in every three U.S. adults in the United States is considered obese (body mass index >30kg/m^2). Obesity contributes to insulin resistance and the subsequent development of chronic metabolic diseases such as Type 2 diabetes. Adipose tissue is an active endocrine organ that plays a role in regulating metabolism. Recently, we demonstrated that adipose-derived exosomes, which are small extracellular vesicles actively secreted by adipose, are altered with obesity. Exosomes contain microRNAs that can control gene expression in distant organs, such as skeletal muscle. Extreme weight loss through bariatric surgery intervention is associated with many improvements in clinical measures such as insulin sensitivity, though the molecular mechanisms driving these improvements are poorly understood. This study hypothesized that bariatric surgery would change microRNA levels in adipocyte-derived exosomes in obese subjects after significant excess body weight loss, and that changes in exosomal microRNA expression after surgery would correlate to improvements in insulin sensitivity.

METHODS

Six obese African-American females, age 27 to 49, were recruited from a bariatric surgery program to participate in the study. Anthropometric measurements and blood samples were obtained two weeks prior to gastric bypass surgery (to avoid any pre-surgical diet effects) and one-year post surgery. Insulin resistance was estimated using the homeostatic model assessment (HOMA) calculation. Adipocyte-derived exosomes were extracted and isolated from the plasma and serum samples using fatty acid binding protein (FABP4) as a sensitive and specific marker for adipocyte-derived exosomes. RNA was extracted, amplified and analyzed using Affymetrix microRNA global microarrays. MicroRNAs affected by surgery and those correlated to clinical changes in insulin sensitivity were uploaded into Ingenuity Pathway Analysis software for biological pathway.

RESULTS

Surgery decreased insulin resistance one-year post-surgery with a 15% reduction in fasting plasma glucose ($p<0.001$) and a 74% reduction in fasting plasma insulin ($p<0.001$) from baseline. Following surgery, 292 mature microRNAs were found to be differentially regulated compared with pre-surgery baseline. After conservative filtering for known microRNAs with mapped mRNA targets, 29 microRNAs remained, targeting 4,266mRNAs. Pathway analysis identified the Insulin Receptor Signaling pathway as being enriched in our dataset (102/167 molecules in pathway represented in the current dataset; pathway p value= 1.41E^{-12}).

CONCLUSION

These data support a possible direct mechanism by which adipose tissue can cause dysregulation in peripheral tissues. Insulin related microRNAs are responsive to gastric bypass and were significantly correlated with improvements in insulin resistance.

STATUS

Graduate Student

AUTHOR

Mallory Epting

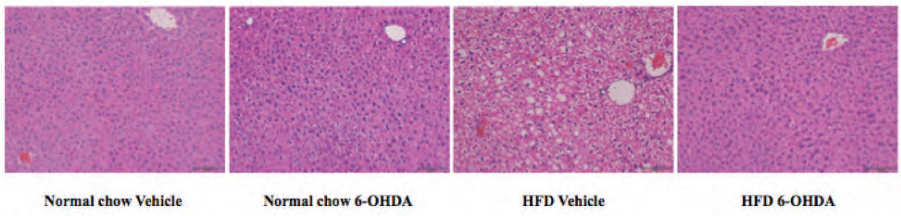
RESEARCH MENTOR/ DEPARTMENT CHAIR

Monica Hubal

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Sympathetic Overactivity Contributes to the Pathogenesis of Non-alcoholic Fatty Liver Disease During Diet-induced Obesity

Non-alcoholic fatty liver disease (NAFLD) is associated with the development of obesity and is a significant contributor to chronic liver, metabolic, and cardiovascular diseases. We have recently shown that hepatic sympathetic nerve activity is significantly elevated in mice fed a high fat diet (HFD; 33±2 vs. 63±5 spikes/s, normal chow vs. HFD; $p<0.05$), although the contribution of the sympathetic nervous system to NAFLD pathology remains unclear. Therefore, we tested the hypothesis that sympathetic overactivity contributes to NAFLD during diet-induced obesity. Male C57B1/6 mice were fed a HFD (60% fat) or normal chow (5% fat) for 15 weeks. 6-hydroxydopamine (6-OHDA, 150 mg/kg i.p.) was then administered to selectively destroy sympathetic nerves, or vehicle control (n=4/group), and mice were sacrificed 3 days later. 6-OHDA treatment did not influence body weight (e.g. 41±3 vs. 40±2 g; HFD-vehicle vs. HFD-OHDA; $p>0.05$) or visceral adipose tissue mass in normal chow or HFD fed animals. However, HFD resulted in significant increases in liver weight (1.0±0.1 vs. 1.8±0.1 g normal chow-vehicle vs. HFD-OHDA; $p<0.05$) and selective ablation of sympathetic nerves rescued HFD-induced hepatomegaly (1.3±0.2 g; $p>0.05$ vs. normal chow). In line with this, histological examination (H&E staining) revealed widespread hepatic lipid accumulation in HFD fed mice, which was reduced to normal levels following 6-OHDA administration (figure). Diet-induced obesity also resulted in elevations in plasma glucose (172±13 vs. 249±20 mg/dl; normal chow-vehicle vs. HFD-vehicle; $p<0.05$), and ablation of sympathetic nerves restored HFD-mediated hyperglycemia (160±7 mg/dl; HFD-OHDA; $p>0.05$ vs. normal chow). Concomitant with this, 6-OHDA administration in HFD fed animals was associated with a reduction in hepatic mRNA markers of gluconeogenesis (e.g. *G6PC* 6.6±1.0 vs. 3.2±0.7 fold normal chow-vehicle; HFD-vehicle vs. HFD-OHDA; $p<0.05$) and lipogenesis (e.g. *Srebp-1c* 2.0±0.3 vs. 0.8±0.3 fold normal chow-vehicle; HFD-vehicle vs. HFD-OHDA; $p<0.05$). Collectively, these findings demonstrate that removal of sympathetic nerve activity rescues obesity-induced hepatomegaly, hepatic steatosis and hyperglycemia, independent of an effect on body weight and adiposity. Moreover, this data reveals a novel role for the sympathetic nervous system in HFD-mediated NAFLD and suggest that targeting hepatic sympathetic overactivity may represent a novel therapeutic approach to treat NAFLD.



STATUS

Staff

AUTHORS

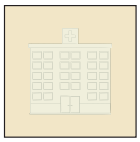
Chansol Hurr

Hayk Simonyan

Colin N. Young

RESEARCH MENTOR/ DEPARTMENT CHAIR

Colin N. Young



MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Public Health Implications of E-cigarette Regulation for African American Youth in Washington, D.C.

To date, inconclusive research exists on the harm reduction effectiveness and long-term health effects associated with electronic cigarette (e-cigarette) use (Goldman, 2014). Without federal e-cigarette regulations, U.S. state governments have implemented state-level regulations. As of August 2015, the U.S. Food and Drug Administration (FDA) is considering the extension of its regulatory jurisdiction to include, or deem, tobacco products not covered in the 2009 Family Smoking Prevention and Tobacco Control Act (FDA Center for Tobacco Products, 2015).

This culminating experience (CE) assesses the public health implications resulting from e-cigarette regulations, including the FDA deeming rule, and lists an optimal set of e-cigarette regulations to maximize health benefits and minimize health risks for African American youth aged 12-17 in Washington, D.C. The health objective is to prevent the onset of illnesses attributed to e-cigarette use and the behavior objective is to decrease the prevalence of e-cigarette use by 20 percent in 5 years. To gather qualitative data, nine key informants completed semi- structured interviews. These data were supplemented with a literature review regarding e- cigarette regulation and a review of public comments submitted to the FDA commissioner on behalf of interviewee stakeholder institutions.

Based on the qualitative results, federal and D.C. e-cigarette regulations should focus on the following provisions to minimize health risks and increase health benefits for the priority population, not all of which are included in the deeming rule: youth access; marketing; flavor bans; taxation; and internet sales. With such restrictions, future surveillance and monitoring research would be necessary to validate these regulatory efforts.

REFERENCES

FDA Center for Tobacco Products (2015). Issue snapshot on deeming: regulating additional tobacco products. http://www.fda.gov/downloads/TobaccoProducts/NewsEvents/UCM397724.pdf. Accessed May 4, 2015.

Goldman, T. R. (2014). E-cigarettes and federal regulation. http://healthaffairs.org/healthpolicybriefs/brief_pdfs/healthpolicybrief_120.pdf. Accessed May 6, 2015.

STATUS

Recent Alumnus

AUTHORS

Armin Aflaki

Caroline Sparks

RESEARCH MENTOR/ DEPARTMENT CHAIR

Caroline Sparks

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Promotion of Drinking Water among Latino Immigrant Youth

OBJECTIVE

To design an innovative intervention to increase drinking water behaviors among Latino immigrant youth.

METHODS

We conducted two rounds of focus groups, totaling 10 sessions (n=61), with Latino immigrant youth, aged 6-18 years, living in Langley Park, Maryland. Participants were stratified into focus groups by age group (elementary, middle, and high school) and language preference (Spanish and English). A professional, bilingual-speaking moderator used a semistructured discussion guide to examine: (1) what youth preferred to drink in different settings and why, (2) their reactions to promotional messages, (3) slogans that would entice them to drink more water in school and at home, and (4) concept testing. The design and analyses were grounded on the social environmental framework to understand how various environments shape drink preferences. The sessions were audio-recorded, transcribed verbatim and translated into English. Two independent coders analyzed the data using an inductive approach to categorize texts according to recurring themes, concepts, and terms. Data were analyzed separately for each age group and language preference. After inter-rater agreement was achieved, final codes and sub-codes were defined in a coding dictionary. All transcribed discussions were entered into the software Atlas.ti and coded using the developed coding dictionary.

RESULTS

Beverage behaviors and preferences depended on (a) availability of water and other drinks, (b) perceived health benefits, (c) level of thirst, and (d) perceptions of taste and safety. There were no major differences in recurrent themes across age groups.

Availability

Youth described that they preferred to drink bottled water at home, since this was what their parents made available to them. At school, however, most youth preferred chocolate milk, which is what was most available to them at lunch time. Youth described that they would not drink fountain water because it did not taste good, and that other forms of water were not available in the cafeteria. Older youth reported that water was often unavailable in vending machines at school.

Perceived health benefits

Youth preferred to drink water to be attractive and to have energy. Concepts emerged around topics related to water makes you run, and athletes that drink water. Reactions to promotional messages that use celebrities were positive, but they did remark that some Latino celebrities endorse soda.

Level of thirst

When really thirsty, youth preferred to drink water and only water to quench their thirst. They also recounted preferring water when it is hot outside. Promotional materials with these concepts received positive reactions.

Taste and safety of tap water

Tap water was considered unsafe and distasteful both at home and at school.

Having both English and Spanish represented in branding and slogans was considered important. Promotional materials were considered appealing if they were visually interesting, included a celebrity or an athlete, and were informative about water.

CONCLUSIONS

A bilingual school- and home-based water promotion intervention that highlights (a) the health benefits of drinking water, (b) the power of water to quench true thirst, and (c) the safety, taste and benefits of drinking tap water is a promising strategy to target some of the barriers around drinking water behaviors among Latino immigrant youth.

STATUS

Graduate Student

AUTHORS

Nicole Barrett

Allison Elkins

Uriyoán Colón-Ramos

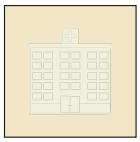
Ivonne Rivera

W. Douglas Evans

Mark Edberg

RESEARCH MENTOR/ DEPARTMENT CHAIR

Uriyoán Colón-Ramos



SCHOOL OF NURSING

The Effect of Community/Public Health Nurses in Hypertension Prevention and Control

BACKGROUND

Maryland participated in the Association of State and Territorial Health Official's Million Hearts State Learning Collaborative in 2014 and 2015. Washington County, Maryland formed a collaboration between the County Health Department, Meritus Health System and the Meritus Health Parish Nurse Network to address undiagnosed and uncontrolled hypertension in the county.

OBJECTIVES

Data from the Meritus Health Parish Nurse Network's Million Hearts Program was analyzed to determine the effect of a community nursing intervention of teaching blood pressure self-monitoring and providing coaching on blood pressure and lifestyle changes in the at-risk and hypertensive population and to create a plan for program dissemination.

METHODS

Within this network of 52 faith communities, 39 faith community nurses provided a three month blood pressure self-monitoring and coaching for lifestyle changes program in 2014 and 2015 to 119 community participants. A secondary data analysis using a repeated measure ANOVA to assess differences in systolic and diastolic blood pressure readings collected before, during and after the intervention and a paired t-test to compare pre- and post-lifestyle scores was completed.

RESULTS

A total of 109 participants completed the program and were included in the analysis showing that blood pressure decreased and that lifestyle satisfaction in six out of seven areas improved across the three-month period.

CONCLUSION

Coaching provided to participants by nurses in the community can create an environment of sustained support to promote improved lifestyle and blood pressure changes over time. This program can be replicated in a variety of community settings to build the evidence-base and support systems-level change in community/public health nursing practice.

STATUS

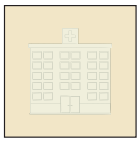
Graduate Student

AUTHOR

Jennifer Cooper

RESEARCH MENTOR/ DEPARTMENT CHAIR

Deborah Chapa



MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

A New Lens on the Changes in Youth Tobacco Use: Zooming In on Single, Dual, and Poly Tobacco Users

Decline in tobacco use prevalence among US Middle and High School youth between 2012 and 2013 (National Youth Tobacco Survey, NYTS), stirred excitement and debate. Controversial findings among high school students centered on decreased cigarette smoking (from 14.0% to 12.7%), increased electronic cigarette use (from 2.8% to 4.5%), and increased use of more than one product (from 9.9% to 12.6%). Our previous research (Ali et al., 2015) demonstrated the importance of forming distinct risk profiles of single, dual, and poly tobacco use, defined as use of only one, any two, and any three or more products. The present study applied this methodology to illuminate changes between 2012 and 2013. 2012 (n=24,658) and 2013 NYTS (n=18,406) data were analyzed using mutually exclusive categories of single, dual, and poly tobacco use in the last 30 days. The same psychosocial factors and twelve tobacco products were analyzed with the addition of flavored cigarettes and cigars in 2013. Multinomial logistic regression facilitated risk profile comparison. In 2012 (n=5,030), the majority of tobacco using youth reported poly use (55.9%), followed by single (28.0%), and dual use (16.1%). 2013 saw the same trend of tobacco using youth (n=4,009) reporting high poly use (53.5%), followed by single (29.2%) and dual use (17.2%). 2012 and 2013 multivariate models showed higher levels of nicotine dependence among poly users compared to single (2012 RRR=3.19, p<0.001; 2013 2.92=, p<0.001) and dual users (2012 2.52=, p<0.001; 2013 1.62=, p<0.05). In 2012, compared to dual users, poly users were more likely to be male, Hispanic, nicotine dependent, influenced by peer cigarette offers, and less likely to be black, have quit intentions, and believe secondhand smoke causes a lot of harm. In 2013, gender, race, dependence, and peer influence held. Quit intention and harm perception findings were no longer significant. The concurrent use of multiple tobacco and nicotine delivery products is a relatively new phenomenon that necessitates a different lens for tobacco control and focused risk assessments to inform tailored interventions for distinct types of tobacco users.

