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"Neuron" by Helen Rynor
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LETTER FROM THE EDITORS

Dear Readers,

We are proud to present the first issue of the fourth volume of the *Florida Medical Student Research Journal* (FMSRJ). This journal was founded in 2015 by two medical students at the Florida International University (FIU) Herbert Wertheim College of Medicine (HWCOM) as a means to showcase the academic achievements of medical students. The FMSRJ publishes work from any health professional or student related to medicine for peer review by Florida medical student editor teams. Through the continued efforts and talent of the student editorial teams, the Journal has developed to represent a venue for innovative, scholarly pursuits.

This year has been unprecedented. Manuscript submissions exceeded all previous years, readership and published materials have expanded beyond FIU, there is collaboration with FIU student journal *Eloquor,* and faculty experts were incorporated into the peer review process alongside student editors.

Our team presents original research representing a range of topics from the bed to the bedside followed by interesting case reports of rare conditions, surgical innovation, and a reminder of the importance of providing thorough, quality care. Readers will then enjoy clinical reviews of related to the fields of dermatology and oncology topics as well as a historical narrative of the role of physicians in early Florida. We are honored to contribute to the existing academic discussions relevant to these articles. In addition to the articles, we also publish the proceedings of the 2019 FIU HWCOM research symposium.

This issue would not have been possible without the generous support of our Executive Advisory Board Drs. Sheldon Cherry, Joe Leigh Simpson, and Juan Acuña as well as the numerous faculty advisors who served as expert reviewers and mentors to the student editors. Thank you to the student editors, authors, administrative personnel, and design team whose guidance, dedication, and work helped to realize the publication of this issue. A special thank you to Helen Rynor, Emily Geisler, and *Eloquor* for the beautiful cover art and art pieces amongst the research. It was truly our pleasure to have this opportunity to work alongside and manage such an incredible team. Lastly, thank you to our families whose unwavering support and example continue to inspire and motivate us to achieve our goals.

We hope this issue will inspire your curiosity and encourage you to continue on the pursuit of your academic aspirations.

Sincerely,

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Dear Readers,

This is the first issue of The Florida Medical Student Research Journal published since I began my tenure as the Dean of Herbert Wertheim College of Medicine. It brings me great joy to be able to address you, the readers, in a forum that is dear to me. Medical education is grounded in social consciousness and a commitment to improving human welfare. As medical professionals involved in basic or clinical research, patient care, and medical education, we share in the noble mission to improve medical care and, thereby, realize better outcomes for all diseases.

Our efforts as scientists, clinicians, and educators are interwoven, addressing the social determinants of disease and the biological basis of disease to improve the human condition. Medical journals such as The Florida Medical Student Research Journal provide forums for disseminating knowledge gleaned through the research, and facilitating translation of that knowledge into actionable strategies that improve patient welfare.

Peer review is essential to the process of validating research findings. The Florida Medical Student Research Journal offers medical students the opportunity to participate in peer-review and to have their own work published. I look forward to collaborating with the students and the readership as we continue to promote scholarly productivity and innovation through medical research.

Our medical school is entering the digital age and presenting information for learning is challenging. The Florida Medical Student Research Journal will be at the forefront in enabling our goals of "bench to bedside" medical care.

On a personal level, I again want to state my great honor and privilege to have the opportunity to work with, and for, each of you to build a very special medical school.

Sincerely,

Robert Sackstein, M.D., Ph.D.

Senior Vice President for Health Affairs
Dean, Herbert Wertheim College of Medicine

Pseudomonas aeruginosa Anti-sigma Factor MucA Shows Essential Similarities to *Escherichia coli* RseA and Other Pathogens

Brett Colbert, B.S.

University of Miami Miller School of Medicine,

Medical Scientist Training Program, Miami, FL, USA

Corresponding Author: Brett Colbert, bmc48@miami.edu

Abstract

Pseudomonas aeruginosa is a Gram-negative, ubiquitous bacterium that often causes respiratory infections in individuals with cystic fibrosis (CF). A major factor contributing to patient morbidity and mortality in these infections is the production of a polysaccharide called alginate that protects the bacterium from the host's immune system and antibiotic therapies. Ordinarily, the sigma factor (AlgT/U) required for alginate biosynthesis is sequestered to the inner-membrane of the cell by MucA, an anti-sigma factor; if MucA is cleaved or mutated, AlgT/U is left free to guide RNA polymerase to transcribe the genes needed for alginate production. MucA is a crucial player in alginate regulation. However, not much is known about the active sites in MucA that play this critical regulatory role. The *Escherichia coli* homolog, RseA, however, has been extensively studied and its active sites have been determined experimentally. This study compared the two, as well as twelve other pathogenic bacteria with homologs to RseA. The protein sequences were aligned and two conserved domains were identified by batch search in PFAM. While there is low overall sequence homology between the various proteins, homology is much higher within the identified domains. Moreover, the residues within the active site necessary for sigma factor binding- as determined experimentally in *E. coli*- were conserved across all species analyzed. These findings will guide future work to verify the results *in vitro* and could lead to the development of an anti-alginate therapy by restoration of MucA functionality or the generation of a synthetic MucA that could sequester AlgT/U.

Key Words: alginate, exopolysaccharide, sigma factor, cystic fibrosis

Introduction

Pseudomonas aeruginosa is a gram-negative, ubiquitous bacterium that is the leading cause of death in those with cystic fibrosis (CF), a common autosomal recessive genetic condition in which a buildup of mucous provides an ideal environment for bacterial colonization[1,2]. One of the major contributing factors to the morbidity associated with *P. aeruginosa* is the production of an exopolysaccharide called alginate[3-5]. Alginate is produced when the cell senses some stress in the environment, such as the oxidative radicals of the immune response, antibiotic therapy, or desiccation. The polysaccharide coats the cell and acts as a physical barrier to the stressor[6]. Isolation of an alginate-producing strain from the lung of a CF patient is indicative of a very poor prognosis[3-5]. More than likely, the patient will die from the infection [5].

Alginate production is metabolically expensive for *P. aeruginosa*. Thus, it is tightly regulated and only expressed when necessary[7-10]. The primary regulatory unit of alginate production is a five-gene operon containing *algT/U-mucA-mucB-mucC-mucD*[11]. The first gene of this operon, *algT/U*, codes for a sigma factor able to bind to RNA polymerase (RNAP), guiding it to transcribe the genes necessary for alginate production[12,13].

Ordinarily, MucA, an anti-sigma factor, sequesters AlgT/U to the inner membrane, preventing it from directing RNAP; however, when *mucA* is mutated or cleaved, AlgT/U is left free to guide RNAP (Figure 1) to transcribe the genes needed for alginate biosynthesis[8,14].

MucA is a 194 amino acid protein which is localized to the inner membrane of the *P. aeruginosa* cell[15]. It has two domains: the cytoplasmic N-terminus that interacts with AlgT/U and the periplasmic C-terminus that interacts with MucB[15] (Figure 1). The transmembrane AlgT/U-MucA-MucB complex (Figure 1) is the bottleneck of the whole alginate regulatory process.

As a result, MucA is a prime target for potential anti-alginate therapies: restoring or enhancing the function of MucA could reduce *P. aeruginosa* alginate production, thereby making the bacterium more susceptible to traditional antibiotic therapies. Knowledge of its active sites could also lead to the generation of a synthetic MucA which could effectively sequester AlgT/U. We investigated the relation of MucA to any functional or structural homologs in other pathogenic bacteria. The *Escherichia coli* homolog, RseA was selected for a central role in this analysis due to the great amount that is already known about this protein experimentally[16,17]. The phylogenetic information could then be used to predict active sites in the *P. aeruginosa* MucA to guide future studies to uncover the precise mechanism of interaction with the sigma factor AlgT/U.

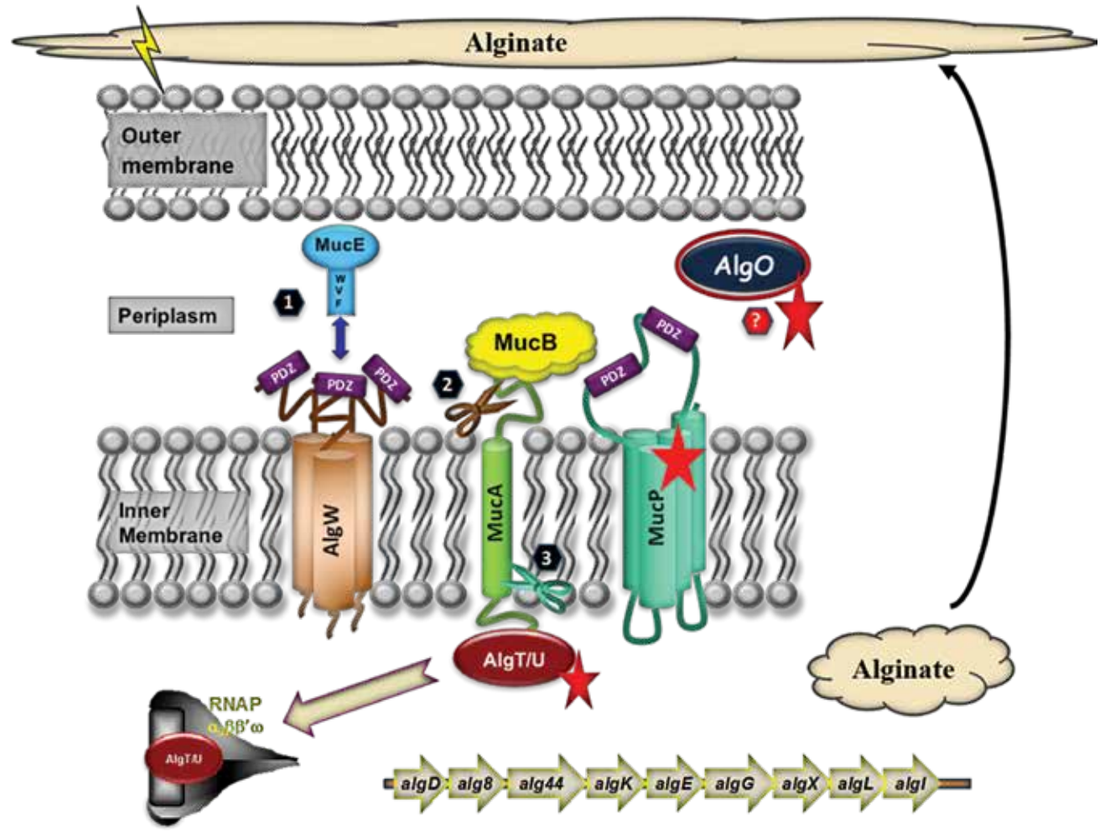

Figure 1: The *Pseudomonas aeruginosa* alginate regulation pathway. Alginate production is controlled by the sigma factor AlgT/U which is ordinarily bound to the inner membrane by the anti-sigma factor MucA to prevent interaction with RNAP. AlgT/U must be freed from MucA to begin alginate production. When stress is sensed, MucE misfolds (1) and induces periplasmic cleavage of MucA by AlgW (2). MucA is also cleaved by MucP (3) within the inner membrane on the cytoplasmic end to release AlgT/U. AlgT/U is now free to interact with RNAP and initiate alginate biosynthesis by transcribing the *algD* operon. When MucA is mutated, it is unable to sequester AlgT/U and alginate production ensues. (Adapted from Pandey *et al.,* 2016.)

Methods

The MucA sequence (Accession: NP_249454.1) was retrieved from the *Pseudomonas* database[18]. The accession number was searched in PFAM to find the domain families it contains (PFAM ID: PF03872 and PF03873). The PFAM sunburst tree was used to select sequences from 12 pathogenic species of bacteria that also have PFAM domains PF03872 and PF03873. The 12 sequences for each domain were then extracted into separate FASTA files. Two strains of *P. aeruginosa* with known MucA mutations that result in alginate production- PDO300 and PA2192- were also included in the analyses.

The 12 whole protein sequences were then submitted to PFAM batch search to identify protein domains.

The sequences were then aligned with Muscle[19] in Jalview[20]. After analyzing these results, Uniprot[21] was used to identify the experimentally determined structure and active sites of the E. coli homolog RseA and then these were compared to the multiple sequence alignment (MSA) to check for conservation of sites across the various species.

Results

A review by Pandey *et al.* compared the homology of the *E. coli* and *P. aeruginosa* stress response pathway proteins (Table 1). This analysis showed that while RseA in *E. coli* and MucA in *P. aeruginosa* are functional homologs, they only share 28.3% sequence homology. Thus, there was a need to investigate if the active sites of the proteins are conserved between the two species.

ORIGINAL RESEARCH

		E. coli K12										
		RpoE	RseA	RseB	RseC	DegP	DegS	RseP	ClpX	ClpP	SspA	SspB
P. aeruginosa PAO1	AlgT/U	66.0	7.8	18.7	15.2	20.7	18.8	21.2	25.4	16.2	9.3	15.7
	MucA	14.4	28.3	22.2	18.2	16.1	15.0	18.6	17.0	13.3	14.9	13.3
	MucB	19.4	16.2	27.6	29.9	17.2	11.4	19.5	18.4	17.0	19.3	18.1
	MucC	15.9	17.2	21.2	30.0	23.2	26.5	24.5	22.5	10.7	17.3	13.3
	MucD	22.0	19.4	17.9	15.0	39.2	33.4	15.4	15.2	23.2	16.9	19.3
	AlgW	17.4	17.6	15.8	23.9	36.8	46.3	17.2	14.3	20.3	18.4	18.7
	MucP	17.3	17.6	19.8	23.2	10.2	16.7	46.9	11.4	17.9	23.5	22.4
	ClpX	23.0	15.3	15.1	19.5	16.2	17.9	12.6	76.6	19.3	21.2	17.5
	ClpP	12.0	11.3	16.1	18.9	18.8	17.4	19.7	17.4	69.6	13.2	14.5
	ClpP2	16.6	12.6	19.4	19.6	14.9	19.4	16.4	22.6	41.5	14.2	15.7
	SspA	13.2	11.5	20.0	20.1	18.6	17.6	19.5	21.2	12.6	53.9	15.2
	SspB	16.3	19.2	20.0	18.0	21.5	20.8	22.2	18.5	16.3	20.0	53.3

Table 1: The numbers refer to percentage homology as determined using ClustalW. The shaded boxes compare the functional homologs. The protein sequences of *E. coli* and *P. aeruginosa* were retrieved from ecogene.com and pseudomonas.com respectively[8].

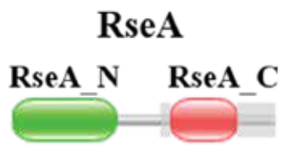

Figure 2: Domain graphic of the two domain families (PF03872 and PF03873) identified by batch search.

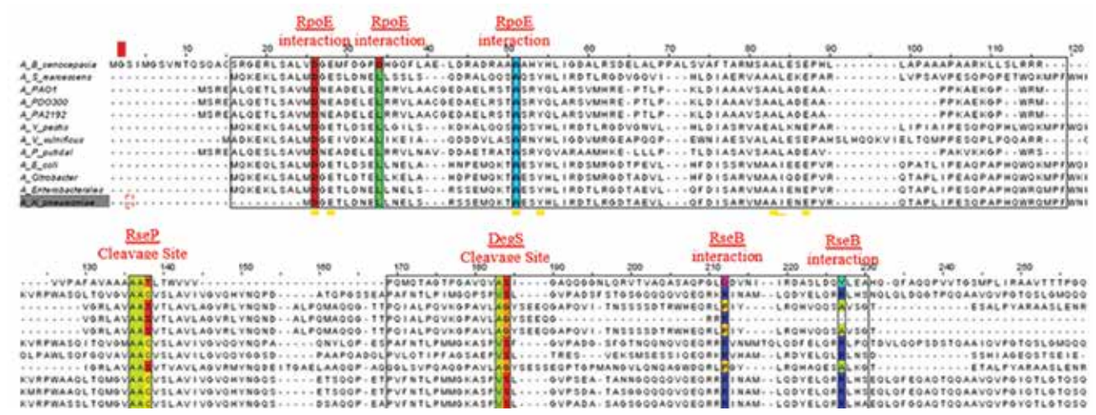

Figure 3: The MSA by Muscle with defaults. The MSA was used to determine conserved residues. The two PFAM domains are in the green boxes, and the conserved active sites are colored with Taylor and labeled by known function in *E. coli*.

Batch search of the chosen sequences uncovered the same two domains for all proteins in the analysis. The first is near the N-terminus and interacts with the sigma factor (PF03872). The second is near the C-terminus and interacts with another periplasmic regulatory protein RseB (PF03873; Figure 2).

The MSA displayed 9 sites that are conserved across all sequences. When compared to the Uniprot data on the active sites of RseA, 5 of the conserved sites are also the active site residues necessary for RseA function, suggesting that these sites are also the active sites of the other, related proteins. There are also highly similar amino acids in the same locations that RseA is cleaved by regulatory proteins (Figure 1, 3).

Discussion

Although MucA is varied in sequence across species of pathogenic bacteria, this study suggests that what is learned from studies on *E. coli* RseA may be applicable to *P. aeruginosa* and the other species we analyzed as well.

It was seen that the same two PFAM domains are present in all the sequences. Despite the lack of sequence homology across the whole protein, the active sites identified experimentally by other authors in *E. coli*[17] are conserved across all sequences. Alignment of the individual domains would further solidify this conclusion. The analysis could also be expanded to include a larger set of pathogenic and non-pathogenic bacterial species.

While mutagenic studies are needed to confirm the active site predictions made in this study, the conservation across the species analyzed at the same locations as the active sites of RseA strongly leads to the hypothesis that these are indeed the active sites in the other species. This will help direct future investigations of MucA. Specifically, the newly-identified, potential active sites can be mutated to verify that they are the active sites in *P. aeruginosa*. Further *in silico* structural analyses could be performed to observe what effect the mutations in PDO300 and PA2192 may have on MucA function as compared to *E. coli* and the *Pseudomonas* wildtype. These two strains are of particular interest since PDO300 harbors the most common *mucA* mutation leading to alginate production (*mucA22*) and PA2192 is a clinical isolate that produces almost twice as much alginate than other mucoid *P. aeruginosa* strains[7,15,22].