STATUS

Graduate Student

AUTHORS

Laurel Curry

Kim Horn

Tiffany Gray

Diane Martinez

Maliha Ali

RESEARCH MENTOR/ DEPARTMENT CHAIR

Kim Horn

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Illustrating the Changing Tobacco Landscape: Risk Characterization of Youth Single, Dual, and Poly Tobacco Users

Little is known about the growing phenomenon of concurrent tobacco use or distinctions among youth who are single, dual, or poly tobacco users. With widespread availability of a myriad of tobacco products, effective prevention and intervention strategies can no longer center on cigarette smoking alone. Tobacco control initiatives must reflect this changing tobacco landscape. It is critical to understand distinct risk profiles of concurrent tobacco users and determine differences in the functional value of various tobacco products. Using data from the 2012 National Youth Tobacco Survey (n=24,658), including US Middle and High School youth, ages 9 to 18 the present study developed *mutually exclusive categories* of single, dual, and poly tobacco use defined as use of *only one, only two, and any three or more tobacco products* in the last 30 days. Multinomial logistic regression established three exclusive tobacco groupings characterized by established risk domains. Resulting risk characterizations were transposed into visual illustrations to foster translation of distinct user profiles to research and practice audiences. Among youth using tobacco in the past 30 days (n=5,030), the majority were poly users (55.9%), followed by single (28.4%), and dual users (16.1%). Multivariable models showed higher levels of nicotine dependence among poly users compared to single (RRR=3.14, p<0.001) and dual users (RRR=2.48, p<0.001). Poly users were less likely to express quit intent compared to single (RRR 0.68, p<0.001) or dual users (RRR=0.77, p<0.05). High tobacco harm perceptions were more likely among dual relative to single product users (RRR=1.54, p<0.05); poly users were less likely to perceive harm (RRR=0.56, p<.0001). Visual illustrations convey distinct profiles, including racial and gender differences. Compared to poly, dual users expressed higher quit intent and risk perceptions suggesting different use motivations. Significant distinctions among single, dual, and poly users suggest tobacco control research should consider these characterizations and the expanding role of non-cigarette tobacco products in future strategies to reduce nicotine addiction among US youth.

STATUS

Graduate Student

AUTHORS

Tiffany Gray

Maliha Ali

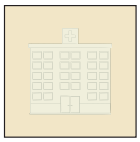
Laurel Curry

Diane Martinez

Kimberly Horn

RESEARCH MENTOR/ DEPARTMENT CHAIR

Kimberly Horn



MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

A Test of the Anger Activism Model: truth® Campaign Advertising-Induced Anger, Self-Efficacy, and Message-Related Cognitions

INTRODUCTION

Although most studies regarding emotion and health messaging have focused on the effects of fear, anger may also have beneficial effects. The extended Anger Activism Model (AAM) contends that efficacy beliefs and anger intensity are critical to determining message-relevant cognitions. This study tested the extended AAM using responses to two advertisements from the truth® youth anti-smoking campaign.

METHODS

Data used in this study is from the online, cross-sectional Truth Initiative Media Monitoring Tracking Survey, which surveys 15-21 year olds. This analysis includes responses from July 2014 through March 2015 (n= 4,792). Self-reported information on anti-tobacco ad-induced anger and efficacy were used to separate individuals into six anger/efficacy groups. Analysis of variance and regression analyses were conducted to understand group differences in anti-tobacco message-relevant cognitions, namely ad-related persuasiveness, receptivity, and conversation.

RESULTS

Results indicated that, as predicted by the model, anti-tobacco message-relevant cognitions were highest among the high anger/high efficacy group and lowest among the low anger/low efficacy group. For the high anger/high efficacy group compared to the low anger/low efficacy group for the two ads, odds of being persuaded by the anti-tobacco ads were 49.78 (95% confidence interval (CI) 20.62 to 120.16] and 18.52 (95% CI 10.35 to 31.55) times higher, odds of being receptive to the anti-tobacco ads were 28.12 (95% CI 14.39 to 54.94) and 23.89 (95% CI 13.53 to 42.21) times higher, and odds of conversing about the anti-tobacco ads were 25.15 (95% CI 13.89 to 45.56) and 12.91(95% CI 8.01 to 20.82) times higher. The relationship between anger/efficacy group and anti-tobacco message-relevant cognitions varied based on advertisement and type of cognition, which suggests that the type of messaging found in advertisements can alter how strongly anger and efficacy impact message-relevant cognitions. However, there was no evidence for the extended AAM's prediction that the relationship between anger intensity and message-related cognitions varies based on level of efficacy.

CONCLUSIONS

This test of the extended AAM found that, as predicted by the model, anti-tobacco messages that incite high anger and high efficacy in combination can have powerful effects. So while fear aroused by anti-tobacco messages featuring health consequences has been shown to be effective, this study suggests that a wider range of emotions – including anger - should be investigated to assess how such emotions might help elicit the desired responses among the target audience, ultimately preventing uptake of tobacco use and reducing rates of smoking.

STATUS

Graduate Student

AUTHORS

Vinu Ilakkuvan

Monique Turner

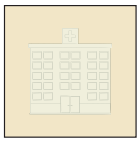
Jennifer Cantrell

Elizabeth Hair

Donna Vallone

RESEARCH MENTOR/ DEPARTMENT CHAIR

Monique Turner



MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

A content analysis of Electronic Health Record (EHR) functionality to support tobacco treatment

BACKGROUND

The adoption of Electronic Health Records (EHRs) in healthcare settings is an opportunity for promoting smoking cessation. EHR functionality related to smoking cessation has potential to shape clinician behavior and standardize best practices. Previous studies have not systematically examined the characteristics of EHRs related to smoking cessation.

OBJECTIVES

The purpose of this study is to review the published literature that describes EHR modifications aimed at supporting cessation and to document the prevalence of EHR functionality using a 5 A's framework (Ask, Advise, Assess, Assist, Arrange).

METHODS

A literature review was conducted and 18 published studies covering 14 unique EHRs were identified. A content analysis for EHR functionality related to tobacco treatment was conducted by two independent coders.

RESULTS

For functionality related to Ask, 100% of EHRs allowed for the documentation of smoking status, in some cases, prompted by an alert (42.8%). Others allowed for the documentation of cigarettes smoked per day (28.6%), tobacco type (35.7%), and previous quit attempts (21.4%). For Advise, 35.7% of EHRs provided functionality helping a clinician provide advice to quit. For Assess, more than half of EHRs included a feature to document a patient's willingness to quit. For Assist, EHRs provided several features, sometimes grouped together in an order set and/or with the presence of an alert. The vast majority provided medication prescribing functionality (78.6%). About half included a feature to refer a patient to the quitline (50.0%), to a tobacco treatment specialist (42.8%), or to educational materials (57.1%). Finally, for Arrange, EHRs helped by scheduling follow-up visits (35.7%) or by linking specialists back to primary care providers (28.6%).

CONCLUSIONS

Studies that have attempted to modify EHRs for tobacco treatment purposes have included modifications across the steps in the 5 A's model, with most supporting documentation of smoking status (Ask) and assisting with medication prescribing (Assist). Future studies need to examine the relationship between the presence of specific EHR functionality and smoking cessation outcomes.

STATUS

Graduate Student

AUTHORS

Jennifer Schindler-Ruwisch

Lorien Abroms

Christina Heminger

Steven Bernstein

RESEARCH MENTOR/ DEPARTMENT CHAIR

Lorien Abroms

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Postpartum Depression Screening in a Pediatric ED: Prevalence in First-Time Moms

BACKGROUND

Postnatal depression (PND) affects about 10-15% of all mothers. , The American Academy of Pediatrics suggests that "routine screening of mothers for postpartum depression by pediatricians will certainly identify women at risk for postpartum depression" While some symptoms may present themselves differently and more severely in some women, one thing is absolutely certain: inadequate treatment could result in long-term damaging effects. Many mothers who present with PND oftentimes blame themselves for not being able to take care of their baby; when in reality, the issue is much deeper and is a concern of mental health. Currently, the most effective screening strategy is the use of the Edinburgh Postnatal Depression Scale (EDPS). With this tool, the mother is asked a series of 10 questions. The scores may range from 0 to 30, with any score greater than 10 being a possible sign of depression.

OBJECTIVE/QUESTION

I will examine the prevalence of PND in non-Hispanic African-American versus non-Hispanic White first-time mothers, and determine if the prevalence is statistically significant for one or both groups of women. I will also examine the prevalence of being previously diagnosed with a mental health condition in non-Hispanic African-American versus non-Hispanic White women, and determine if it presents as significant in first-time mothers.

METHODS

The Postnatal Depression (PND) study staff is conducting an ongoing prospective, cross-sectional survey using a convenience sample of mothers with infants aged zero to six months presenting in the emergency department for non-acute care. The study excludes non-birth mothers, as well as mothers who do not speak English or Spanish. Demographic data—i.e., race/ethnicity, age, insurance type, and zip code – are collected electronically. Mothers who screen positive for PND are contacted via a follow-up phone call using scripted interview questions. The staff is screening for two hundred fifteen positive mothers overall; and all non-Hispanic African American and non-Hispanic White first-time mothers who were screened will be included—ideally a sample of at least 100 people.

RESULTS

To be determined.

CONCLUSIONS

To be determined.

STATUS

Graduate Student

AUTHOR

ShaQuilla Bell

RESEARCH MENTOR/ DEPARTMENT CHAIR

Olga Price

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Culture and Psychosis: A Case Study

BACKGROUND:

Multiple descriptive studies utilizing disease vignettes called short explanatory model interviews (SEMI) were undertaken in a rural district of Tamil Nadu, India to explore regional disease models of psychosis. Among community health workers, 87% attributed SEMIs to non-medical explanations. A similar study found community members believed social and financial problems resulted from violence, self-destructive behavior, sadness and alcoholism while possessions, hallucinations, irrelevant talk and bizarre behavior resulted from spirits, witchcraft and magic. Overwhelmingly, they believed violence/aggression required intervention which could be administered at a hospital or religious center. A study among a cohort of schizophrenic patients found that 70% attributed their situation to spiritual or mystical factors; only 22% attributed it to a disease model.

CASE PRESENTATION:

Our patient was a 60 year-old Hindi speaking man with a history of hypertension, diabetes mellitus and alcohol dependence presenting with command auditory hallucinations (CAH), visual hallucinations (VH) and suicidal ideation (SI). Clinical interviews were conducted through an in-person translator who also served as a cultural broker assisting interpretation of our patient's beliefs. Our patient immigrated 22 years ago from rural India. He reported that his wife had affairs with family members after he came to the US. CAH were of his wife and in-laws instructing him to commit suicide, bequeathing them his property. VH were family members poisoning his food. He started drinking 1/4 L of alcohol daily at age 16. He reports AH before drinking; as the voices increased he coped with increased drinking. He was sober for 1.5 years, during which time hallucinations continued. He lost his job due to drinking. He did not interpret CAH/VH as depression (Hamilton-D score: 13) or as illness but felt this bad luck was due to black magic perpetrated by his family. He wants the hallucinations to stop and believes they impair daily functioning by necessitating drinking.

DISCUSSION:

It is important to highlight the emic perspective of diagnosis and assess psychosis against cultural standards. Black magic is a commonly held belief in India but it is general, not directed at individuals. Therefore, belief of personal black magic persecution, as held by our patient, is an abnormal thought process.

CONCLUSION:

Given our patient's disordered beliefs of personal black magic persecution and his CAH/VH, outside the context of alcoholism, which impaired functioning, he was diagnosed with paranoid schizophrenia. This case highlights the importance of culturally competent care and considering culturally appropriate disease models in diagnosis.

STATUS

Medical Student

AUTHORS

Patricia Carr Reese

Rayna Sobieski

Christina Marlow

Veronica Slootsky

RESEARCH MENTOR/ DEPARTMENT CHAIR

Veronica Slootsky

PSYCHIATRY/MENTAL HEALTH

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Marijuana use in the immediate 5-year premorbid period is associated with increased risk of onset of schizophrenia

Several studies suggest that adolescent marijuana use predicts earlier age at onset of schizophrenia, which is a crucial prognostic factor. Yet, many investigations have not adequately established a clear temporal relationship between the use and onset. We enrolled 247 first-episode psychosis patients from six psychiatric units and collected data on lifetime marijauna/alcohol/tobacco use, and ages at onset of prodrome and psychosis in 210 of these patients. Cox regression (survival analysis) was employed to quantify hazard ratios (HRs) for effects of diverse premorbid use variables on psychosis onset. Escalation of premorbid use in the 5 years prior to onset was highly predictive of increased risk for onset. Through the analysis of time-specific measures, we determined that daily use approximately doubled the rate of onset (HR = 2.2, p b 0.0005), even after controlling for simultaneous alcohol/tobacco use. Building on previous studies, we were able to determine that cumulative marijuana exposure was associated with an increased rate of onset of psychosis (p=0.007), independent of gender and family history, and this is possibly the reason for age at initiation of marijuana use also being associated with rate of onset in this cohort. These data provide evidence of a clear temporal relationship between escalations in use in the five years pre-onset and an increased rate of onset, demonstrate that the strength of the association is similar pre and post-onset of prodromal symptoms, and determine that clearly adult use may be just as important as adolescent use in these associations.

STATUS

Medical Student

AUTHORS

Thomas Reed

Beth Broussard

Anthony Crisafio

Michael T. Compton

RESEARCH MENTOR/ DEPARTMENT CHAIR

Michael T. Compton

PSYCHIATRY/MENTAL HEALTH

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Auditory Hallucinations in a deaf patient: a case study

BACKGROUND

To date, one case report of auditory hallucinations in a deaf patient has been published. Larger population-level assessments estimate that psychotic disorders occur equally in both hearing and non-hearing populations. There are a few distinct difficulties in making the diagnosis of a thought disorder in a non-hearing patients. Language-deprived deaf patients display difficulties with language that mimic the types of language production errors seen in patients with thought disorders. The majority of deaf children are born to hearing parents resulting in early language deprivation and interference with the ability to infer the mental states of others and to recognize affect. These language production errors include limited vocabulary, lack of sequential organization to stories, inappropriate syntax, excessive use of gesture, emotional disconnectedness and social withdrawal. The added difficulty of using an American Sign Language (ASL) interpreter further complicates the clinical picture. Interpreter subjectivity can lead to the reformulation and repetition of questions. The assessment tools currently utilized to diagnose thought disorders are verbal and standardized for hearing patients.

CASE PRESENTATION

Our patient was a 20 year old woman with a history of congenital deafness presenting with an attempted suicide by drowning who reported auditory hallucinations (AH) and past commanding visual hallucinations (CVH). Clinical interviews were conducted through a translator certified in American Sign Language (ASL). Our patient had been diagnosed with deafness at the age of two years old. AH were narrations of the patient's actions and were not command in nature. AH were present during her clinical time with our team. She was not able to discern the gender of the voice, tone or intonation of the voice. The patient also reported CVH of a shadow shape that gestured for her to hurt herself in different ways. These CVH were not present while the patient was in our care. The AH and CVH did not cause her significant distress.

DISCUSSION

It is important to critically assess the tools that are currently used to diagnose thought disorders in deaf patients. These many challenges may further exacerbate the health disparities seen in the deaf community.

CONCLUSION

Our patient met the criteria for major depressive disorder while in our care. This case highlights the importance of the development of assessment tools and cultural competence to enhance the diagnosis and treatment of non-hearing patients with mood and thought disorders.

STATUS

Graduate Student

AUTHORS

Rayna Sobieski

Patricia Carr-Reese

Christina Marlow

RESEARCH MENTOR/ DEPARTMENT CHAIR

Veronica Slootsky

QUALITY IMPROVEMENT

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Enhancing physician-nurse communication by improving attendance during bedside rounds

OBJECTIVE/AIM

Enhance physician/nurse communication by improving nurse attendance to bedside rounds by 50% by the end of the academic year.

BACKGROUND

Communication between different health professionals is crucial to achieving high quality patient care. A review of literature revealed that effective communication led to: improved information flow, more effective interventions, improved patient safety, enhanced employee morale, increased patient and family satisfaction and decreased lengths of stay. As such, rounds are important to patient care, as different team members discuss and agree on a particular management plan, and it is the main venue to target for our project. Research has shown that Nurse-Physician rounding increased communication, and lessened the need to page doctors for questions. Which greatly improved workflow for both physician and nurses.

QUALITY IMPROVEMENT METHODS

We targeted patients on 5 south at The George Washington University, which is an Internal Medicine ward. First PDSA cycle was conducted between 1/27-2/5, excluding call days. Each day, the nurse distribution sheet was collected by a team member, which contained contact numbers for health care professionals for every patient on the floor. Every nurse was called before rounds and invited to join. In addition, if a nurse did not show up, a team member was left behind to provide updates, and this was called "Left behind briefing" which was used a balancing measure.

RESULTS

During the 10 day period, 5 day worth of data was collected, and the percentage of attendance (day) was 80 (1), 72 (2), 100 (6), 50 (7) and 100% (8). The rest of the 5 days, data were not collected. Number of "left behind briefing" (day) was 1 (1), 2 (2), 0 (6), 2 (7) and 0 (8).

CONCLUSION

Calling nurses prior to rounds was an effective way to increase attendance for rounds, as all recording achieved target of 50%. Number of "left behind briefing" did not increase during that period. On half of the recorded days, no records were logged, as the process was not initiated by physician team. This was likely due to lack of reminders, which will be added to next PDSA cycle.

STATUS

Resident

AUTHORS

Nawaf Abaalkhail

Rami Alsharif

Alia Khoja

Caitlin Willemann

Qusai Al Saleh

Omar Siddique

Ashley Noisette

Nika Safaie

RESEARCH MENTOR/ DEPARTMENT CHAIR

Nupur Mehta

QUALITY IMPROVEMENT

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Medical Student Competency in Wound Care Guidelines

INTRODUCTION

Chronic wounds that have failed to heal after 3 months of appropriate wound care affect approximately 6.5 million people in the US with a prevalence of 1% and costs estimated at $25 billion per year. Medical students currently receive limited wound care training, yet to effectively manage chronic wounds, providers must both understand the biology of healing, and also remain up-to-date with wound care guidelines published by the Agency for Healthcare Research and Quality (AHRQ). The purpose of this student-led project was to investigate medical students' knowledge and comfort with wound care guidelines.

METHODS

This study was approved by the George Washington University IRB (011639). A questionnaire of 11 questions testing the fundamentals of chronic wound management, developed based on AHRQ guidelines, was administered using the REDCap survey tool to students via the GWU SMHS year group listservs. Participants were evaluated for didactic exposure as well as participation in certain electives. Student comfort level of managing chronic wounds was assessed using a self-reported subjective grading scale.

For the purposes of analysis students were grouped into two groups: pre-clinical (years 1 and 2), and clinical (years 3 and 4). Data was analyzed using T-test, Fisher's Exact and Chi Square performed using GraphPad Prism 5.0.

RESULTS

Data was available from 48 students, 21 pre-clinical and 27 clinical. Knowledge of wound care guidelines was suboptimal in both groups, with clinical students correctly answering 34.68% of questions and pre-clinical 29.0% (p=0.188). Students reported a mean of 1.77 ± 0.88 hours of didactics on wound healing, tissue injury or wound management with no significant differences between preclinical and clinical groups.

For most questions there were no significant differences in correct response rate between clinical and pre-clinical groups. However, for the question pertaining to recommended frequency of diabetic foot examination, 9.52% of preclinical students responded correctly compared to 55.56% of clinical students (p=0.0019). Comfort level of medical students in managing chronic wounds was not correlated with correct answers on this survey. However, we did note that individuals reporting higher subjective comfort scores had received more wound related didactic hours (2.38 ±0.74 compared to 1.61±0.84, p=0.02).

CONCLUSION

This survey shows that despite the prevalence and healthcare costs of chronic wounds, medical students are currently not receiving adequate training on guideline based management of chronic wounds.

STATUS

Medical Student

AUTHORS

Sophia Akhiyat

Sean McNish

Anirban Banerjee

Kara Couch

Victoria K. Shanmugam

RESEARCH MENTOR/ DEPARTMENT CHAIR

Victoria K. Shanmugam

QUALITY IMPROVEMENT

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Improving Adherence to Screening and Immunization Guidelines Among Medical Residents in the Internal Medicine Clinic

PURPOSE

Our goal was to improve adherence to The United States Preventive Services Task Force (USPSTF) screening and immunization guidelines among medical residents at the internal medicine clinic.

METHODOLOGY

Using the Abdominal Aortic Aneurysm(AAA) screening compliance rate as a surrogate marker for other screening and immunization compliance rates, we observed the screening rates within a group of 99 internal medicine residents. Baseline screening rates were obtained by reviewing medical records of patients who had received a health maintenance exam between June 23rd and August 22nd, 2015. We then introduced intervention methods with the intent to improve screening rates. For our first intervention, residents attended a short educational session, during which a primary care physician outlined the AAA screening recommendation. For the second intervention, an email was sent to all internal medicine residents to reinforce the AAA screening guideline. The third intervention involved sending an email to supervising attendings, informing them of the recommendation and the screening rate among their residents. They were also urged to remind their residents to perform AAA screening when indicated. At the end of each intervention period (each week-long cycle, totaling to 5), retrospective data, including the screening rate, were calculated and compared to both the baseline and prior week's results using the Chi-square test. In our final intervention, we plan to work with the clinic's information technology team to integrate all screening tests and immunization recommendations into the electronic health record.

RESULTS

The initial AAA screening rate was 2.5% between June 23rd and August 22nd, 2015. Over the next five weeks, following the first intervention method, this rate improved significantly from 2.5% to 15% with a p-value < 0.01. We suspect that this was due to the fact that no previous AAA screening guideline lecture had been given. Conversely, topics such as mammography, colonoscopy, and Papanicolaou(Pap) smear screening have been taught consistently. During the next two interventions, the rates were 12.5% and 33.3%, with p-values of 0.48 and < 0.01, respectively. We suspect these results are due to the complexity of patient concerns, along with high patient volume, which can make it difficult for internal medicine residents to address all necessary screening tests. The final intervention is still underway.

CONCLUSIONS

Our quality improvement project examined the baseline AAA screening rate and the effectiveness of various educational and systemic interventions for improving these rates. Education proved to have a significant role in improving residents' adherence to screening guidelines. Another way to enhance guideline adherence is to incorporate the guidelines into the medical record software. Having a tab for "Screening/immunization" as a set of orders and as part of the patient's "History and Physical Note" template can help physicians address these matters on a more consistent basis.

STATUS

Medical Resident

AUTHORS

Talal Alzahrani

Joseph Delio

Nejat Naser

Lauren Choi

Brandon Anderson

Brandon Rieders

Jason Gendell

Erin Vipler

RESEARCH MENTOR/ DEPARTMENT CHAIR

Erin Vipler

QUALITY IMPROVEMENT

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Evaluating Impact of Resident Feedback on Diabetic Patient Outcomes

INTRODUCTION

Residents are often unaware of their performance in clinic as compared to that of their peers. The intent of this project was to improve resident compliance with best care practices for diabetic patients using a novel feedback system to gauge performance in clinic. Per American Diabetes Association guidelines, diabetics should be screened annually for kidney disease with a urine microalbumin/creatinine ratio. Routine screening is integral in preventing and/or treating diabetic nephropathy, which is the leading cause of kidney failure in the United States. Diabetics with proteinuria benefit from close medical follow up to ensure tight blood pressure and glucose control.

METHODS

The study was conducted at an urban academic ambulatory center. The study population consisted of members of a categorical internal medicine residency program, with a 4+1 ambulatory model. Our sample was comprised of 19 residents with an even distribution among PGY-1, PGY-2, and PGY-3. A total of 249 patients were evaluated.

First, we reviewed the charts of patients seen in clinic by our 19 residents over the previous two ambulatory weeks. Patients with "diabetes mellitus" listed as a medical problem by ICD code were identified. Then, we surveyed these patient's records for a urine microalbumin/creatinine checked within the past year.

Subsequently, the residents were presented with individual and group compliance rates, and the recommendations for screening were reviewed through a short teaching module. The data was communicated via PowerPoint presentation at a weekly didactics session. Residents were notified that their performance would be reviewed again after another two ambulatory weeks. We hypothesized that there would be a significant increase in compliance with screening after administration of the feedback and education intervention.

RESULTS

Pre-intervention data analysis showed that 63% of the 99 diabetic patients seen in clinic over the course of two ambulatory weeks had a screening urine microalbumin/creatinine within the last year. During the two ambulatory weeks post-intervention, there was a 74% screening rate for 150 diabetic patients seen. Nine of 19 residents had screening rates of greater than 80%. The P-value was 0.06 for pre- and post-intervention comparison.

CONCLUSIONS

While subjective feedback for residents from attending physicians is well-documented and frequently provided, objective feedback via chart audit is a less common component of residency programs. Though our initial data was not significant, it suggests a positive clinician behavioral shift in response to receiving data about patient management performance. A major limitation of this study is the small sample size. A potential confounding bias is that post-intervention data was collected later in the year, when residents were likely more experienced. In the future, we plan to expand this intervention to a larger sample of residents. We also anticipate monitoring appropriate initiation of ace inhibitors for patients with microalbuminuria.

STATUS

Staff

AUTHORS

Meghana Bhatta

Srikar Kumar

Celia Mouyal

John Tiu

Sruti Chintameneni

Charlie Lee

RESEARCH MENTOR/ DEPARTMENT CHAIR

Cherinne Arundel

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Improving post-hospital transitions of care by facilitating follow-up appointment creation

BACKGROUND

Transitions of care are important to patient safety and care. They are a known period of risk and often patients can suffer an adverse event, resulting in hospital readmissions. Within the George Washington University Hospital, data has shown that over 50% of patients admitted to the internal medicine wards that are readmitted within 1 month do not have a follow-up appointment scheduled prior to initial discharge. A study at the University of Colorado Hospital showed that patients lacking timely follow-up after an inpatient stay were ten times more likely to be readmitted. Our project aims to improve the rate of follow-up appointments made and documented by 25%.

METHODS

Baseline data was collected in December 2015 from four internal medicine wards teams tracking the number of daily patient discharges, follow-up appointments, and time to follow-up appointment from discharge. Our intervention was to provide all internal medicine wards team members with local clinics' contact information. Data was again collected after the intervention as a comparison.

RESULTS

Baseline data identified 50 patients that were discharged from medicine teams. Average length of stay was 13.5 days. 19 patients (38%) had follow-up appointments made at time of discharge. Average time from discharge to appointment date was 15 days. After the intervention, 58 patients were discharged from medicine teams. Average length of stay was 4.8 days. 36 patients (62%) had follow-up appointments made at time of discharge. Average time of discharge to appointment date was 8 days.

CONCLUSIONS

By providing internal medicine residents with contact information for local clinics, we were able to increase the percentage of patients who have appointments made at time of discharge by 24%. Results also show a decrease in the average time from discharge to appointment date, indicating timelier follow-up. The next steps will be to determine if this correlates to a reduction in readmission rates, which are costly to both the hospital and the patient.