Conclusion

There is an urgent need for some form of an anti-alginate therapy. Mucoid *P. aeruginosa* infections are the leading cause of death in CF[5]. This therapy will likely be a combination therapy with various classes of antibiotics: the anti-alginate compound could expose the bacteria allowing the antibiotic to be effective. As of yet there is no approved and effective anti-alginate therapy. The only current therapeutic option is higher and higher doses of last resort antibiotics that are nonetheless failing. The sum of the present analyses and the proposed studies could lead to therapies that enhance the functionality of MucA in *P. aeruginosa* or generate synthetic MucA homologs that sequester AlgT/U, thereby lowering the alginate production and alleviating the morbidity and mortality concomitant upon infection with an alginate producing strain of *P. aeruginosa*.

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Investigation of Fanconi Anemia: The Downstream Genetic Pathway

Bianca Nguyen, Juan Acuna, MD, MSc, and Wenrui Duan, PhD

Herbert Wertheim College of Medicine, Florida International University, Miami, Florida 33199

Corresponding Author: Bianca Nguyen, bnguy027@med.fiu.edu

Abstract

Introduction: A key response mechanism to DNA damage is the Fanconi Anemia (FA) repair pathway, which involves homologous recombination DNA repair. A FA repair deficiency is considered to increase the sensitivity of tumors to DNA-targeted agents and may prove to be a target of cancer treatment. We aim to explore the association between the FA repair pathways and downstream genes that influence tumor growth.

Methods: To generate FANCD2 knockdown cells, human lung cancer cell line A549 was transduced with FANCD2-specific short hairpin RNA (shRNA) expressing and puromycin-resistant lentiviral particles or control shRNA lentiviral particles. The cells were cultured and successful FANCD2 knockdown was confirmed by western immunoblot analysis. Significant gene expression changes between knockdown FANCD2 and control samples across the A549 cell line was determined, defined as a five-fold change in upregulation or downregulation. The fold change was calculated by dividing FANCD2 deficient expression by FANCD2 efficient expression.

Results: 13436 genes were evaluated and 10 selected genes demonstrated gene expression change by at least 5-fold with FANCD2 knockdown in the A549 cell line. Of the five downregulated genes, four of these genes had literature supporting oncogenic function. Three upregulated genes had literature supporting oncogenic function.

Conclusion: As FANCD2 is considered to promote cell proliferation, upregulation of tumor suppressor genes and downregulation of oncogenic genes expression was expected with FANCD2 knockdown. Our results provide a starting point for developing targets to downstream genes associated with FA deficient tumors, which may prove to limit cancer progression.

Key Words: Fanconi Anemia, Lung Cancer, Gene Expression, DNA Repair

Introduction

DNA repair processes are essential for cells to maintain genome stability and to prevent genetic mutation[1]. Perturbations of DNA metabolism prevent the completion of replication and trigger DNA response pathways[2]. It has been recognized that DNA repair checkpoints are critical for hindering induction of neoplasms, rooting from defects in DNA damage response pathways[2]. Abnormalities in oncogenes and tumor suppressors can drive mutations to initiate onset and progression of cancers[3]. Known DNA repair proteins such as BRCA1 and FANCD2 can be detected in cancer cells and serve as markers for competent DNA repair function[4].

A key response mechanism to DNA damage is the Fanconi Anemia (FA) pathway, which involves homologous recombination DNA repair[4]. The Fanconi Anemia pathway is activated through mono-ubiquination of the FANCD2 protein[4]. Homologous recombination repair (HRR) is essential to prevent genomic instability related to double strand DNA damage and stalled DNA replication forks[5]. Deregulation of homologous recombination repair genes such as FANCD2 have been identified in Non- small cell lung cancer, although it is not known whether carcinogenesis is associated with a functional HRR deficiency[5]. The identification of homologous repair-deficient tumors is a significant challenge in oncology research, particularly when taking into consideration the complexity of the DNA damage response system[5] HRR deficiency may increase the sensitivity of tumors to DNA-damaging agents such as platinum or targeted agents such as PARP inhiibtors[5,6]. FA homologous repair deficiency may therefore prove to be a target of cancer treatment, as long as appropriate biomarkers become available to identify patients with these tumors[7]. Currently, there is a growing appreciation of DNA repair deficiencies in lung cancer prevention and treatment, given the high prevalence of lung cancer and increased efficacy of DNA-damaging drugs[7]. A study conducted by Duan, et.al reported the detection of 22% of NSCLC to be FA functionally inactive by the Fanconi Anemia Triple Staining Immunofluorescence test, indicating the clinical relevance of the detection and targeted treatment for patients with FA deficient tumors[7].

The FA pathway includes multiple genes which form foci of DNA repair on chromatin during the S phase of the cell cycle and during DNA damage[7]. The FA proteins encoded by these genes are thought to work cooperatively in a common signaling pathway to repair intercross links[7]. The FA repair mechanism contains 16 complementation groups, and eight of the proteins are subunits of the FA-core complex-1, which activate FANC\D2 in response to DNA damage[7]. As deregulated FANCD2 (FANCD2 knock-down cell) foci formation is associated with tumorigenesis, we hypothesize that lung cancer cells with reduced FANCD2 expression will

demonstrate downregulation of associated tumor suppressor genes and we expect oncogenic genes to demonstrate upregulation[7].

As the FA pathway is responsible for repairing DNA cross links and double-strand breaks in coordination with the HRR pathway, it is plausible that cancers with impaired FA pathways are more sensitive to platinum-based chemotherapy[7]. Given that multiple genes collaborate to influence the FA pathway, pinpointing downstream genes in FA deficient tumors can aid in understanding the FA repair response and the increased sensitivity of specific tumors to DNA damaging agents[7]. Evaluation of studies focusing on FA deficiency and tumor progression provides a basis for clinical application of certain therapies to a subset of lung cancer patients. However, few studies have examined the functionality of genes associated with FA deficient lung cancer cells. The A549 cell line is commonly studied in lung cancer lab research studies. We modified the A549 cell line to create a FANCD2 knockdown cell line. Our goal is to identify the FA associated genes that regulate cancer cell cycle progression.

Methods

To generate FANCD2 knock-down cells, human lung cancer cell line A549 was transduced with FANCD2-specific short hairpin RNA (shRNA) and puromycin-resistant lentiviral particles or control shRNA lentiviral particles. Using FANCD2- specific shRNA, we induced degradation of FANCD2 mRNA to create knockdown cells. The cells were cultured in RMP1640 growth medium, and successful FANCD2 knock-down was confirmed by western immunoblot analysis. The western blot was used to evaluate the amount of FANCD2 protein amount. RNA deep sequencing was completed with Illumina RNA-Seq to compare gene expression of the FANCD2 deficient cells to control cells. Biometrics software and bioinformatics personnel analyzed the data, providing the fold change for the FANCD2 knockdown and FANCD2 efficient cells. Given the inventory of genes associated FANCD2 knock-down cells from lung cancer patients, we compared gene expression between knock-down FANCD2 and control samples and ranked significant gene expression changes, defined as a five-fold change in upregulation or downregulation. The fold change was calculated by dividing FANCD2 deficient expression by FANCD2 efficient expression. The function of the genes deemed to have significant change were determined via a PubMed search using the gene bank.

Gene	Fold Change in A549 deficient (A549D2)/ A459 efficient (A549E)
AC011558.5	-79448541.38
RP11-350N15.6	-8752673.04
PLA2G4B	-3169698.70
RP4-635E18.7	-429066.13
RP11-321N4.5	-313697.26

Table 1: Downregulated genes associated with FANCD2 knock-down in A549 cancer cell line. Five selected genes demonstrated gene expression change by at least 5-fold with FANCD2 knockdown in the A549 cell line. The most significant gene expression change in the A549 cell line was the AC011558.5 gene. Four of these genes associated with the FA repair pathway had literature supporting oncogenic function.

Gene	Fold Change in A549 deficient (A549D2)/ A459 efficient (A549E)
RNA5S16	19122373.25
RP11-801F7.1	259353.62
RP11-360L9.7	648539.22
RP11-298I3.5	30443.26
AC114546.1	21818.55

Table 2: Upregulated genes associated with FANCD2 knock-down in A549 cancer cell line.

Results

Five selected genes demonstrated gene expression change by at least 5-fold with FANCD2 knockdown in the A549 cell line The RNA5S16 gene demonstrated the most significant gene expression change. Gene expression profiles were evaluated for these significant genes, and three upregulated genes had literature regarding oncogenic functionality. The genes with significant alterations in expression with FANCD2 knock-down are listed in tables 1 and 2. Of the five downregulated genes, four of these genes had literature supporting oncogenic function.

Downregulated genes AC011558.5, RP11-350N15.6, PLA2G4B, RP4-635E18.7, and RP11-321N4.5 demonstrated significant expression change in the A549 cell line. The most significant gene expression change in the A549 cell line was the AC011558.5 gene, with a range of -79448541.38 to -3.04. No literature was found concerning the function of this gene. PLA2G4B displayed a significant downregulation with -3169698.70 fold change in the A549 cell line. This gene was found to be expressed in head and neck squamous cell cancer, and in breast cancer cells[8,9]. RP4-635E18.7 exhibited a significant fold change in the A549 cell line, with a change of -429066.13 folds. This long noncoding RNA is associated with prognosis of patients with glioblastoma multiforme[10]. RP11-321N4.5 downregulation was correlated to FA knockdown by a significant fold change of -313697.26 in the A549 cell line. The RP11 gene is associated with increased ovarian cancer risk and increased transcriptional activity [11,12]. The RNA5S16 gene demonstrated the most significant gene expression change, with a change of 19122373.25 fold. No literature was found regarding function of this gene. RP11-801F7.1 displayed an upregulation in the A549 cell line, with a change of 53319.09 fold. RP11-360L9.7 is another isoform of the RP11 gene, exhibiting a significant gene expression change of 648539.22 folds. RP11-298I3.5 displayed moderate fold change compare to other RP11 variants. The RP11 gene is associated with increased ovarian cancer risk and increased transcriptional activity [11,12]. The AC114546.1 gene demonstrated significant upregulation with FANCD2 knockdown, with a fold change of 21818.55. No literature found concerning function of this gene.