STATUS

Staff

AUTHORS

Caitlin Biedron

Angela Basen

Kanika Gupta

Nishant Magar

Kristen Millado

Vani Pyda

Matthew Tick

RESEARCH MENTOR/ DEPARTMENT CHAIR

Chavon Onumah

QUALITY IMPROVEMENT

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Severity of Pain is not associated with Urgency of Diagnosis in ED Patients with Abdominal Pain

BACKGROUND

Abdominal Pain is the most common cause of visits to US Emergency Departments (EDs) and the causes range from urgent to non-urgent diagnoses. Distinguishing urgent versus non-urgent causes of abdominal pain is done through the use of clinical exam, lab studies and diagnostic imaging such as CT scans. There are no validated clinical decision rules to assist physicians in discriminating urgent from non-urgent causes of abdominal pain or which patient needs a CT scan. There is controversy regarding the use of CT scans for patients with abdominal pain due to the increased cost, radiation exposure and length of stay.

OBJECTIVE

The objective of this study is to compare the demographics, pain score and CT utilization for patients with urgent versus non-urgent causes of abdominal pain.

METHODS

At an academic ED, a convenience sample of patients with abdominal pain was prospectively enrolled by research assistants during the ED visit. Research assistants abstracted treatment information from the electronic medical record for the ED and hospitalization if applicable. Finally, enrollees were telephoned 2 weeks after the index ED visit to ascertain symptom resolution and treatment outcomes. Following establishment of final diagnosis, patients were classified as having an urgent or non-urgent diagnosis based upon published peer-reviewed criteria. Risk differences in pain severity, CT scan utilization and demographics were compared to urgency of diagnosis and a paired t-test was used to estimate differences in initial clinical characteristics.

RESULTS

In a model of 725 patients, 144 had urgent diagnoses and 561 had non-urgent diagnoses. There was no distinction in insurance type, income level, mean age or pain score in the two groups. Ct scan utilization was higher in patients with urgent diagnoses (42.4% versus 16.4%).

CONCLUSION

20.4% of patients had an urgent diagnosis for the abdominal pain. There was no difference in the pain score for patients with urgent versus non-urgent diagnosis. While work-up bias is a potential limitation, CT scan utilization was higher in patients with an urgent diagnosis suggesting appropriate clinical judgement. Future studies will need to look at ways to target the testing to more high-risk patients who present with undifferentiated abdominal pain.

STATUS

Medical Student

AUTHORS

Ryan Brunetti

Caitlin Davis

Lorna Richards

Melissa McCarthy

Andrew Meltzer

RESEARCH MENTOR/ DEPARTMENT CHAIR

Andrew Meltzer

QUALITY IMPROVEMENT

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Implementing Diabetes Screening Guidelines in Resident Clinic

The U.S. Preventative Service Task Force now recommends screening all adults over the age of 45 for diabetes and pre-diabetes as of November 2014. Previously, the recommendation was to screen only those patients who had risk factors for diabetes such as obesity and hyperlipidemia. The goal of this project was to increase awareness of the screening guidelines among internal medicine residents and to improve the rate of appropriate diabetes screening in our patient population. We determined the baseline diabetes screening rate in a cohort of resident physicians. Our goal was to improve the baseline screening rate by at least 30% after three cycles of interventions. Our interventions included emails reminders, flyers posted in all exam rooms in clinic, and educational presentation during resident morning conference. Overall, we found that the baseline diabetes screening rate was 11% and that over 4 months, there was a sustained improvement of the screening rate to 21%. This project helped achieve an improvement in age appropriate diabetes screening by 50%.

STATUS

Staff

AUTHORS

Nathan Calabro

Shuo Chen

Jacob Elkon

RESEARCH MENTOR/ DEPARTMENT CHAIR

Anne Cioletti

QUALITY IMPROVEMENT

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Improving Care Coordination between a Community-Based Primary Care Clinic and a Subspecialty Clinic: the Implementation of a Pilot Direct Phone Line

BACKGROUND

Effective coordination between primary and subspecialty care is important for providing high quality comprehensive healthcare. Administrative and process barriers against effective patient care coordination between Bread for the City (BFTC), a local FQHC-look alike, and subspecialty care at Medical Faculty Associates (MFA) include efficient appointment scheduling and difficulty in timely record transfer between primary care and specialists. Based on prior consultations, this project develops a direct phone line between BFTC and the MFA Gastroenterology department.

METHODS

A pilot direct phone line between BFTC and the MFA Gastroenterology department, aims to reduce time spent on scheduling and improve the process of records transfer, compared to other divisions as controls. Call tracking forms will be used to assess a number of indicators such as improving call times, transfer of medical records, and referral processes. As initial results from this first PDSA cycle are returned, interventions will be adjusted to improve quality of the interventions. Additional interventions will be developed and implemented according to needs and initial metrics.

RESULTS

Multiple stakeholder meetings with staff and administration of both MFA and BFTC sites were held to develop buy-in and support of the quality improvement interventions. A protocol and tracking form was developed to collect information about the referral process on the day of referral, including the call times. Administrative staff at BFTC were trained in the study protocol and tracking form to record aspects of their usual duties in assisting patients coordinate specialist appointments. The time course of specific aspects of the referral process of the GI direct call line will be analyzed compared to the other MFA Internal Medicine Departments to assess if there was improvement in the process.

DISCUSSION

Improving referral processes across institutions requires streamlining of individual institutional procedures. A critical lesson for this intervention was the initial level of coordination and training of administrative staff at both institutions. An important factor for the success of this intervention was the willingness of leadership and staff at both institutions to improve the processes in order to provide improved quality of care to patients through these care linkages. Initial consultations provided at an earlier stage of this project was important for engaging the buy-in of BFTC staff who felt that interventions were developed in response to needs that they identified. It is important for community-based partnerships to incorporate this level of communication to address community needs through developing tailored interventions.

STATUS

Resident Physician

AUTHORS

Tingyin Chee

Adrienne Poon

Aneesha Hossain

Jillian Catalanotti

David Popiel

Randi Abramson

RESEARCH MENTOR/ DEPARTMENT CHAIR

Jillian Catalanotti

QUALITY IMPROVEMENT

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Increasing Resident Dissemination of Ambulatory Clinic Visit Information to Patients

BACKGROUND

One of the most critical components to good patient care is communicating information between patient and physician. It has been reported that only 43% of patients leave an ED visit correctly informed about diagnosis, planned examinations, and follow up.1 Few studies have been conducted to determine patient retention after outpatient clinic visits. The first step in aiding the retention and dissemination of clinic visit information is having the provider communicate that information to the patient. The GW Internal Medicine Residency Clinic currently has a "discussed" section embedded in the EMR system to print out and give to patients after their clinic visit, a cumbersome computer process; however, it is unknown how often this summary is actually provided to the patient. The purpose of this study is to evaluate how often residents at GW are providing their patients with after visit information and if a pre-printed form would aid in more patient information being disseminated.

AIM STATEMENT

The creation of an "After Visit Summary" form will increase resident dissemination of clinic visit information of medication changes, lab work, follow-up, and referrals to patients by 20% in a 15 week period at the GW MFA resident clinic.

METHODS

Survey of residents in residency clinic was given to assess baseline for number of residents providing information summarizing clinic visits. "After Visit Summary" forms were created and dispersed at the GW MFA resident clinic. Announcements were made through person and email that the forms were available to use in lieu of the "Discussed" section that is currently in the EMR if not being utilized. A survey was given to the residents to assess if the "Discussed" section was being used, and if not, how often the "After Visit Summary" was given to patients. Multiple PDSA cycles were performed that changed location and color of the form, with resident surveys following the changes to assess any change in use of the form. A retrospective sub-analysis was also undertaken to determine if there was an increase in the "Discussed" section in the EMR being printed after awareness of "After Visit Summary" availability was made.

RESULTS

Only 56% (n=18) of residents gave their patients some form of written information after their clinic visit, with 33% (n=6) of those residents providing the "Discussed" section from the EMR. Further results pending (Will be complete on 3/10/16).

DISCUSSION

Pending results.

STATUS

Medicine Resident

AUTHORS

Nicholas Dallas

Raeva Malik

Mitalhi Mehta

Shalenee Singh

Alex Aldrich

Kusha Davaar

Steven Tessla

Anne Cioletti

RESEARCH MENTOR/ DEPARTMENT CHAIR

Anne Cioletti

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Outcomes of Prolonged Minimally Invasive Myomectomy Compared to Open Procedures

BACKGROUND

Myomectomy is the only fertility sparing surgical approach for the management of fibroids and is increasingly being performed via minimally invasive surgery (MIS). Although MIS has proven clinical benefits over laparotomy, longer operative times in both MIS and laparotomy are associated with adverse outcomes. Little evidence exists to identify patients at risk of excessive operating time. Furthermore, no evidence exists to differentiate an operative time at which risk increases for either approach.

METHODS

Using the American College of Surgeons National Surgical Quality Improvement Program, laparoscopic and abdominal myomectomies were identified from 2005 to 2013 by CPT code. Procedures were split into laparoscopic and open, and then stratified based on operative time: < 1 hour, 1 to <2 hours, 2 to <3 hours, ≥ 3 hours. Outcomes in open cases were compared to those of laparoscopic cases by time.

RESULTS

In all, 2403 laparoscopic and 3436 open procedures were analyzed. In general, open abdominal procedures had worse 30-day outcomes than laparoscopic procedures. Longer surgeries were associated with African American race, higher BMI, lower hematocrit, HTN, age, and large or numerous fibroids. Surgery time was longer for laparoscopic procedures compared with open procedures. Wound complications, clotting, sepsis, UTI, bleeding, return to OR, hospital LOS > 3 days, and a composite complications outcome were significantly associated with surgery time. For most outcomes, there was an increased rate with increased surgery time. After adjusting for confounders, there was no difference in complications between laparoscopic procedures < 1 hour, 1 to < 2 hours, and 2 to < 3 hours long. However, laparoscopic procedures ≥ 3 hours had a higher odds of complications compared with laparoscopic procedures < 1 hour (OR 5.46 [1.31-22.75]; p=.02)). For open procedures, there was no difference in odds of complications for cases < 1 hour and those 1 to <2 hour. However, open procedures of 2 to <3 hours had a higher odds of complications when compared to those < 1 hour long (OR 3.70 [2.20-6.23]; p<.0001).

CONCLUSIONS

Surgical time was predictive of complications in both laparoscopic and open myomectomy. Laparoscopic myomectomy had a lower complication rate overall. For laparoscopic cases, there was an increase in complications at > 3 hours compared to < 1 hour and for open cases there was an increase in complications at > 2 and < 3 hours compared to < 1 hour. Careful patient counseling and preparation to increase surgical efficiency should be prioritized for either approach.

STATUS

Medical Student

AUTHORS

Kathryn Denny

Maria Victoria Vargas

Samantha L. Margulies

Cherie Marfori

RESEARCH MENTOR/ DEPARTMENT CHAIR

Maria Victoria Vargas

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Natural Language Inputs for Medication Reconciliation: A Feasibility Study

INTRODUCTION

Medication errors and adverse events are common throughout the health care continuum, often at transitions of care. The clinical and financial impact of these events is significant, both to the patient and the healthcare system. In 2005, The Joint Commission identified medication reconciliation as National Patient Safety Goal No. 8 in effort to reduce errors and subsequently improve patient outcomes. Our study aims to address medication reconciliation using an innovative approach that leverages a mobile natural language processing (NLP) software application for vocal medication intake. In this study we captured recordings of medications spoken in a variety of dialects from laypersons in order to determine the accuracy and sensitivity of voice recognition with natural language processing in various environmental settings.

METHODS

The study protocol was approved by the IRB. We recruited and interviewed adult volunteers who spoke English on the National Mall in Washington, DC. Participants completed a demographics survey and were asked to recall up to five medications, supplements, or vitamins of their choosing to speak into the IOS mobile application run on an iPhone. The application processed the input by recognizing the speech from the voice recognition engine and then matching recognized medications with a grammar derived from a limited National Drug Code (NDC) directory. If identifiable, the screen displayed text listing the items spoken.

RESULTS

Forty-seven participants were recruited and forty-six inputs were suitable for analysis. Participants represented four countries and seventeen US states.

We used industry standard measures for speech recognition Word Error Rate (WER) and information retrieval measures of Precision and Recall in order to gauge the accuracy of the application at medication recognition. Without accounting for medications spoken that were not listed in the NDC directory, the application had a Recall rate of 97% with Precision of 77% and WER of 29%. Including only identifiable medications, Recall remained 97% and Precision increased to 82%.

CONCLUSIONS

The results of this feasibility study suggest that the use of voice recognition and NLP for medication intake can be effective. We found that even with a variety of layperson inputs recorded against a wide range of background noise levels, the NLP software accurately detected medication inputs from laypersons with high precision and recall rates. In future testing, we plan to include more common names of medications to improve recognition. We also want to control ambient noise by testing in task-appropriate environments, including the home, clinic or hospital.

STATUS

Medical Student

AUTHORS

Marquise Hopson

Neal Sikka

Charles Jankowski

Ann Thyme-Gobbel

RESEARCH MENTOR/ DEPARTMENT CHAIR

Neal Sikka

QUALITY IMPROVEMENT

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Care Team Fact Sheets: An Intervention to Improve Communications, Understanding, And Satisfaction Between Patient And Provider

Hospitalized patients often have a large number of physicians caring for them including primary hospitalist and additional consultant teams. Further, in a teaching hospital, residents and fellows can multiply the number of providers a patient meets, often leading to patient confusion and ineffective communication. Our research objective is to study whether Care Team Face Sheets with labeled photographs of the patient's primary medical team will improve hospitalized patients' ability to identify at least one of their primary hospital physicians by name. Further, we will assess if these sheets are associated with improvements in important patient measures including physician communication, plan-of-care understanding, and overall satisfaction with their hospitalization. We hypothesize that patients in the intervention group may have a better relationship with the physicians in their treatment team, which could lead to better communication, understanding, and satisfaction scores than a control group.