Discussion

Gene expression profiles were determined in order to identify genes and associated pathways differentially regulated upon FANCD2 knockdown. Five genes were determined as very significant in terms of downregulation in response to FANCD2 knockdown. These genes include: AC011558.5, RP11-350N15.6, PLA2G4B, RP4-635E18.7, and RP11-321N4.5.

The Phospholipase A2, group IVB (PLA2G4B) gene was downregulated with FANCD2 knockdown and exhibited a -3169698.70 change in the A549 cell line. Fusion of PLA2G4B with JMJD7 has been reported in head and neck squamous cell cancer (HNSCC)[8]. This read-through fusion gene modulates phosphorylation of Protein Kinase B (AKT) to promote HNSCC tumor survival[8]. This suggests the oncogenic function of PLA2GB4, as ablation of this fusion gene inhibited proliferation of cancer cells by promoting G1 cell cycle arrest and increased starvation-induced cell death compared to JMJD7- only knockdown HNSCC cells[8]. Additionally, basal expression of this gene was higher in breast cancer cells HCC1143, further supporting the oncogenic function of this lipolytic gene[9].

RP4-635E18.7 is a long noncoding RNA (lncRNA) that is associated with glioblastoma multiforme (GBM) [10]. A study conducted by Lei, et al analyzed lncRNA expression profile in GBM and found that this gene was involved in cell to cell signaling, and was related to the mitogen-activated protein kinase signaling pathway[10]. This gene served as a biomarker for the prognosis of GBM, providing a more accurate prediction of survival, and suggesting oncogenic function of this gene[10].

Five significantly upregulated genes in response to FANCD2 knockdown include RNA5S16, RP11-801F7.1, RP11-360L9.7, RP11-298I3.5, AC114546.1. These findings do not correlate with our hypothesis, as we postulated that knockdown of FANCD2 was associated with upregulation of genes promoting cell cycle arrest. The upregulated genes may be related to cell cycle arrest; however, there is no current literature reporting this function. RNA5S16 and AC114546.1 genes did not have literature supporting gene function.

Five variants of RP11 were identified with at least a five-fold change gene expression. Two RP11 variants were downregulated, and three variants were upregulated. RP11, also identified as pre-mRNA processing factor 31 homolog (PRP31), was found to be associated with risk of invasive disease in a study assessing gene correlation with ovarian cancer risk[11]. The PRPF31 gene is known to encode the ubiquitous splicing factor PRPF31[12]. Another study by Rose et al. in 2012 found that one functional polymorphism was identified in the PRPF31 promoter that increased transcriptional activation[12]. RP11-350N15.6 and RP11-321N4.5 exhibited significant downregulation in the A549 cell line, which

is consistent with our hypothesis of gene downregulation with FANCD2 knockdown. Conversely, RP11-801F7.1, RP11-360L9.7, and RP11-298I3.5 genes resulted in a significant upregulation in the A549 cell line, suggesting that different isoforms of RP11 are influenced by different regulatory mechanisms with FANCD2 knockdown.

Genes related to cell proliferation are expected to be downregulated with FANCD2 knockdown, as FANCD2 is considered to promote cell growth through interactions with cell proliferation pathways such as PI3K-AKT-mTOR pathway[13]. Inhibited oncogenic function due to FA pathway knockdown is expected to reduce cell proliferation. However, the literature suggests that the 3 upregulated genes also have oncogenic function. These genes may have other functions beyond the scope of carcinogenesis, which may explain gene upregulation with FANCD2 knockdown.

Evaluation of genes in FA deficient lung tumors was assessed by FANCD2 knockdown and evaluating concurrent gene expression changes. Identifying genes with significant expression change in FA deficient tumors, such as PLA2G4B and RP11-350N15.6, can direct the genetic-based therapy for treatment of NSCLC with alterations in the FA repair pathway. Genes such as RP4-635E18.7 and PLA2G4B were found in other cancers, further supporting the role of gene regulation in tumorigenesis for these specific genes. Given that these genes expressed significant change in regulation in lung cancer cells with FANCD2 knockdown, it may be valuable to further investigate the role of these genes in normal and malignant cells. FA homologous repair deficiency may prove to be a target of cancer treatment, as long as appropriate biomarkers become available to identify patients with these tumors[7].

Our results provide a strong starting point for the development of treatments targeting genes associated with the FA pathway and the understanding of the mechanism of action of the repair pathways in lung cancer cells. Identification of FA downstream genes may provide insight on DNA repair networks which alter or compensate for defective FA repair pathways and consequently affect tumor growth. It is possible that the microRNA associated with these genes were upregulated upon FANCD2 knockdown, causing increased degradation of mRNA for the genes listed in Table 1 and 2. Further investigation is needed to determine how FANCD2 interacts with these genes to promote cell proliferation.

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Clinical Perspectives on Using a Standardized Hand-off Protocol to Reduce Medical Error

Sandya Muchimilli, MPH

Herbert Wertheim College of Medicine, Florida International University, Miami, FL

Corresponding Author: Sandya Muchimilli, smuch007@med.fiu.edu

Abstract

Introduction: Various forms of medical error exist: misdiagnoses, miscommunication, and malpractice. A standardized handoff checklist is a common medical error reduction initiative designed to improve transfer of medical information in a clinical setting. Few studies exist regarding clinicians' perspectives around such initiatives. This study examines clinicians' perspectives on medical error reduction initiatives, adds to the limited literature, and seeks to answer the question: "What are clinicians' views towards a standardized checklist used as an approach to reducing miscommunication-related medical error in an in-patient setting?"

Methods: This is a qualitative pilot study of the implementation of a standardized handoff checklist conducted at a large academic hospital between April and May 2017. Clinician interviews were conducted using a standardized, semi-structured guide, recorded, and transcribed for analyses using a comprehensive, iterative coding process. Major themes were identified.

Results: Definitions of medical error amongst the interviewed were diverse. Most appreciated the standardization and structure the checklist provided, found the introduction aspect to the checklist helpful for team dynamic, and had an overall positive view on medical error reduction initiatives.

Conclusions: Clinicians' views on defining medical error and appreciation for standardization are important to consider when constructing and implementing new medical error reduction initiatives. Healthcare institutions should consider studying clinical perspectives and implementing medical error reduction initiatives aligning with clinician preferences in order to reduce medical error.

Keywords: Medical Error Reduction, Patient Hand-Off, Checklist

Introduction

The ambiguity of defining and identifying medical error systematically, the subjectivity of clinical decisions from provider to provider, and the complexity of healthcare delivery, adds to the current persistence of medical errors within healthcare systems across the United States.[1, 2] It has been well established over the years that medical error is a critical problem in regard to public health and patient safety in the United States; therefore, defining the term explicitly is important.[1,2] Within the current literature, the most often cited definition of medical error is "an unintended act (either of omission or commission) or one that does not achieve its intended outcome."[1] Other generally accepted definitions of medical error include "the failure of a planned action to be completed as intended (an error of execution), the use of a wrong plan to achieve an aim (an error of planning), or a deviation from the process of care that may or may not cause harm to the patient." [3,4] These definitions from current literature show the lack of standardization in defining the term "medical error," underlining the need for a universally accepted definition to categorize mistakes and standardize improvement initiatives.[3,4]

In recognizing the diversity of medical error, its definition should encompass both the outcome-dependent and process-dependent aspects of medical care.[3] The outcome-dependent aspect refers to the occurrence of adverse outcomes and injuries such as malpractice (i.e. amputating the wrong leg) or negligence (i.e. giving the wrong dosage of a medication that results in prolonged hospitalization). On the other hand, the process-dependent aspect of medical care refers to "near-misses." "Near misses" are system failures that cause error by exposing patients to risk, but that do not result in harm (i.e. giving a patient in a shared room the other patient's medications, but the patient realizing the mistake and informing the nurse).[3,5] A common factor within these two categories of medical error is miscommunication.

Miscommunication is a complex, yet important factor in regard to medical error occurrence. The hand-off of patients between departments is a crucial point where miscommunication-related medical errors occur.[6]Therefore, a group of physicians at Boston Children's Hospital developed a hand-off curriculum for pediatric residents between June 2010 and February 2014 as a component to the Inpatient Settings Accelerating Safe Sign-outs (I-PASS) Study. Elements of the disseminated handoff process that is a part of the curriculum follows the same mnemonic: 'I' for illness severity, 'P' for patient summary, 'A' for action items, 'S' for situation awareness and contingency planning, and 'S' for synthesis by receiver.[6] A prospective intervention study of the hand-off program during 10,740 patient admissions demonstrated an association between the implementation of the I-PASS hand-off and significant reductions in medical error.[6,7]

In regards to the rates of medical error and its persistence over the years, the most cited estimate of the incident rate of death from medical error, suggesting 44,000 to 98,000 deaths per annum, is the

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1999 Institute of Medicine (IOM) report.[8] This report was based on research conducted by the Utah and

Colorado Study and the Harvard Medical Practice Study from 1992 and 1984, respectively.[9,10] Although the IOM report is the most cited reference in regards to deaths from medical error, it is outdated and its estimate is too low, as argued by more recent literature. Recent studies reveal higher incidence rates, with the Agency for Healthcare Quality and Research reporting an estimate of 575,000 deaths from medical error in the Medicare population between 2000 to 2002 and the US Department of Health and Human Services reporting 180,000 deaths from medical error in the Medicare population in 2008.[11,12] More recently, Makary et al. used studies since the IOM report and extrapolated to the total number of hospital admissions in 2013 to calculate an average rate of death from medical error; they estimated an annual incidence rate of 251,454 deaths from medical error.[4] When compared to CDC rankings, this estimate suggests medical error as the third leading cause of death in the United States.[4,13] A recent Johns Hopkins study also estimated that more than 250,000 Americans die each year from medical errors, ranking it as the third leading cause of death as well.[4]

Systematic patient safety initiatives are often preventative in nature and seek to reduce medical error rates. They are often referred to as "medical error reduction initiatives." Some examples include hospital root-cause analysis committees, departmental morbidity and mortality conferences, and standardization of inter- and intra- departmental hand-offs of patients and information.[14]

An in-patient department of a large academic medical center in New England recently implemented a medical reduction initiative by standardizing the patient hand-off between the department and another in-patient department within the hospital in 2016. Along with incorporating all of the I-PASS elements (detailed in Figure 1), the new standardized hand-off is a checklist that also requires introductions of all care team members (Figure 1). The checklist is used primarily by the physicians and the residents but contains tasks and responsibilities for other care team members present during the handoff as well.

This study seeks to further explore the complexity of miscommunication in healthcare delivery and its relationship to medical error in healthcare systems at an academic medical center in New England that standardized the hand-off of patients from one in-patient department to another. By understanding clinical perspectives around the medical reduction initiative that was implemented within this hospital, this paper hopes to shed light on how actors at the frontline of healthcare delivery view medical reduction initiatives that are intended to instill greater patient safety and positively change practice. These findings may potentially be extrapolated to other healthcare systems in the United States.

Few studies have sought to examine clinicians' perspectives on such initiatives, and this study seeks to add to the limited literature. Attention needs to be directed towards understanding clinicians' perspectives around medical error reduction initiatives in order to improve upon the ways of reducing medical error. This study seeks to answer the question: "What are clinicians' views towards a standardized hand-off checklist protocol as an approach to reducing miscommunication-related medical error in an in-patient setting?"

Methods

The qualitative method of grounded theory was used to accomplish the research goal. Grounded theory is useful when no relevant existing framework exists, and important themes emerge upon the analysis of collected data on participants' own experiences.[6] Semi-structured individual telephone and in-person interviews were used as the method of collecting data because it encourages open commentary and allows for the in-depth exploration of individual experiences. The experience of using a hand-off protocol such as a standardized checklist is personal, and semi-structured interviews provided the opportunity to delve deeper into specific aspects of people's views and thoughts on the hand-off protocol. Because different levels of participants (attending physicians, residents, and other clinical staff such as nurses and physician assistants) interact in a hierarchical manner which may lead to sensitivities and unique perspectives in regards to the new hand-off protocol, interviews were conducted on an individual basis.

All clinicians who had experience of both the old and new hand-offs within an in-patient department at an academic medical center in New England were invited to participate via e-mail by the convenience sampling method in April 2017. Those that did not respond received a follow-up e-mail 20 days later. Participation was voluntary. The study received approval by the Dartmouth College Institutional Review Board (IRB).

Within an in-patient department of a non-profit academic medical center in New England, 60% of the clinicians were recruited to participate in this study. The clinicians included physicians, physician assistants, and nurse providers. During May 2017, phone interviews were conducted with physicians and other clinicians within the in-patient department. All participants received and acknowledged an information sheet for the study prior to the phone call that served as the consent form. Each interview lasted approximately 20 minutes and was audio-recorded. Each interview was conducted using a scripted, semi-structured interview guide and followed-up with probes as necessary. Interview guide can be provided upon request. The interview guide was drafted, piloted on non-participants, and refined on the basis of their comments. All but one of the audio-recordings were transcribed verbatim using Trint™, a secure online audio transcription software, and were de-identified before analysis. One audio-recording was not transcribed verbatim due to a lack of recording clarity; however, notes were taken while listening to the recording. These notes were then coded using the same coding structure as the rest of the transcribed data. The total number of participants (n) whose comments were coded under respective themes are only provided if the count is ten or more. This approach was used to maintain participant confidentiality.

Consistent with the grounded theory methodology, analysis started simultaneously with data collection to establish that the interviews were capturing intended collected data and to consider potential new topics to include in subsequent interviews.[7] Transcripts were read during the open coding process and a group of advisors frequently met to compare and discuss emerging themes. The coding structure was refined over two weeks until no further codes or categories emerged from the collected data, the coding structure seemed stable, and the group of advisors agreed upon the coding structure. Upon reaching consensus of the coding structure, theoretical saturation was reached.[8] All interviews were coded with the coding structure and the coded data were analyzed to elicit themes surrounding medical error, the old handoff method, and the new standardized checklist. Major themes revolving around describing medical error and descriptions of the old versus new handoff methods are discussed below in the order that participants were asked about their thoughts as per the interview guide. The term "negative code" refers to coding that suggested dislike or disapproval of a topic and the term "positive code" refers to coding that suggested liking, appreciation or approval of a topic.

Results

Participants' descriptions of medical error evolved over the course of the interview. When ***initially*** asked how they would define 'medical error,' all of the interviewed clinicians mentioned an unplanned element. At the ***end*** of the interview when asked about how the implementation of the standardized checklist might have changed their perspective on medical error, participants' descriptions shifted towards the idea that mistakes are inevitable. However, all other codes to the initial question regarding defining medical error and the latter question in regard to how their perspective changed from the recent medical error reduction initiative were the same for each respective participant. As seen in Table 1, some participants described medical error as harming the patient, systemic failure, and care-related problems (Table 1). A few participants also mentioned that the complexity of healthcare results in medical error.

When asked to describe what they liked and disliked about the old handoff methods used before the standardized checklist was implemented, the majority of participants reported that they did not receive enough information in the past and that different providers would give contradictory information. However, no nurse mentioned the latter issue. In general, the participants described the old handoff to be unstructured and lacking in standardization. Some participants also mentioned hesitance to raise issues when they did not personally know everyone present for the handoff. Having to ask too many questions after the handoff had occurred was also a commonly cited problem. One physician mentioned that there were care coordination issues (such as not being notified about a patient's arrival) with the old handoff. As seen in Table 2, interviews only contained negative codes for participants' descriptions of the old handoff methods (Table 2).

All participants responded that the new standardized checklist provided more structure during information transfer and found the introduction piece of the checklist to be helpful and have a positive effect on team dynamic. One participant, however, did mention they found the introduction "stilted" and too formal. Many participants said that everyone listened and paid more attention to each other since only one person talks at a time with the new standardized checklist. Physicians specifically commented on the fact that introductions helped in terms of knowing roles—knowing what their own and others' responsibilities were in regard to the information transfer during the handoff. As seen in Table 3, almost all of the coded interviews only contained positive codes for participants' descriptions of the new standardized checklist; only one negative code was applied (Table 3).

Overall, negative codes were used to describe the old handoff and positive codes were used to describe the new standardized checklist. The only concern mentioned about the change in the handoff was that the other department felt that the new standardized checklist might take too much time; this concern was only cited by physicians. All of the physicians also mentioned that the change in the handoff instilled a culture of improvement within the department.

Participants defined medical error as harming the patient and a systematic failure. Medical error was also described as having an unplanned element and being related to care. The complexity of healthcare and the fact that mistakes are inevitable were also cited during participants' discussions of medical error. Participants felt that they were not receiving enough information and often received contradictory information from the other department. A lack of structure, formality, and standardization was also attributed to the old handoff method. Clinicians also mentioned the issues of not knowing people in the room and having to ask too many questions with the old handoff method. In terms of the new standardized hand-off checklist, all participants cited greater structure and standardization. All of the participants also appreciated the introduction aspect to the checklist. Many participants felt they knew who was in the room and what each person's role was; they also felt that colleagues were listening better and paying more attention during the handoff. It is interesting to note that only one participant mentioned a negative code when describing the new handoff. Although appreciative of the introduction's purpose, one participant found the introduction piece of the new checklist to be somewhat artificial in nature. It could be possible that other participants might have felt similarly but may not have felt comfortable opening up about negative aspects to the new checklist. Other clinicians that were not interviewed within the two in-patient departments could also have felt similarly. Lastly, physicians mentioned they were initially worried the new checklist would take considerably longer after hearing about the process from others. However, they also mentioned the standardized checklist instilled a culture of quality improvement in the department and was worth the marginal increase in time.