Because this intervention a novel multistep process of navigating a dedicated website to create the Face Sheet, then providing it to the patient as part of the physician introduction, we predict that widespread adoption will not be immediate and preliminary survey data support this. Our aim is for the Face Sheet to be distributed to at least 60 percent of patients on hospitalist teams prior to the final data collection for our primary research objective. Multiple PDSA cycles have been performed to increase adoption of the Face Sheet among hospitalist teams, with interventions including educational, authoritative, visual reminders, and serial adherence assessment with direct feedback. Data collection and PDSA cycling is currently ongoing for intervention adoption.

Our study includes hospitalized adults on the academic hospitalist service for whom English is a preferred language. Patients were screened for inclusion and baseline data collected prior to the Face Sheet intervention. The process above will be repeated after the successful introduction (defined as greater that 60 percent distribution) of Face Sheets on the academic hospitalist service. We will use an intention to treat analysis to compare a post-intervention sample to pre-intervention controls.

STATUS

Resident

AUTHORS

James Howard

Angela Ryan

Veeshal Modi

Jennifer Schwenk

Caitlin Mingey

Anne Cioletti

RESEARCH MENTOR/ DEPARTMENT CHAIR

Anne Cioletti

QUALITY IMPROVEMENT

SCHOOL OF MEDICINE AND HEALTH SCIENCES

The Patient Passport: A patient-centered discharge intervention to reduce readmissions

BACKGROUND

The transition of care from the inpatient to outpatient setting is complicated, often resulting in adverse events and subsequent readmissions, higher costs, and worse patient outcomes. Inadequate patient education, incomplete discharge instructions, and lack of patient understanding of medication changes, post-discharge follow up plans, and their reason for hospitalization remain significant areas for improvement. Efforts to address these challenges in transitions of care are at the forefront of many Quality Improvement (QI) endeavors.

This QI study focuses on a specific step in the complicated discharge process by implementing a patient-centered discharge tool called a Patient Passport, with the goal of improving patient understanding of the discharge plan in attempt to reduce avoidable readmissions by 10% by December 2016.

METHODS

Five PDSA cycles were carried out over six months, with the primary objectives being to design an effective, evidence-based Patient Passport, assess how to best incorporate it into the current discharge process, evaluate barriers to completion and collection of the survey, and pilot incremental changes to the survey and its distribution and collection process. The primary outcome measure is reduction in readmission rates to the Medicine floor at GW Hospital. Interim process measures that are currently being used include: Number of Passports distributed per PDSA cycle; number of Passports collected per PDSA cycle; number of Passports completed per PDSA cycle; and barriers to distribution and collection.

RESULTS

Barriers were encountered in piloting the Patient Passport for discharge, ranging from logistical issues (pen availability), to time constraints for the nursing and medical staff, to lack of a systemic distribution and collection system for the Patient Passport, resulting in Passports getting lost. These barriers will be systematically addressed in future PDSA cycles, as noted below.

CONCLUSIONS & NEXT STEPS

A patient-centered intervention to improve the transition of care from the inpatient to the outpatient setting has great potential in reducing avoidable readmissions. At GW Hospital, a systematic process needs to be put in place to distribute and collect the Patient Passport such that the implementation can be scaled up, and the percentage of readmissions appropriately measured. Subsequent PDSA cycles will focus on the design of a distribution and collection process with the initial scale up to be completed on the Gold Team on the cardiac floor of the hospital. Active participation of nursing staff, medical staff, and hospital administrators will be essential in ensuring the success of this endeavor to reduce readmissions.

STATUS

Resident

AUTHORS

Elizabeth Kidder

Sripooja Satya

C. Harrison Fischer

Tanuka Datta

Tushina Jain

Paul Blair

Kelli Gilmer

RESEARCH MENTOR/ DEPARTMENT CHAIR

Nupur Mehta

QUALITY IMPROVEMENT

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Accuracy and the Proper Use of the Point-of-Care Analysis in Hemoglobin A1C Measurement

Serum hemoglobin A1C level is often used as a surrogate marker for the average serum glucose of an individual over the previous three months. At George Washington Medical Faculty Associates (MFA), hemoglobin A1C can be measured either by laboratory or point-of-care (POC) analysis. Some clinicians use POC values alone in glucose monitoring while others confirm the value with the additional laboratory testing. Thus, it is important to compare A1C measurements obtained by the two modalities in order to determine the proper use of these tests.

One hundred and fifteen patients were identified to have both POC and laboratory A1C values ordered on the same day, between August 2013 and August 2014. The differences between the two A1C values were analyzed and the average difference and coefficient of determination (R2) was calculated. We also computed the sensitivity and specificity of the POC method in diagnosing diabetes while using laboratory analysis as the gold standard. The impact of ordering both A1C measurements on medical management was also evaluated by reviewing clinic notes post testing.

The differences between the two measurements ranged from 0 to 3.2 with an average difference of 0.2% of A1C. The Kappa statistic is 0.761 and the coefficient of determination, R2, was 0.938. Eighty-four percent of measurements had laboratory measurements greater than POC. The POC method has a sensitivity of 88.6% and specificity of 96.3% in diagnosing diabetes. We also found that in only 4% of cases, medical management was changed based on the difference between POC and laboratory values.

In conclusion, the difference in A1C measurements between POC and laboratory methods is arguably insignificant in making clinical decisions during routine outpatient management of diabetes.

STATUS

Staff

AUTHORS

Lei Lynn

Dana Kay

Naji Younes

Sabyasachi Sen

Vivek Jain

RESEARCH MENTOR/ DEPARTMENT CHAIR

Vivek Jain

QUALITY IMPROVEMENT

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Is there an operative time at which minimally invasive hysterectomy becomes inferior to open hysterectomy?

BACKGROUND

Despite the well-established benefits of minimally invasive hysterectomy, the evidence suggests longer operative times in comparison to laparotomy. Longer operative times in both minimally invasive approaches and laparotomy have been associated with adverse outcomes. Little evidence exists to guide surgeons in both identifying patients at risk of excessive operating time and determining if the at-risk patient may then benefit from an alternative surgical approach. Furthermore, no evidence exists to differentiate an operative time at which a prolonged minimally invasive hysterectomy becomes inferior to a quicker laparotomy.

PATIENTS AND METHODS

Using the American College of Surgeons National Surgical Quality Improvement Program, laparoscopic and open hysterectomies were identified from 2005 to 2013 by CPT code. Procedures were split into open and laparoscopic and then stratified into operative time categories: < 1 hour, 1 to < 2 hours, 2 to < 3 hours, 3 to < 4 hours and > 4 hours. Outcomes in open cases were compared to those of laparoscopic cases by time.

RESULTS

There were 30,160 open cases and 33,356 laparoscopic cases analyzed. Laparoscopic hysterectomies were more likely to have longer surgery times. Overall, bleeding, return to OR and wound complications were all significantly higher in open cases. Laparoscopic cases remained superior to open cases up until > 4 hours, at which time there was no difference in bleeding or wound events when compared with open cases < 2 hours, and a higher odds of return to the operating room when compared to open cases lasting 1 to < 2 hours (OR 1.66 [1.28-2.15], P=.0001). When assessing laparoscopic cases > 3 and < 4 hours, even open cases < 1 hour duration had a higher odds of the composite complication variable (OR = 2.20 [95% CI 1.89-2.56] P<.0001). A total of 11.5% of laparoscopic hysterectomy cases lasted > 4 hours.

CONCLUSIONS

Laparoscopic hysterectomy had superior outcomes than abdominal hysterectomy overall. However, a significant rise in complications was seen with at > 4 hours, at which point there was no longer a benefit to laparoscopy when compared to abdominal cases < 2 hours. Relatively few laparoscopic cases lasted > 4 hours. Careful patient counselling, preparation to increase surgical efficiency and potentially an open approach should be considered in laparoscopic hysterectomies anticipated to be > 4 hours long.

STATUS

Medical Student

AUTHORS

Samantha L. Margulies

Maria Victoria Vargas

Kathryn Denny

Cherie Marfori

RESEARCH MENTOR/ DEPARTMENT CHAIR

Maria Victoria Vargas

QUALITY IMPROVEMENT

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Assessing severity, immediacy, and ideal setting in emergency department patients: A pilot study on inter-rater reliability

OBJECTIVES

We conducted a pilot study to assess the inter-rater reliability of ED physician assessments of three simple ED visit attributes – severity, immediacy and ideal setting, with long-term goal of developing a novel ED categorization system.

METHODS

Using 2010 National Hospital Ambulatory Care Survey (NHAMCS) data, we randomly selected 300 ED patient records for review by six board-certified emergency medicine physicians. Each physician reviewed 100 cases where each visit was assessed by two raters on visit severity and immediacy using a 7-point Likert scale, and which of six settings was "ideal" for the visit. De-identified patient demographics, complaints, time of day, day of week, triage assessment, ED care delivered (i.e. testing and medications), disposition and final diagnosis were used for assessments. Respondents classified the certainty of each assessment into "Very Certain" v. "Less Certain". Weighted kappa and interclass correlation coefficients were used to assess inter-rater agreement.

RESULTS

The included study population assessed represented a wide range of illnesses, demographics, diagnoses, ED care and disposition: age averaged 38 years, 56% were female, 34% were non-white, and 13% admitted. For severity, immediacy, and ideal setting there was fair to moderate agreement between the two raters with a weighted kappa of 0.33 (95% confidence interval [CI] 0.27-0.40), 0.30 (95% CI .23-.36), and 0.28 (95% CI 0.21-.34), respectively. When both raters felt "Very Certain" about their assessments weighted kappas were higher, but still only demonstrated fair to moderate agreement for severity 0.42 (95% CI 0.34-.51) and immediacy 0.35 (0.27-0.44). Ideal setting was not stratified by rater certainty.

CONCLUSIONS

In this pilot study, rater agreement was fair to moderate for severity immediacy, and "ideal" treatment settings for a random sample of ED patients, and only somewhat improved when the raters felt "Very Certain" about assessments. Therefore, even when assessed by expert reviewers, reliably rating ED visit characteristics is a challenge, demonstrating a fundamental validity issue in categorization systems for ED visits.

STATUS

Medical Student

AUTHORS

Michael McMullen

Jesse Pines

RESEARCH MENTOR/ DEPARTMENT CHAIR

Jesse Pines

QUALITY IMPROVEMENT

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Implementation of a Systematic Standardized Hospital Screening Protocol for Sepsis at the George Washington University Hospital

BACKGROUND

Medical interventions specific to the Emergency Department (ED) have come a long way in executing quality improvement efforts of sepsis management, as outlined in the Surviving Sepsis Campaign guidelines. Although many clinically guided recommendations have been made thanks to the therapeutic advances of large, multicenter randomized control trials (ProCESS, ARISE, PROMISE), there has been no clear superior evidence-based method of screening. Furthermore, the optimal treatment of severe sepsis and septic shock is a dynamically evolving process. Rapid response in identifying these patients and administering aggressive treatment within the initial hours of suspected physiological changes is not only crucial to improve the odds of survival, but also can greatly influence long term outcomes.

OBJECTIVE

The goal of this study is to evaluate the impact of a newly-designed systematic protocol to screen adult patients presenting with possible sepsis risk to an academic ED at a University Hospital, a site that lies at the 80th percentile in 2014 for overall sepsis mortality among its teaching hospital counterparts. We hypothesize that early screening and intervention, in addition to improvement initiatives such as education training programs for ER staff, will decreased time from triage to antibiotics administration (TTAA) which will lower hospital mortality septic patients.

METHODS

A multidisciplinary hospital sepsis committee consisting of physician, nursing, and pharmacy leadership, was established to address late sepsis recognition and above average mortality at GW. Based on the committee recommendation, a formalized screening process was suggested to quickly assess and treat patients with a potential sepsis in the ER. The screening protocol consists of two branches. The first mechanism identifies patients during triage through a nurse driven screening process (Figure1). The second mechanism is implemented when a patient who was not identified septic in triage and develops signs of sepsis in the ED. The implementation stage of the screening protocol involved multidisciplinary team education, including nurses and ED Physicians, and rewarding of timely sepsis screening and treatment.

RESULTS

We identified 100 sepsis patient over around 10 weeks before and after the intervention (Figure2). We applied a liner regression model to look at the reduction of TTAA vs days of service (DOS) which showed a significant reduction at p value of 0.0466 (Figure3). As a last step we applied Generalized Additive Model (GAM) to TTAA vs DOS and Mortality vs DOS (Figure4,5).

CONCLUSIONS

We think applying this intervention will lead to early detection of septic patient and early antibiotic administration.

Fig 1

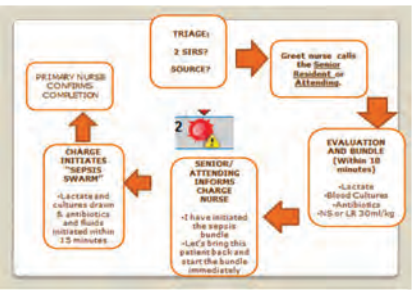


Fig 2

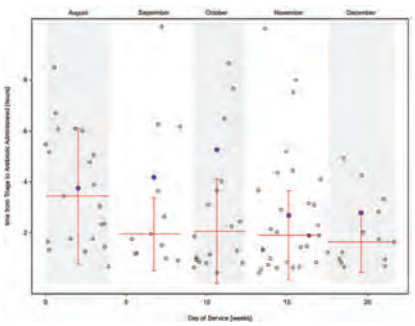


Fig 3

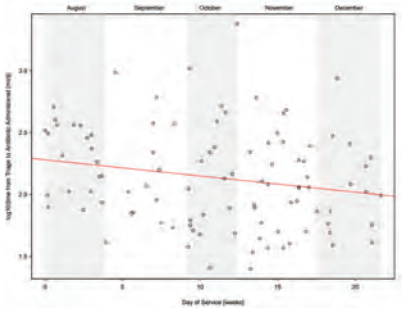


Fig 4

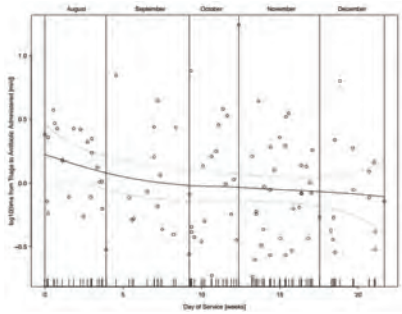
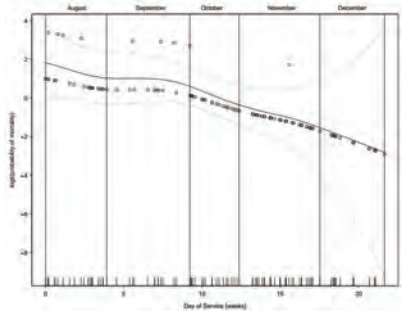


Fig 5



STATUS

Graduate Student

AUTHORS

Aleksandra Smith

Eussra El-Magbri

Imad Khojah

Ivy Benjenk

Christian Sprang

Griffin Davis

Robert Shesser

RESEARCH MENTOR/ DEPARTMENT CHAIR

Robert Shesser

QUALITY IMPROVEMENT

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Improving Advance Care Planning in Primary Care

End of life care has become an increasingly important aspect of health care in the past decade. Primary care physicians play an important role in advanced care planning (ACP) and thus end-of-life care by starting advanced care discussions with patients early on in their patient-physician relationship.