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Theme	Description
Unplanned	– Something was done incorrectly, missed, went off-plan, or happened unexpectedly and could have been avoided – Near-miss that doesn't reach the patient
Mistakes are inevitable	– It is human nature to make mistakes – Errors occur throughout the hospital, but efforts are being made to prevent them – Can't get rid of medical error completely
Care-related problems	– Patient's care is affected – Healthcare delivery is impacted negatively
Harming patient	– An adverse or negative outcome occurs
Systemic failures	– Policies are not in place, and therefore errors go unnoticed
Occurs due to complexity of healthcare	– Healthcare delivery is complex and therefore error is inevitable – There are multiple levels of healthcare and therefore medical error is a spectrum, from individual to systemic failures, from harm to near-misses, etc. – Many environments and process points at which medical error can occur

Table 1: Emergent Themes from Descriptions of Medical Error

Theme	Description
Not receiving enough information	– Having to go back through records because information was missed either by receiver or giver
Receiving contradictory information	– Different clinicians reporting different information at different times
Lack of structure	– The information was not given in any particular order
Lack of formality and standardization	– Providers in the room would have side-conversations with each other – Everybody talked on and over each other
Not knowing people in the room	– Not knowing newer providers, such as rotating residents
Having to ask too many questions	– Asking a question that may have already been answered – Having to bother another clinician with multiple questions for more information

Table 2: Emergent Themes from Descriptions of the Old Handoff Method

Theme	Description
Having introductions	– Knowing who is in the patient room – Everyone knows who everyone else is
Listening and paying attention	– Only one person talks at a time so everyone else is listening and getting more information – Everyone pays attention to each step of the handoff allowing for more complete information transfer
Knowing roles	– Everyone knows what others' responsibilities and obligations are – Everybody knows what to expect in terms of who is responsible for receiving and giving specific information pieces
More structure and standardization	– The handoff is not chaotic and no one is talking over another – There is an order to delivering the information during the handoff – Attention is drawn to irregular or out-of-place reporting because it may have to do with patient's health status and/or care

Table 3: Emergent Themes from Descriptions of the New Standardized Checklist

Discussion

Since this was a small pilot study, there were significant limitations in study sampling and logistics. Logistical limitations included a 1-month period of data sampling and collecting interview data remotely. In regard to the study sample, there were four main limitations. First, a convenience sampling method was used because it was the quickest and easiest way to recruit participants. This is not the most ideal form of sampling and introduces sampling bias; therefore, the results of this study may not be generalized to the rest of the population. In addition, the sample size was small. In order to maintain confidentiality, counts were not provided and an in-depth comparison across different provider roles was not done; only a surface level comparison and analysis of role differences was done. It should also be noted that only one of the two in-patient departments (the *receiving* department) involved with the new hand-off checklist was interviewed. Ideally, both in-patient departments should have been interviewed. Lastly, since the nature of clinicians' daily schedules is generally busy and hectic, recruiting participants was difficult, leading to scheduling difficulties and a small sample size.

Future studies should use a larger sample size—this would allow for a comparison of perspectives of different types of providers and a more robust analysis in terms of numbers and statistics. Future studies should also look at both departments involved in a hand-off initiative such as the one studied; participants should be from both the department *giving* the information and the department *receiving* the information in order to get a more accurate representation of how clinicians feel towards a particular handoff initiative. Larger studies could compare clinicians' perspectives from multiple departments on standardized hand-off checklists within the same hospital or between different hospitals. Future studies could also look at how clinicians view the "standardized checklist" initiative as compared to other hand-off medical error reduction initiatives specifically or other medical error reduction initiatives in general.

Clinicians within an in-patient department of an academic medical center in New England had a diversity of definitions for the term "medical error." They also found a recently implemented standardized hand-off checklist to be a helpful and effective medical error reduction initiative. Since this pilot study was limited in scale, identified diversity in defining medical error, and elucidate a positive response from clinicians in regard to a new standardized handoff checklist, further research should be conducted on clinical perspectives on medical error definitions and reduction initiatives in order to better understand and support healthcare quality improvement projects. This study underlines the benefit of and appreciation for more standardized processes such as checklists; therefore, healthcare institutions should continue to implement such medical error reduction initiatives.

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Performance of a Student-Run, Community Outreach Program at Reaching At-Risk Populations in Miami-Dade County

David Patrice Dorcius*, Eli Levitt*, Alyssa McCauley, Jake Levine, Lena Carleton, Greisy Martinez Harvell, Maryse Pedoussaut MD, Julia Bisschops MD, Alan Wells PhD, Frederick Anderson MD

* Co-first authors

Herbert Wertheim College of Medicine, Florida International University, Miami, FL, USA

Corresponding Author: David Dorcius, ddorc006@med.fiu.edu

Abstract

Introduction: Medical Students Working to Improve Society and Health (MedSWISH) is a student run organization, whose goal is to provide health screenings, health education and referrals for long-term care to community members at health events in Miami-Dade County. The purpose of this paper is to describe the health event population that MedSWISH has seen thus far so that future services may be tailored to meet the community's needs.

Method: A group of medical students from Florida International University, supervised by a licensed physician, attended 10 different health events. There, they provided all willing adults with health screenings on their body mass index (BMI), body fat percentage, blood pressure and blood sugar. Once the screenings were completed, participants were asked to share the results of their health screenings, their zip code as well as whether they have access to a primary care physician and insurance.

Results: Out of the 331 participants consented from the ten individual events, 41.3% of them were obese, 38.1% fell within the hypertensive range and 13.0% fell within the diabetic range. There was a significant difference in the screening metrics between the individual health events.

Conclusion: This preliminary analysis provided valuable insight as to the characteristics of participants that attend MedSWISH health events. Though much more research is needed to fully understand the characteristics of the different populations, this research is integral in MedSWISH's mission to improve and individualize the services provided at the health events.

Key Words: MedSWISH, Medical Student, Health Fair, Community Outreach

Introduction

The factors that influence patient health and wellbeing are multifactorial in nature. However, studies have shown a strong relationship between a lack of access to health care and the prevalence of chronic disease.[1] According to a study using the National Health and Nutrition Examination Survey, between 1999-2004, over eleven million patients who suffered from chronic illness in the United States were uninsured.[1] The study revealed that those patients that suffered from a chronic disease, who also did not have health insurance, were more likely to forgo routine care and utilize emergency departments as their primary care facility. Their lack of access to long-term care combined with their uncontrolled chronic disease lead to an increase in the risks associated with their conditions.[1–3] Chronic uncontrolled hypertension, as well as uncontrolled diabetes, can each increase the risk of developing a myocardial infarction, stroke, visual impairment, renal impairment and heart failure.[2–4] Studies have shown that continuity of care plays an important role in improving both patient outcomes and satisfaction.[5,6] The impact of continuous care was found to be even more pronounced in patients suffering with a chronic illness.[5] Access to long-term care alongside prevention and management of chronic disease can reduce the risk of these long-term effects and thereby improve patient outcomes.[7]

Access to affordable health care is one of the greatest factors that contributes to health disparities in America.[8] According to the United States Census Bureau, 19.4% of the population in Miami-Dade under the age of 65 was uninsured in 2016.[9] Medical Students Working to Improve Society and Health (MedSWISH), is a student run organization from FIU HWCOM that strives to close this gap. Students in MedSWISH provide free health screenings and education to community members at different health events in Miami-Dade County, such as health fairs, farmers markets and parades. If barriers to access to health care are identified, participants are referred to local organizations that can provide them with long-term care. By offering body mass index (BMI), body fat percentage, blood pressure, and blood glucose screenings, MedSWISH aims to increase awareness of personal health indicators as well as to educate participants on lifestyle modifications that could improve their overall well-being and health. MedSWISH volunteers work alongside other medical student organizations to educate participants on exercise, diet, smoking cessation, mindfulness, stroke awareness, and cancer screening awareness. The goal of this organization is to decrease adverse outcomes such as myocardial infarction, stroke, heart failure, and renal disease by focusing on screening and education for chronic illnesses that serve as risk factors, such as diabetes mellitus, obesity and hypertension.[2,10–12] MedSWISH strives to increase access to health care in our most vulnerable areas, which are defined by the Neighborhood Health Education and Learning Program (NeighborhoodHELP), by connecting health event participants with local resources in order to improve their health outcomes.[13]

NeighborhoodHELP is a program offered by the Florida International University, Herbert Wertheim College of Medicine (FIU HWCOM). Through the NeighborhoodHELP program, patients are provided the opportunity to have long-term access to care.[13,14]health disparities persist, resulting in medicine's renewed emphasis on the social determinants of health and calls for reform in medical education. APPROACH The Green Family Foundation Neighborhood Health Education Learning Program (NeighborhoodHELP Members that are enrolled in the program may be assigned to a diverse team composed of a medical student, a physician assistant student, a social work student, a law student and a nursing student. Every household team is supervised by a licensed physician and supported by an outreach worker, in order to aid in improving the clinical and social needs of the household.[13,14] NeighborhoodHELP patients have access to law, education, and social work services, which work to address the social determinants of health that can act as a barrier to patient care. Long-term care is available through household visits and the Mobile Health Center a mobile clinic that provides patients with free medical care by FIU HWCOM health professionals.

In order to better cater to the medical and educational needs of the local community, MedSWISH has begun an Institutional Review Board (IRB) approved research project to assess the population served at its health events. The purpose of this paper is to describe the population that MedSWISH has served over the last year. By evaluating the demographics and health metrics of the communities served, MedSWISH aims to improve the health screenings and health education provided, by tailoring them to their respective health event.