The objective of our quality improvement project is to improve the rate of ACP discussions in the primary care setting as well as the documentation of these discussions. More specifically, our aim is to increase the documentation of advance directive discussions in routine physicals performed by internal medicine resident physicians for patients age 50 and older by 20% in each PDSA cycle. Interventions (of which PDSA cycles will be built around) to increase discussions and documentation include 1) adding questions regarding advance care directives to the intake history and physical form 2) providing clear, concise information regarding ACP as a reference for patients and physicians (to be discussed during the same-day history and physical or during a subsequent visit dedicated to discussing advance care planning), 3) informing attending physicians of the above changes, and 4) providing more training regarding ACP discussions in a didactic setting via a Geriatric/Palliative Care physician.

Data collection is ongoing. Data from prior PDSA cycles indicated that interventions should target teaching residents practical skills and methods to have end of life discussions with their patients and in familiarizing residents with resources and reading materials that can be shared with their patients.

STATUS

Resident Physician

AUTHORS

Sheldon Steiner

Suneeta Ganji

Anokhi Shah

Anne Cioletti

RESEARCH MENTOR/ DEPARTMENT CHAIR

Anne Cioletti

QUALITY IMPROVEMENT

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Quality Improvement: Utilizing Telemetry Monitoring As Indicated

BACKGROUND

The utilization of telemetry services has been characterized by immense practice variation and is rife with overuse. Such programs are expensive and labor intensive, however, studies have shown that arrhythmia detection affects clinical management in only 3.4% to 12.7% of patient cases. Estimates also show that the typical 400-bed hospital could slash costs by $250,000 annually by reining in undue utilization of cardiac monitoring. By curtailing the discretionary use of these services, health care costs may also be lessened without impairing patient outcomes and other measures of quality.

AIM STATEMENT

This quality improvement plan entailed the use of education in an effort to reduce unwarranted use of telemetry services by at least 25% among the inpatient medicine ward teams. The first PDSA cycle of educational intervention was tested over a 2-month period. The educational content was tailored for residents, and included a pre-lecture quiz, a 5-minute review of indications and common misconceptions, and a handout was given that reviewed indications for residents to keep with them for future reference.

METHODS AND RESULTS

For 4 weeks before the educational intervention, telemetry usage data was collected on a daily basis (Monday through Friday) for general internal medicine inpatient wards teams only. Pre-educational conference quizzes were also administered randomly to gauge resident understanding of telemetry indications at baseline. Cumulative telemetry usage each week was noted to be 108, 153, 87, and 104 respectively. Post-intervention usage was noted daily for 2 weeks (due to holiday scheduling), totaling 82 and 94 patients, respectively. The average usage post-intervention dropped by 22%. Out of the 13 randomly selected residents who performed the pre-intervention quiz, 100% had no formal telemetry usage education previously, and the average quiz score was a mere 46% correct.

DISCUSSION

Telemetry indications are rarely formally taught, as demonstrated by our random sampling of resident data. Succinct, lecture-style education is a relatively simple and efficient way to begin to inform resident physicians in charge of placing orders for these patients on admission, and has had an impact in decreasing telemetry usage as seen in this brief resident-led pilot study. The next steps of this study will include additional 2-month PDSA cycles studying various modalities of education. If successful, then consideration for placing order alerts in the electronic medical record system may help curb usage in the long-term, and span all the various medical specialties.

STATUS

Resident Physician

AUTHORS

Sonia Taneja

Rami Alsubail

Hani Al-Hamoud

Saria Izzeldin

Teja Mandava

Greg Piech

Nathan Punwani

RESEARCH MENTOR/ DEPARTMENT CHAIR

Alan Wasserman

QUALITY IMPROVEMENT

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Sweet! Resident-driven QI leads to 50% improvement in DM2 screening

BACKGROUND

Type 2 diabetes mellitus, a chronic degenerative metabolic disease, affects more than 400 million people worldwide. Early treatment has been shown to avoid morbidity and mortality (1). Recent evidence suggests that systematic screening benefits a larger population than previously thought and prevents the development of Type 2 diabetes and associated morbidity (2).

AIM STATEMENT

To increase the appropriate screening rate for Type 2 diabetes mellitus by fifty percent over a seven month period (as defined by the 2015 guidelines by the U.S. Preventative Services Task Force).

METHODS

a. Measures:

The percentage of patient visits in resident clinic, in which screening at the interval recommended by current USPSTF recommendations had been performed (every three years in individuals at increased risk). Individuals at increased risk include those aged 40 to 70 with a BMI of 25 or greater, women with a history of gestational diabetes or PCOS, and individuals with a family history of diabetes or those of certain ethnic groups.

b. Interventions:

The authors performed resident education both through electronic reminders alone (Intervention I) as well as combined with lectures about the new practice guidelines and the efficacy of systematic screening to reduce the burden of diabetes related disease (Intervention II). Senior attendings who are supervising residents were informed about and invited to discuss the new guidelines with residents as part of their preceptor role (Intervention III).

RESULTS

The baseline rate of adequate screening was 60.00 percent of the eligible patient encounters (96/160). Following Intervention I, the rate remained virtually unchanged at 60.81%. Following Intervention II, the screening rate increased to 72.55 percent (111/151). This improvement was maintained the following month (130/183; 71.04%). Following Intervention III, screening rate improved to 96.00 percent (24/25; preliminary data). (Fig. 1)

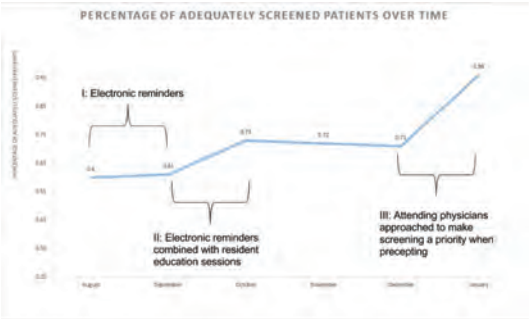


Figure 1: Changes in Screening rates over time and timing and nature of interventions

continued on following page

STATUS

Staff

AUTHORS

Dianne Thompson

Cory Bolinger

Christian Geier

Samantha Ober

Anne Cioletti

RESEARCH MENTOR/ DEPARTMENT CHAIR

Anne Cioletti

continued from previous page

In the primary-care setting, the interventions increased the percentage of adequately diabetes-screened patients from 60% to 96%. The initial interventions, which were targeted at residents alone, were followed by a slight increase in screening rates, more so when combined than in isolation. The third intervention, which included senior physicians showed the greatest improvement.

DISCUSSION/NEXT STEPS

Our observations are consistent with research regarding quality improvement in hand hygiene which suggests that bundles of measures are more effective, and that multimodal approaches e.g. those including leadership personnel, are more effective than interventions that provide education alone (3). We are hopeful that the improvements will lead to decreases in morbidity and mortality in our patient population. Going forward, the authors plan to construct an annual physical template to serve as a memory aid to alert physicians when diabetes screening is indicated or if funding can be obtained create a software based support system to standardize screening practices and continue to improve quality of care and the health of our patients.

REFERENCES

1 Siu, Albert L., and on behalf of the U.S. Preventive Services Task Force. "Screening for Abnormal Blood Glucose and Type 2 Diabetes Mellitus: U.S. Preventive Services Task Force Recommendation Statement." *Annals of Internal Medicine* 163, no. 11 (December 1, 2015): 861. doi:10.7326/M15-2345.

2 Nathan, David M. "Diabetes: Advances in Diagnosis and Treatment." *JAMA* 314, no. 10 (September 8, 2015): 1052. doi:10.1001/jama.2015.9536.

3 Pronovost, Peter. "Toward More Reliable Processes in Health Care." *Joint Commission Journal on Quality and Patient Safety / Joint Commission Resources* 41, no. 1 (January 2015): 3.

QUALITY IMPROVEMENT

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Vancomycine Quality Improvement Project

BACKGROUND

Vancomycin is one of the most widely used intravenous antibiotics in the United States for the treatment of severe gram-positive infections, specifically methicillin-resistant *Staphylococcus aureus*. Under-dosing of this medication may result in ineffective treatment and an increased risk of vancomycin resistance. Over-dosing may increase the risk of side-effects such as nephrotoxicity. Troughs are used to guide dosing of vancomycin in order to maintain a therapeutic concentration (15-20 mcg/mL) that achieves a steady-state before the administration of the fourth dose. Therefore, a vancomycin trough must be timed just prior to the fourth dose to ensure that a therapeutic steady-state has been achieved. It is important for any medical facility to implement a system to determine whether medications are within their therapeutic window to reduce the risk of such complications.

OBJECTIVE

To improve quality of care by increasing the percentage of appropriatelytimed vancomycin troughs through nursing education and the institution of a vancomycin order-set.

METHODS

Data was collected through retrospective chart review of patients admitted to George Washington University Hospital who received greater than 4 doses of vancomycin before a trough was reported. Patients who received oral vancomycin, were dosed in the emergency department, received less than four doses, and those with an estimated GFR < 40 were excluded. Afterwards, the percentage of properly timed troughs was calculated. The interventions we plan to implement include: nursing and resident education regarding the necessity of proper timing in obtaining vancomycin troughs, coordination with the pharmacy in order to label bags of vancomycin with reminders, and an EMR order-set for ordering vancomycin along with an appropriately timed trough. Data collection and analysis will be repeated after each intervention.

RESULTS

Data collection reveals that in the month of October 2014, 1550 doses of vancomycin were administered to 270 patients in the GWUH. Of these, 106 patients met inclusion criteria. Only 36 out of these 106 patients (34%) were identified to have appropriately timed vancomycin troughs.

CONCLUSIONS

The initial analysis of this study has revealed that only 34% of vancomycin troughs were timed properly. This confirms that there is much need for improvement in vancomycin level monitoring at GWUH to reduce the risks of the aforementioned complications. With interventions such as nursing education and order-set implementation, we hope to improve the efficacy of antibiotic therapy at GWUH.

STATUS

Resident Physician

AUTHORS

Vladislav Tsaltskan

Bryan Senisi

Michael Elliott

Stanley Liu

RESEARCH MENTOR/ DEPARTMENT CHAIR

Anne Lesburg

QUALITY IMPROVEMENT

SCHOOL OF MEDICINE AND HEALTH SCIENCES

The medical field's views on the lack of structure and licensing among yoga therapists

Patient use of yoga therapy has increased steadily in recent years, but the field of yoga therapy is still widely widely unstructured and lacks a standardized national credentialing process. Only self-regulation via organizations such as the International Association of Yoga Therapists currently exists. This means that there is no quality control measure in this field, and there is no officially recognized license to practice. Integrative medicine centers that recommend yoga therapy each have their own unique system for vetting yoga therapists to work with patients. The goal of this project is to compile and analyze the current standards the medical community requires a yoga therapist to meet in clinical practice, and the current feeling the integrative medicine community has regarding the lack of a national yoga therapist credential. To do this, a survey was sent to heads of integrative medicine centers across the US. It inquired about the yoga therapists that currently work within those centers, what level of training the center requires a yoga therapist to have, and what these doctors believe are important steps toward forming a national yoga therapy credential. The data collected showed a wide variety of requirements for yoga therapists among the different centers. Only one-third of respondents reported an internal credentialing process at their center, but each doctor did report a list of requirements for the yoga therapists that work with them. The lowest level of training reported was RYT-200, and the highest was RYT-500 plus a masters degree. A third of the doctors require a minimum of 2 years teaching experience from the yoga therapists, and the number of years of therapy experience varied from zero to four, with one institution having the yoga therapists do in house therapy clinical training before they can officially practice. Of the survey respondents, two-thirds believe that a national standard is needed. Many different barriers to forming a national credential were reported, the most common being a lack of standardized yoga teacher training programs. The legal difficulties of forming a license were also mentioned. The survey results clarify the specific requirements the integrative medicine community needs from yoga therapists. A review of the data collected shows that the respondents overall were very responsive to the formation of a national credential for yoga therapists; the medical community is receptive to yoga therapy as a clinical profession if the practice can be standardized and regulated.

STATUS

Medical Student

AUTHORS

Sarah Van Remmen

RESEARCH MENTOR/ DEPARTMENT CHAIR

Mikhail Kogan

QUALITY IMPROVEMENT

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Nationwide Sampling for Blood Loss Requiring Transfusion in Elective Lumbar Fusion Procedures: An ACS-NSQIP Data Analysis

In the United States, there are approximately 400,000 elective lumbar fusions performed annually according to the Healthcare Cost and Utilization Project. In elective lumbar fusion cases, a blood transfusion is considered a "hit" by centers participating in the American College of Surgeons – National Surgical Quality Improvement Program (ACS-NSQIP). Recognizing there is a shortage of banked blood nationwide, unnecessary transfusions should be avoided.

Using the ACS-NSQIP database from 2005-2012, we extracted all lumbar fusion cases using identifying CPT codes along with the primary data-point on patients receiving blood transfusions. Univariate and bivariate analysis were conducted and the Wilcoxon Mann-Whitney test was used to assess for statistical significance.

The results showed statistical significance for blood transfusion between orthopedic surgeons and neurosurgeons, 21% and 14% respectively. In analyzing the odds ratio for the fusion type and number of levels performed, we determined that osteotomy had the highest odds ratio of 6.24 (95% CI: 4.19-9.29) and two-level surgeries were associated with an almost 3-fold (OR: 2.92; 95% CI: 2.43-3.50) increased risk of blood transfusion while three-level surgeries were associated with a 3.7-fold (OR: 3.66; 95% CI: 3.21-4.18) increased risk relative to one-level surgeries.

Lumbar fusion surgery has an increased propensity of having a blood transfusion. Knowing the risk factors and improving surgical techniques will allow spine surgeons to judiciously utilize the depleting supply in the blood banks.

STATUS

Resident

AUTHORS

Richard Young

Justin Shafa

Pinyao Rui

Anthony J. Caputy

RESEARCH MENTOR/ DEPARTMENT CHAIR

Anthony J. Caputy

QUALITY IMPROVEMENT

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Use of Macros for Improvement of Speed and Quality: Ensuring Accurate and Timely Patient Documentation

This study hopes to increase the speed and quality of resident documentation at GW Hospital by expanding the use of macros at George Washington University Hospital's general cardiology service.

The project will focus on medical residents who are rotating on the Gold Team service (general cardiology service). A baseline survey was recently administered to query residents regarding time spent on writing comprehensive discharge instruction sheets for patients, self-assessed quality of discharge instructions written, and baseline use of macros templates. Macros templates for discharge instructions for the most common Gold Team diagnoses (heart failure exacerbation, non-cardiac chest pain, myocardial infarction, and syncope) will be composed by the study investigators under guidance and approval from cardiology attendings.

The principal investigators will also compare discharge instructions before and after the intervention by randomly selecting 4 discharges per each of 8 Gold Team residents at baseline, and 4 discharges per each of 8 Gold Team residents during the intervention period. The instructions will be graded using a standard discharge grading form that is currently used in the Department of Medicine discharge clinic for rotating residents and has been validated in the literature. Each discharge instruction sheet will be graded by both investigators, and discrepancies will be resolved by discussion to consensus.

Among 38 Internal Medicine residents who have thus far responded to our baseline survey, 80% have indicated that composing one set of discharge instructions requires approximately 10-20 minutes on average, with 40% indicating a ten minute average. When extrapolated to the large throughput of patients that typically occurs on Gold Team, this documentation creates a significant time burden on busy house-staff—time that necessarily is spent away from direct patient care and resident education. In terms of self-assessed quality of discharge instructions, 47% believe their instructions to be of average quality and 31% believe their instructions to be of below average to poor quality. Seventy-three percent of respondents have never used macros to assist in creation of their medical record documentation. This provides a prime opportunity to expand the use of macros in documentation to achieve the goals above.

We hypothesize that the uptake of macros for the creation of discharge instructions will be high and that their use will both decrease the perceived time burden associated with composing discharge instructions and improve the quality of discharge instructions given to patients.

STATUS

Medical Resident

AUTHORS

David Zarkowsky

Freba Farhat

Ivan Pena

Christina Sensabaugh

RESEARCH MENTOR/ DEPARTMENT CHAIR

Anne Cioletti

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Inter-rater Reliability of the Berg Balance Scale with Individuals with Multiple Sclerosis at Risk for Falls

PURPOSE

The Berg Balance Scale (BBS) is a useful, objective measure to assess balance in persons with Multiple Sclerosis (MS). Each of the 14 items on the scale is scored from 0-4 based on the participant's level of independence in performing static and dynamic balance tasks. The purpose of this study was to examine the inter-rater reliability of BBS scores between two raters across 29 subjects with MS as part of the *Free from Falls* study, a collaboration between GW and the National MS Society.

SUBJECTS/MATERIALS/METHODS

The BBS was used to assess changes in balance between the experimental group (n = 15), who participated in an 8 week fall prevention program, and control group (n = 14). Each balance assessment was videotaped for scoring. Fifty-four trials were independently rated by two different examiners, which represented pre-tests and post-tests for 29 and 25 subjects respectively. Raters were trained prior to the video analysis to establish a baseline interpretation of the scoring system. Analysis of the reliability of the total BBS score was performed by an independent investigator using intraclass correlation coefficient (ICC) Model 2, and on each individual item using kappa correlation coefficients.

RESULTS

BBS total scores between raters had excellent reliability (Pre-test ICC=0.9695; Post-test ICC=0.9579). In addition, the kappa analysis for individual items on the Berg demonstrated excellent rating (Kappa > 0.75) for Items #1, 2, 3, 6, 7, 8, 11, 13, and good rating (Kappa = 0.4-0.75) for Items #5, 9, 10, 14. Items #4 and #12 had poor reliability (kappa = 0.31).

CONCLUSIONS

The BBS total score demonstrated excellent reliability between two raters for this population. Training prior to rating may have contributed to the consistency in scoring between the two raters. Two items emerged from the ratings that showed poor reliability, including the stand-to-sit and the alternating lower extremity toe-taps on a step.

CLINICAL RELEVANCE

This study suggests that two specific BBS items may be problematic for different raters. Accurate ratings could affect documentation of achieving goals, including the minimal clinical important difference (MCID), for a given patient on an outcome tool.

STATUS

Faculty

AUTHORS

John Kofmehl

Elizabeth Ruckert

David A. Scalzitti

Joyce Maring

Costello

RESEARCH MENTOR/ DEPARTMENT CHAIR

Elizabeth Ruckert

SCHOOL OF NURSING

Evidence-Based Health Assessment: The Impact of Hypertensive Disorders of Pregnancy on Future Cardiovascular Disease

Women who experience preeclampsia and other hypertensive disorders in pregnancy are at significantly increased risk for subsequent cardiovascular disease and mortality. Preeclampsia more than doubles a woman's long-term risk of cardiovascular disease (CVD) (Brown et al., 2013; McDonald et al., 2008) and nearly doubles her risk for fatal or non-fatal stroke (Bellamy et al., 2007; McDonald et al., 2008). In 2011, the American Heart Association published an update to their guidelines for the prevention of CVD. In the preventative algorithm, the first step is an evaluation of risk that includes an assessment of pregnancy complications (Mosca et al., 2011). Despite the known association between hypertension in pregnancy and CVD, many texts on health assessment, primary care, obstetrics and midwifery do not make mention of this critical link. This reflects a serious lag between research and education. Further, there is a knowledge gap among practitioners. A recent published study demonstrated that 27% of obstetricians and 45% of internists did not identify the association between hypertensive disorders in pregnancy and CVD (Wilkens-Haug, Celi, Thomas, Frolkis & Seely, 2015). With nearly 1 in 2 women developing cardiovascular disease in her lifetime, prevention is key to effective women's health care (Lloyd-Jones et al., 2006).

To further investigate this critical gap, researchers from the GW School of Nursing evaluated the knowledge of nurse practitioner and nurse-midwifery clinicians and students and found gaps similar to that reflected for physicians in the research. In addition, a review of current textbooks across disciplines was conducted. This presentation will provide the results of these investigations and make recommendations for improvement in education and practice for this critical issue for women's health care providers.

STATUS

Faculty

AUTHORS

Linda Briggs

Mayri Sagady Leslie

RESEARCH MENTOR/ DEPARTMENT CHAIR

Christine Pintz

SCHOOL OF NURSING

Does Educational Level or Specialty Certification Influence the Level of Breast Feeding Support that Nurses Provide to Newly Delivered Mothers?

BACKGROUND

Breastfeeding is the optimal method of feeding for infants in the first year of life. Support for breastfeeding begins in the hospital after delivery, yet often, adequate informational, technical, and emotional support is not provided, and formula supplementation is initiated. This limits the rate of exclusive breastfeeding. A better understanding is needed of the factors that influence support of new mothers in their breastfeeding attempts.

OBJECTIVE

This study was conducted to determine what, if any, correlation existed between nurses' level of education and specialty certification, and their support of new mothers in their quest to breastfeed their babies. It examined the relationship between a nurse's educational level and the supportive attitudes and behaviors regarding breastfeeding that he/she demonstrated. It also examined the relationship between certification status and the supportive attitudes and behaviors regarding breastfeeding that he/she demonstrated.

METHODS

Utilizing the 64 item Nursing Support for Breastfeeding Questionnaire, a quantitative study that utilizes a descriptive comparative survey design was performed. Registered nurse participants rated their level of support and attitudes about breastfeeding using a seven point Likert type scale for each question. A sample of 150 Labor and Delivery, Mother/Baby and Neonatal Intensive Care nurses in a large urban teaching hospital in the Northeastern portion of the United States was given the opportunity to complete the survey. Thirty five nurses returned the survey and 30 (n=30) met the inclusion criteria.

RESULTS

An independent samples t test was utilized to compare the results reported by nurses that held specialty certification in women's and children's nursing against those who did not. Nurses without certification reported a mean score of 5.85, while nurses with certification reported a mean score of 6.19. Significance was found to be .092, which was not considered to be statistically significant ($p<.05$). An analysis of variance (ANOVA) was done between the different educational levels. The mean score for nurses with an associates degree was 6.08, nurses with a bachelors degree was 6.03, and nurses with a masters degree was 5.51. Significance was found to be .094, which was also not statistically significant ($p<.05$). Age and years of maternal child health experience were secondarily analyzed by the same methods and also found not to be statistically significant predictors of a nurses' willingness to provide breastfeeding support to new mothers.

CONCLUSIONS

The variables of educational level and certification status were not a statistically significant predictor of a nurse's willingness to provide support to breastfeeding mothers while in the hospital for delivery. Additional research is needed with larger sample sizes to validate these results.

STATUS

Graduate Student

AUTHORS

Linda Cassar

Stephanie Wright

Pearl Zhou

Gretchen Wiersma

RESEARCH MENTOR/ DEPARTMENT CHAIR

Stephanie Wright

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Childhood violence, adult relationship violence, & adult health outcomes among South Asian women in the US

BACKGROUND/SIGNIFICANCE

The devastating effects of experiencing violence in childhood are seen well into adulthood. This has been particularly difficult to assess among South Asians (SAs) living in the US due to a lack of race-specific data.

OBJECTIVE/PURPOSE

A cross-sectional study of SA adult women living in the US was conducted to better understand the relationship between childhood exposure to violence, and gender-based violence and health behaviors in adulthood.

METHODS

A quantitative survey with over 500 SA women living in the US measured socio-demographics, exposure to violence as a child (verbal, sexual and physical), adult relationship violence, suicide, body esteem, and subjective well-being. Multiple logistic and linear regression models examined whether childhood violence was associated with suicide ideation and attempt; adult intimate partner violence; body esteem and subjective wellbeing. All models adjusted for age, household income, country of origin, and acculturation.

RESULTS

The models on suicide ideation and attempt, yielded significant findings for childhood verbal abuse (OR 5.22; 95% CI 3.06 – 8.91 and OR 4.91; 95% CI 2.34 – 10.32, respectively); childhood physical abuse (OR 3.71; 95% CI 1.56 – 8.79 and OR 5.18; 95% CI 1.96 – 13.67, respectively); sexual abuse (OR 2.17; 95% CI 1.33 – 3.55 and OR 4.36; 95% CI 2.04 – 9.34, respectively); and having a battered mother (OR 2.12; 95% CI 1.21 – 3.72 and OR 2.68; 95% CI 1.22 – 5.81, respectively). Significant associations were found between childhood verbal abuse and body esteem ($\beta = -0.18$, $p<0.001$); childhood verbal abuse and subjective well-being ($\beta = -0.20$, $p<0.001$); and childhood physical abuse ($\beta = -0.12$, $p<0.01$) and having a battered mom ($\beta = -0.11$, $p<0.01$).

DISCUSSION/CONCLUSIONS

To date, this is the first study to examine childhood violence and its relationship to adult violence and health among South Asian women in the U.S.

STATUS

Graduate Student

AUTHORS

Nitasha Chaudhary

Amita N. Vyas

Karen M. McDonnell

Loretta DiPietro

RESEARCH MENTOR/ DEPARTMENT CHAIR

Amita N. Vyas

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Smoking Characteristics and Psychiatric Comorbidities of Pregnant Smokers: An Analysis of Quit4Baby Randomized Controlled Trial

BACKGROUND

Text messaging or short message service (SMS) programs have been shown to be effective in helping adult smokers quit smoking (Abroms et al., 2014). However, to our knowledge, no prior research has examined psychiatric comorbidities associated with smoking in the text messaging context. The risk of smoking has been shown to increase as a function of the number of psychiatric illnesses with which a person is diagnosed (Aubin, Rollema, Svensson, & Winterer, 2012). The current study examined this association and other correlates of smoking-psychiatric comorbidity in a sample of U.S. pregnant smokers enrolled in Quit4Baby, a smoking cessation text messaging program for pregnant smokers that was adapted from Text2Quit.

METHOD

Pregnant women enrolled in Text4baby and who were current smokers or recent quitter (N=505) were enrolled in a Quit4Baby efficacy study. Those under the age of 14, not pregnant, without a cell phone for personal use, and not currently smoking were ineligible. Participants were surveyed at baseline, and self-report measures of psychiatric conditions and smoking outcomes were assessed.

RESULTS

Consistent with previous studies, the number of comorbid diagnoses was significantly associated with heavy (>20 cigarettes/day) smoking. Moreover, among current smokers, there was a significant difference between groups on number of cigarettes smoked by number of psychiatric comorbidities as determined by one-way ANOVA ($F(3, 503) = 7.789$, $p = <0.001$) A Tukey post-hoc test revealed that the number of cigarettes smoked was significantly higher for pregnant smokers with 1 comorbidity (9.64 ± 8.469, $p = <0.001$) and 3 comorbidities (8.88 ± 6.374, $p=.026$) compared to those with no psychiatric comorbidity (6.36 ± 4.938). Pregnant smokers with 2 comorbidities (8.23 ± 6.761, $p= 0.056$)was marginally significant. The regression analysis also showed odds ratio of 7.58 for having a Fagerstrom Test for Nicotine Dependence (FTND) sum score of 6 or higher for three psychiatric diagnoses compared to no psychiatric diagnosis.