Methods

This comparative cross-sectional study was approved by the Florida International University's IRB. Between January 2018 and October 2018, health screening participants provided verbal consent, consistent with IRB-approved informed consent procedures, to collect data for analysis on their screening results. Included on those results was data on participants' blood pressure, blood glucose, body mass index, body fat percentage, insurance status and access to a primary care physician (PCP). MedSWISH's community activities are funded by the Office of Student Affairs at FIU HWCOM. No additional funding was required to conduct this study. A team of medical students, supervised by an FIU HWCOM physician, attended 10 community health and wellness events between January 2018 and October 2018. There, they provided all participants over the age of 18 with voluntary health screenings. All the medical students in attendance were volunteers who had been trained by MedSWISH on the proper technique to measure BMI, body fat percentage, blood pressure and blood glucose. The health events were organized by local community partners who invited MedSWISH, as well as other organizations and vendors, to provide services. The community partners were responsible for reaching out to the community and advertising the health event.

On the day of the event, MedSWISH provided participants with information on their weight, BMI, body fat percentage, blood pressure and blood sugar. Any participant that presented with an elevated reading on any of the metrics was subsequently seen by the supervising physician. Once the screening completed, participants were transferred to the check-out station, where a second group of medical students provided them with further health education on the results of their screenings, in adherence to United States Preventive Screening Task Force (USPSTF) and Eighth Joint National Committee (JNC8) guideline recommendations on obesity, hypertension and diabetes.[2,12,15,16] An individualized approach was used, whereby medical students partnered with the participants to create a suitable plan for the latter to improve their health metrics. These recommendations included evidence-based diet modifications programs, such as the DASH diet and MyPlate, as well as increases in their physical activity levels in adherence to the American Heart Association recommendations.[17,18] Depending on participants' needs and access to health care, they were connected to local community health resources for further long-term support. Those resources included Federally Qualified Health Centers (FQHC), as well as the FIU NeighborhoodHELP program.[13,14] Participants were then consented to take part in this IRB-approved study. In order to be eligible for the study, participants had to be over the age of 18 and live in Miami-Dade County. Eligible participants were then asked to share the results of their health screenings, including their BMI, body fat percentage, blood pressure and blood sugar. They were also asked to share their zip code, information on their health insurance status as well as whether they had access to a primary care physician (PCP).

For the purposes of the health screenings, MedSWISH used Etekcity digital body weight scales (Model: EB9380H) for all body weight measurements. Omron fat loss monitors were used to measure the BMI and the body fat percentage, and Omron Automatic blood pressure monitor (Model: BP742) for all blood pressure measurements. For the blood glucose measurements, MedSWISH used Contour Next EZ blood glucose monitoring system (Model: 9628).

A preliminary descriptive analysis was run on the first 331 participants' data collected from 10 different health events in Miami-

Summary of Health Events			
	n	%	SD
# of events	10	-	-
Total Patients Screened	500	-	-
Number of Patients Consented	331	-	-
Age ≥ 65 Years Old	78	24.6	-
Sex			
Male	86	30.7	-
Female	194	69.3	-
Race/Ethnicity			
Asian	1	0.4	-
Black	188	72.9	-
Hispanic	57	22.1	-
White	10	3.9	-
Other	2	0.8	-
Health Coverage			
Uninsured	93	28.3	-
Lack of PCP	90	27.3	-
Screening Results			
BMI	29.4		6.0
Obese	131.0	41.3	
Body Fat %	33.7		9.5
Blood Pressure Systolic - Mean	131		19.9
Blood Pressure Diastolic - Mean	81		11.4
Hypertensive Range[a]	122	38.1	
Glucose (Fasting) - Mean	122.0		64.2
Glucose (Non-fasting) - Mean	123.6		56.7
Diabetic Range[b]	40	13.0	

Table 1: Description of MedSWISH Health Events. Abbreviations: PCP, primary care physician; BMI, Body mass index. Superscript: [a]: anyone with systolic Blood Pressure ≥140 or/and Diastolic Blood Pressure ≥ 90. [b]: Anyone with a fasting blood sugar ≥ 126 or a non-fasting blood sugar ≥ 200. [c]: only patients younger than 65 years old. [d]: Data was taken from the US census bureau, Miami-Dade County quick facts, population estimates as of July 1st, 2017. [e]: Data was taken from Miami Matter's project from the Health Council of South Florida.

Dade County. The events were organized by roman numerals I - X, in the order in which they were attended in 2018. The descriptive analysis of the participants' data was assessed using SPSS version 23. Frequencies and central tendencies of the participants data were compared to that of the average population in Miami-Dade County, using data from the 2010 census as well as the Miami-Dade Matter's health indicator database **(Table 2)**.[9,19–21] A two-sided Pearson chi-square test was used to compare the demographic characteristics (age, gender, race/ethnicity) and health indicators (BMI, blood pressure, blood sugar, access to PCP and insurance) by the different health events. An alpha level of 0.05 was chosen.

For the purpose of this study, hypertensive range was defined as any individual with a one-time systolic blood pressure reading greater than or equal to 140 mmHg and/or a one-time diastolic blood pressure reading greater than or equal to 90 mmHg.[2] Diabetic

Population Summary	
	%
Age	
≥ 65 Years Old	16.0[d]
Sex	
Male	48.6[d]
Female	51.4[d]
Race/Ethnicity	
Asian	1.6[d]
Black	18.2[d]
Hispanic	68.6[d]
White	13.2[d]
Other	1.2[d]
Health Coverage	
Uninsured	19.3[c,d]
Lack of PCP	N/A
Screening Results	
BMI	-
Obese	25.3[e]
Body Fat %	-
Blood Pressure Systolic – Mean	-
Blood Pressure Diastolic – Mean	-
Hypertensive range[a]	32.7[e]
Glucose (Fasting) - Mean	-
Glucose (Non-fasting) - Mean	-
Diabetic Range[b]	9.2[e]

Table 2: Description of Miami-Dade Population. Abbreviations: PCP, primary care physician; BMI, Body mass index; N/A, Not Available. Superscript: [a]: anyone with systolic Blood Pressure ≥140 or/and Diastolic Blood Pressure ≥ 90. [b]: Anyone with a fasting blood sugar ≥ 126 or a non-fasting blood sugar ≥ 200. [c]: only patients younger than 65 years old. [d]: Data was taken from the US census bureau, Miami-Dade County quick facts, population estimates as of July 1st, 2017. [e]: Data was taken from Miami Matter's project from the Health Council of South Florida.

range was defined as any individual with a one-time fasting blood sugar level greater than or equal to 126 mg/dL or a non-fasting blood sugar greater than or equal to 200 mg/dL.[12]

Results

The dataset comprises 331 participants from 10 health events in Miami-Dade County. Demographic characteristics of the data reveal that 25% of the sample was aged 65 years or older. As for gender, it showed that 69% of the sample was female. When measuring the rate of insurance, 28.3% of the sample reported not having had insurance at the time of the screening. As for the health screening results, 41.3% of the sample was obese. Furthermore, 38.1% of the participants that fell within the hypertensive range while 13.0% of the participants fell within the diabetic range (Table 1).

To help put this data in perspective, according to the United State Census bureau's 2017 Population Estimate Program, in Miami-Dade County, 16.0% of the population was aged 65 years or older, while 51.4% of the county was female (Table 2).[6,9] According to the Census bureau's 2016 Small Area Health Insurance Estimates, 19.4% of the population under the age of 65 was uninsured.[9] According to Miami Matters, an interactive information platform initiated by the Health Council of South Florida, as of 2016, 25.3% of the population of Miami-Dade County is obese.[19] In addition, 32.7% of the population has been diagnosed with hypertension while 9.2% has been diagnosed with diabetes.[19–21]

For each metric collected, there was a significant difference in the results between individual events (Table 3). There was a lower percentage of female participants in events II and VI compared to the other fairs (P = 0.016). The percent of uninsured participants was 28.3%. The highest prevalence of insurance was in event I, II, III and V (P = 0.07). The percentage of people who lacked a PCP was 27.3%. A higher percentage of participants had access to a PCP in events I, II and III compared to the other health events (P = 0.012). The average BMI of the total sample was 29.4 (SD = 6). Event V had the lowest rate of obesity compared to event I, IV, IX and X (P = 0.007). Event I, III, IV, IX and X had the highest percentage of participants in the hypertensive range

(P=0.003). Finally, 13.0% of the sample's blood sugar readings fell within the diabetic range. Event X had the highest prevalence of participants with a blood sugar reading in the diabetic range. On the other hand, health events II, V, VI and VIII had the lowest prevalence of participants with a blood glucose reading in the diabetic range (P = 0.009).