CONCLUSIONS

The current findings of increased rates of mental disorders among smokers and nicotine-dependent smokers in the pregnant women population are supported by this study. The intention to stop smoking should be proactively supported among these comorbid pregnant smokers. Upon the conclusion of the Quit4Baby randomized controlled trial, the effectiveness of text messaging interventions on psychiatric comorbid pregnant smokers will be examined.

STATUS

Graduate Student

AUTHORS

Shawn Chiang

Lorien Abroms

Jennifer Schindler-Ruswich

Leah Leavitt

RESEARCH MENTOR/ DEPARTMENT CHAIR

Lorien Abroms

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Media Utilization and Perceptions of Gender Inequality/Girls' Education in India

BACKGROUND

Gender inequality is a pervasive issue in India, particularly for adolescent girls. Adolescent girls are commonly married young, quickly become mothers, and are then burdened by stringent domestic and financial responsibilities. Many studies have illustrated how investments in girls' education lead to better health and well-being at the individual, family, and community level. Specifically, studies have linked education with reduced child and maternal death; improved child health; and lower fertility. At the same time, utilization of media in India has grown rapidly in recent years. Previous studies have found that media plays a critical role in in shaping attitudes and behaviors, and further, mass media can play a strong advocacy role by creating awareness and bringing about action. To that extent, this study will examine whether media utilization (i.e., watching TV, using social media, and listening to the radio) influences a person's perceptions of gender norms and girls' education.

METHODS

Secondary data analysis of a cross-sectional study lead by the Girl Rising India team will be conducted. A representative household sample of lower-middle/middle class adults (n=1607) ages 18 to 65 living in urban/peri-urban regions of eight states in India were recruited for a quantitative survey. Descriptive and multivariate analyses will be conducted to explore relationships between hours of TV watched, hours of radio listening, hours of Internet/web use, social media use, and perceptions of gender inequality and girls' education.

RESULTS

Results will include frequencies and means on sociodemographic and other key variables. Bivariate and multivariate analyses will be conducted for each media utilization variable and perceptions of gender inequality and girls' education.

CONCLUSION

Findings will provide a better understanding of whether media use influences gender perceptions. In addition, this study will help determine how to better target this audience with gender equality messages. Future programs will be able to create effective media campaigns to reduce gender inequality in India.

STATUS

Graduate Student

AUTHOR

Pooja Chumble

RESEARCH MENTOR/ DEPARTMENT CHAIR

Amita Vyas

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Pregnancy and Birth Outcomes in Women with an Intrauterine Device in situ

BACKGROUND

Pregnancy with an *in situ* intrauterine device (IUDs) is associated with increased incidence of abortion. However, if abortion does not occur, pregnancy outcomes with IUDs are not well described.

OBJECTIVES

The objectives of this study is to determine the association between IUDs present during pregnancy and the occurrence of abortion (spontaneous or induced), preterm Delivery (PTD), and small for gestational age (SGA) newborns.

METHODS

We analyzed the National Inpatient Sample (NIS) database for the years 2010 and 2011. The NIS is a database of all-payer inpatient hospital stays collected from about 1000 hospitals across the United States from different hospital settings, care levels and diverse population. We identified the presence of an *in situ* IUD during delivery, spontaneous or induced abortion, PTD, and SGA using International Classification of Diseases codes (ICD-9). We used chi square and Fisher's exact tests to calculate odds ratios (ORs) of abortions, PTD and SGA in women with IUDs compared to those without. We repeated the analysis using logistic regression models to control for possible confounders including maternal race, age, hypertension, diabetes, infections, obesity, smoking and many others.

RESULTS

We studied 8,597,284 maternal birth records. The prevalence of IUD *in situ* was 0.02%. Patients with an IUD *in situ* experienced greater risk for spontaneous abortion (OR= 7.2; CI: 5.1 – 10.1, p <.001) and induced abortion (OR=23.1; CI: 15.6-34.4, p<.001) than patients without an IUD in place. When compared to women without IUDs, women with IUDs *in situ* had significantly increased risk for PTD (adjusted OR=2.04; CI: 1.7-2.4, P <.001) after adjusting for associated demographic and clinical variables. IUDs were not associated with increased risk to deliver SGA newborns (adjusted OR= 0.56; CI: 0.34-0.92, P = 0.022).

CONCLUSIONS

Presence of an IUD in situ during pregnancy was associated with increased risk for spontaneous and induced abortions. IUDs were also associated with preterm deliveries but not with small for gestational age infants.

STATUS

Graduate Student

AUTHORS

Sandy Fulkerson Schaeffer

Mohamed Mohamed

RESEARCH MENTOR/ DEPARTMENT CHAIR

Mohamed Mohamed

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Maternal depression and child externalizing behaviors

About 10.97% of women with children aged 1 to 4 years old are identified with depression. Children of mothers with depression are more likely to exhibit externalizing behavior problems, and these problems have been reported to appear more frequently in male children. We examined the association between maternal depression and externalizing behavior in toddlers, and whether child sex moderated these effects, as previous studies have shown child behavior to be linked to both child sex and maternal depression.

The sample included 186 mother/child dyads (95 male children) who were recruited in the first trimester of pregnancy from an urban hospital. We measured maternal depression using the Beck Depression Inventory-II at 24 months of child age. Mothers were identified as having high or low levels of depression based on the clinical cutoff score of 17 or higher. Externalizing behavior was measured at 36 months of child age using maternal reports on the Child Behavior Checklist (CBCL). The raw scores on the CBCL were then converted into t-scores and used in analyses. We used univariate analysis of variance to examine differences in externalizing behavior, with high vs. low levels of maternal depression and child sex as the independent variables and scores on the externalizing behavior subscale as the dependent variable.

There was a significant association between maternal depression at 24 months and externalizing problems at 36 months ($F=201.344$, $p=0.045$). Mothers at or above clinical cut-off for depression at 24 months of child age later reported higher externalizing problems in their child at 36 months of child age. There was no main effect of child sex, or an interaction of child sex and maternal depression. Thus, this association was not different for boys and girls.

These results suggest mothers who have clinical levels of depression at toddler age have children with higher maternal reports of externalizing problems at preschool age. This association did not vary as a function of child sex. This result contradicts the expected result that externalizing behaviors in male toddlers would be more severe than in female toddlers. One implication is that treating maternal depression during early childhood may decrease the prevalence of externalizing behaviors in children. This may lead to healthier social development of these children.

STATUS

Graduate Student

AUTHOR

Julia Gruspier

RESEARCH MENTOR/ DEPARTMENT CHAIR

Rina Eiden

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Food allergy and health-related quality of life in a racially diverse sample

RATIONALE

Food allergy (FA) prevalence and health-related quality of life (HRQoL) may differ among demographic groups, but most studies have focused on predominantly Caucasian populations. This study characterizes FA and HRQoL among a racially diverse sample.

METHODS

An online survey assessed demographics, perceived risk of allergen exposure, perceived severity, FA worry, and HRQoL (Food Allergy Quality of Life– Parental Burden questionnaire) among 103 caregivers recruited from the pediatric allergy clinic at Children's National Medical Center.

RESULTS

Caregivers were 8.7% Hispanic, 44.4% Caucasian, 26.2% African American, 8.7% Asian American, and 9.7% Non-Hispanic Other. Mean child age was 5.28 years (SD = 4.35); mean FA number was 2.85 (SD = 1.95). Prevalence of individual FAs were comparable among racial/ethnic groups; there were no significant differences in FA number, $p > .05$. Controlling for age, Asian Americans reported a significantly higher perceived risk of allergen exposure than African Americans, $F (4, 92) = 2.89$, $p < .05$. After controlling for age, there were no significant differences in perception of FA severity, FA worry, or HRQoL among racial/ethnic groups, $p > .05$, but notably, Asian Americans reported the highest perceived FA severity, African Americans were most worried, and Hispanics reported the worst HRQoL.

CONCLUSIONS

Results from a diverse allergy clinic indicate no racial/ethnic differences regarding FA prevalence. Variations regarding FA perceptions and HRQoL were apparent. Additional research is needed with larger, diverse samples to further elucidate patterns of FA perceptions and HRQoL among racial/ethnic groups.

STATUS

Medical Student

AUTHORS

Linda Herbert

Elizabeth Flory

Hemant Sharma

RESEARCH MENTOR/ DEPARTMENT CHAIR

Linda Herbert

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Maternal Leisure-time Physical Activity and Risk of Preterm Birth: A Systematic Review of the Literature

BACKGROUND

Preterm birth is a leading cause of infant death and regular physical activity may reduce the risk for preterm birth because of its beneficial effects on pregnancy complications such as preeclampsia, excessive weight gain, and gestational diabetes. On average, however, pregnant women report lower levels of physical activity compared with those who are not pregnant. This systematic review examined low, moderate and vigorous leisure-time physical activity (LTPA) during pregnancy and the outcome of preterm birth.

METHODS

Key words related to preterm birth and physical activity were used to search relevant databases (Medline, Cochrane, CINAHL, Sports Discuss and Scopus). Studies were excluded if they did not measure physical activity as an exposure in pregnant women, did not provide information on gestational age at delivery, and were not published in English. All study designs and sample sizes were considered.

RESULTS

The search generated 1472 studies. There were 27 studies included in this review of which 23 received high quality reporting scores. A total of 13 studies reported a significant protective effect of LTPA on the risk of preterm birth. Physical activity of both moderate and vigorous levels was associated with a lower risk of preterm birth in a number of studies, with relative risk estimates ranging from 0.08 to 0.90. Low-intensity activity was also significantly associated with a lower odds of preterm birth, provided the duration of such activity was ≥8hr/day at weeks 23-26 (OR=0.56, 95% CI=0.36, 0.87) or >20min/day during the second trimester (aOR=0.36, 95% CI=0.16, 0.78). Fourteen studies reported null findings, while only two studies detected a significantly higher risk of preterm birth with LTPA during pregnancy.

CONCLUSION

This review of literature up to 2014 provides evidence to support the assertion that healthy pregnant women can engage in low, moderate, and even some vigorous levels of LTPA without risk for preterm birth.

STATUS

Alumna

AUTHORS

Mira Kahn

Kimberly Robien

Loretta DiPietro

RESEARCH MENTOR/ DEPARTMENT CHAIR

Loretta DiPietro

WOMEN/CHILD HEALTH

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Impact of Sexual Health Knowledge Acquired in Adolescence on Incidence of Sexual Violence in Young Adulthood

Rates of sexual violence victimization are incredibly high among young women in the United States. Although these high rates exist, many young people do not receive formal comprehensive sexuality education, which could help to prevent the occurrence of sexual violence. Currently, little research has been conducted on the long-term impacts of sexual health knowledge obtained during high school, or on the relationships between sexuality education and experiences of sexual violence victimization. This study aims to examine the long-term impacts of sexual health knowledge on sexual violence victimization. The dataset used in this study is a subset of the National Longitudinal Study of Adolescent to Adult Health, Waves I and IV. This survey was conducted by administering an in-home questionnaire to a nationally representative sample of adolescents who have been followed through four waves of data collection since 1994. Multivariate analysis will be conducted using Stata 14 to determine the relationship between the level of sexual health knowledge individuals demonstrate during high school, and whether or not they experience sexual violence victimization after high school. Results of this analysis will inform future research on the impact of sexuality education policy, and contribute to the body of knowledge that is used to inform programs and policies aimed at preventing sexual violence.

STATUS

Graduate Student

AUTHOR

Brittany Perrotte

RESEARCH MENTOR/ DEPARTMENT CHAIR

Karen McDonnell

WOMEN/CHILD HEALTH

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

The Effect of the Liberian Civil Wars on Maternal and Child Health

In 1989 Liberia broke out in the first of two civil wars that would last until 2003. As a result of both wars, approximately 200,000 people were killed and another 1.5 million were forced to flee their homes. Once peace was achieved, Liberia's health system was in state of disarray. The majority of health facilities were destroyed and the entire state only had 30 physicians. Ellen Johnson Sirleaf was elected to office in 2005 and made repairing Liberia's health system one of her top priorities. One of her main focuses was maternal and child health. This study examines data from Liberia pre-civil war, immediately post-civil war, and the most recent data available. The data used is from the Demographic Health Surveys made available by USAID. The aim of the study is to demonstrate if Liberia's two civil wars had an impact on its maternal and child health indicators and the change that has occurred since. Ghana is used as a control due to its geographic proximity and absence of civil war. While final results of this study are still pending, initial results demonstrate that Liberia is developmentally behind Ghana in maternal and child health indicators.

STATUS

Graduate Student

AUTHOR

Hallie Stevens

RESEARCH MENTOR/ DEPARTMENT CHAIR

Karen McDonnell

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Investing in Girls: Do Gender Perception and Attitudes Matter?

BACKGROUND

India is one of the most challenging nations to be a girl and gender discrimination is pervasive across a girls' lifespan. The prevalence of child marriage, maternal mortality, violence, and malnutrition are particularly high in India. Further, 40% of girls do not make it past class 8. When a community invests in a girl's education, she marries later, experiences less violence, and has healthier children. Understanding gender norms and attitudes is critical to addressing programs and policies that ensure healthy and educated girls and women.

METHODS

A representative sample of adults (n=1607) ages 18 to 65 living in urban/peri-urban regions of eight states in India was recruited for a cross-sectional survey. The survey instrument measured attitudes toward gender, perceptions of secondary education, and perceived self-efficacy. Descriptive analyses will be conducted to assess overall perceptions and attitudes towards gender equality and girls' education, and whether they vary by gender, age, socioeconomic class, number/gender of children.

RESULTS TO DATE

Preliminary analyses suggest variability in attitudes toward gender and education by socioeconomic class, gender, and age. Women and participants ages 50 to 65 were significantly more likely than men and younger participants to identify the importance of a girl's education. Participants ages 50 to 65 were more likely to have positive attitudes toward girls' education than younger participants.

CONCLUSIONS

Findings from this study will provide insight on attitudes toward gender and girls' education, which is critical to the development of interventions and policy. Further, results will guide the development of more robust and reliable gender attitude scales specific to adolescent girls.

STATUS

Graduate Student

AUTHORS

Amita Vyas

Jordan Genovese

RESEARCH MENTOR/ DEPARTMENT CHAIR

Amita Vyas