Discussion

This study aimed to describe the different health fair participants who received health screenings by health event. The goal of this

ORIGINAL RESEARCH

Characteristics	Antioch Fresh Start Healthy Initiative	Miami Lakes Farmers Market	CARE Miami Gardens	Northside 7th Day Adventist	Miami Beach Gay Pride Parade	North Miami Health Fair	Little Haiti Health Fair	Sweetwater Health Fair	Little Haiti Soccer Park Health Fair	Little Haiti Griffin Park Health Fair	P (Value)
Event #	I	II	III	IV	V	VI	VII	VIII	IX	X	
	N(%)	N(%)	N(%)	N(%)	N(%)	N(%)	N(%)	N(%)	N(%)	N(%)	
Age											
18-64	22(73)	24(100)	18(62.1)	46(78)	18(94.7)	21(84.0)	¥	33(86.8)	23(67.6)	34(57.6)	< 0.001
>65	9(26.7)	0(0.0)	11(37.9)	13(22.0)	1(5.3)	4(16)	¥	5(13.2)	11(32.4)	25(42.4)	< 0.001
Gender											
Male	7(23.3)	10(41.7	5(17.2)	22(36.7)	12(63.2)	6(24.0)	¥	¥	7(20.6)	17(28.8)	0.016
Female	23(76.7)	14(58.3)	24(82.8)	38(63.2)	7(36.8)	19(76.0)	¥	¥	27(79.4)	42(71.2)	0.016
Ethnicity											
Asian	0	¥	¥	0	¥	0	0	1(2.6)	0	0	< 0.001
Black	28(93.3)	¥	¥	45(76.3)	¥	17(70.8)	9(69.2)	3(7.9)	31(91.2)	55(93.2)	< 0.001
Hispanic	2(6.7)	¥	¥	12(20.3)	¥	6(25.0)	4(30.8)	27(71.1)	2(5.9)	4(6.8)	< 0.001
White	0(0.0)	¥	¥	2(3.4)	¥	1(4.2)	0(0.0)	7(18.4)	0(0.0)	0(0.0)	< 0.001
Other	0(0.0)	¥	¥	0(0.0)	¥	0(0.0)	0(0.0)	0(0.0)	1(2.9)	0(0.0)	< 0.001
BMI											
Normal/Overweight	15(53.6)	15(65.2)	18(66.7)	26(44.1)	18(94.7)	17(73.9)	9(69.2)	23(63.9)	15(48.3)	30(51.7)	0.007
Obese	13(46.4)	8(34.8)	9(33.3)	33(55.9)	1(5.3)	6(26.1)	4(30.8)	13(36.1)	16(51.6)	28(48.3)	0.007
Hypertension[a]											
Normal/Prehypertensive range	17(58.6)	16(72.7)	15(55.6)	31(51.7)	16(88.9)	19(76.0)	9(81.8)	29(78.4)	19(59.4)	27(45.8)	0.003
Hypertensive range	12(41.4)	6(27.3)	12(44.4)	29(48.3)	2(11.1)	6(24.0)	2(18.2)	8(21.6)	13(40.6)	32(54.2)	0.003
Diabetes[b]											
Normal/Prediabetes range	25(86.2)	22(100)	23(88.5)	49(84.5)	16(94.1)	23(95.8)	11(91.7)	35(97.2)	28(84.8)	36(70.6)	0.009
Diabetic Range	4(13.8)	0(0.0)	3(11.5)	9(15.5)	1(5.9)	1(4.2)	1(8.3)	1(2.8)	5(15.2)	15(29.4)	0.009
Insured											
No	3(10.0)	4(16.7)	3(10.3)	21(35.6)	3(15.8)	8(32.0)	6(46.2)	9(23.7)	12(35.3)	24(41.4)	0.007
Yes	27(90.0)	20(83.3)	26(89.7)	38(64.4)	16(84.2)	17(68.0)	7(53.8)	29(76.3)	22(64.7)	34(58.6)	0.007
PCP											
No	3(10.0)	2(8.3)	3(10.3)	24(40.0)	6(31.6)	8(32.0)	5(38.5)	11(28.9)	8(23.5)	20(34.5)	0.012
Yes	27(90.0)	22(91.7)	26(89.7)	36(60.0)	13(68.4)	17(68.0)	8(61.5)	27(71.1)	26(76.5)	38(65.5)	0.012

Table 3. Characteristics of the sample by health event. Abbreviations: PCP, primary care physician; BMI, Body mass index. Superscript: [a]: anyone with systolic BP ≥140 or/and Diastolic BP ≥ 90; [b] Anyone with a fasting blood sugar ≥ 126 or a non-fasting blood sugar ≥ 200; ¥: Due to difficulties with the data collection form, researchers were unable to collect this data.

study was to use the data collected to better characterize the population seen, so as to tailor MedSWISH's services to match each community's needs. A significant difference was found between health events in terms of age, gender, ethnicity, BMI, blood pressure, insurance and PCP rate. The pattern of these differences was consistent throughout the different metrics measured, with events I, II and III having consistently better access to health care in terms of health insurance and access to a PCP. On the other hand, events V, VI and VII had consistently better health screening results compared to other events with regards to the percent of participants within the obese, hypertensive or diabetic range. Health events I, III, IV, IX, and X, had the highest prevalence of participants with a blood pressure reading in the hypertensive range. On the other hand, fairs I, IV, IX, and X had the highest rate of participants with blood sugar readings in the diabetic range. The pattern seen at different events might be due to several factors, including the social determinants of health affecting the respective communities, the methods used to advertise the event, and the specific resources and incentives made available to participants by the organizing body. These differences could have resulted in an inherent preference of sicker or healthier participants presenting to the respective events.

Though the people that attended health events V, VI and VII had lower readings in terms of BMI, blood pressure and blood sugar, this does not take away from the importance of these health events in their communities. These same locations still suffered from a relative lack of access to health care, emphasized by the elevated number of participants without insurance or a primary care physician. This lack of longitudinal care predisposes these participants to worsened health outcomes and a potential increased utilization of emergency services as mode of primary care.[5,6] An increased focus by MedSWISH on ways to increase access to care is warranted.

This data though preliminary, has brought valuable insight as to the population that attended different health events in which MedSWISH was present. Based on this analysis, MedSWISH will plan to take to tailor the services provided at different health events, to improve its ability to meet the anticipated needs of the respective communities. For example, the data collected from event II reveals an elevated prevalence of participants in the obese, as well as the hypertensive range. Interestingly however, none of the participants screened for this same event had a blood sugar reading that fell within the diabetic range. These important differences provide MedSWISH the opportunity to focus on interventions for blood pressure and obesity in the future. Interventions may include more frequent education on evidence based dieting programs such as the DASH diet, presentations on ways to lead a more active lifestyle, informational sessions on the risks associated with obesity and hypertension, and information on local pharmacies with discounted prices for blood pressure medications.[2,17]

This study has several limitations. First, many participants, though diagnosed with hypertension or diabetes, had their metrics well controlled with medication. This, compounded by the fact that only one time point was taken per participant, limited the study's ability to capture the prevalence of hypertension and diabetes in the study population. Second, ethnicity data in three health events were not collected, which might have skewed the population average for that metric. Third, data on the participant's race and ethnicity was not collected separately, which could have clouded this study's ability to better characterize the population seen. Finally, the only patient health information (PHI) collected was zip code, making it impossible to ascertain whether any of the data points belonged to the same participant.

Conclusion

This study is an interim analysis, characterizing the health metrics of the populations screened at MedSWISH health events between January and October 2018. The results of this study will be used to guide the services that the organization provides at future health events. Event volunteers will be advised on the specific comorbidities present at each event and will be provided with community specific resources to help them better individualize their care and education to each participant. MedSWISH plans to expand this study to include a larger number of participants and health events. MedSWISH will also begin to collect additional variables, including race, smoking history, personal history of diabetes as well as hypertension, and information on the referrals made. These additional variables will increase MedSWISH's ability to study the impact that the organization may have on the event participants' awareness and access to care, with the ultimate goal of improving participant awareness of chronic diseases and improving participant health outcomes.

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Ethnic Disparities and Chest X-rays in the Emergency Department

Nicolas Ramsay, BS, Athena Failla, BS, MPH, Ana Martinez, BS,
Marcia Varella, MD, PhD, MHS, Juan M. Lozano, MD, MSc
Herbert Wertheim College of Medicine, Florida International University, Miami, FL, USA
Corresponding Author: Nicolas Ramsay, nrams016@med.fiu.edu

Abstract

Introduction: Community acquired pneumonia (CAP) is a common cause of hospital admission for pediatric patients. Evidence of racial disparities were reported for the diagnosis and management of CAP in pediatric patients in the Emergency Department (ED). We investigated whether Hispanic/Latino pediatric patients presenting to the ED throughout the United States with a differential of pneumonia received different quality of care when compared to non-Hispanic/Latino patients.

Methods: Secondary data analyses were conducted using the National Hospital Ambulatory Medical Care Surveys from 2009 to 2014. Pediatric (ages 1-17) ED visits including "pneumonia" in the differential were analyzed using ICD-9 codes 480 through 487. The outcome was receiving a Chest X-Ray (CXR), and the independent variable was ethnicity (being Hispanic or Latino vs. non-Hispanic and non-Latino). Multivariate logistic regression was used to assess independent associations of ethnicity with performance of a CXR. Sensitivity analyses were conducted to account for missing data on ethnicity, age, race, or insurance.

Results: 587 pediatric patients with a differential diagnosis including pneumonia and were included in the study. Hispanic/Latino patients appear to be slightly less likely to receive a CXR when compared to their Non- Hispanic/Latino counterparts, yet results were not significant [unadjusted odds ratio (OR) 0.8, 95% Confidence Interval (CI) 0.3-1.9, p=0.600)]. After adjusting for age, gender, race, location, and insurance type, the association remained not significant (OR= 0.8, 95% CI 0.3-2.5, p=0.744).

Conclusions: We fail to find evidence for disparities in the use of CXR for diagnosis of pneumonia for Hispanic/Latino patients presenting to the ED with symptoms of pneumonia. However, power limitations might have contributed to these results. Further research is warranted.

Keywords: pneumonia, disparity, emergency, CXR, chest X-ray, pediatrics

Introduction

Community acquired pneumonia (CAP) is a common cause of hospital admission for pediatric patients, and it is still an important cause of morbidity in children even in developed countries.[a]

Diagnosis and management of pediatric CAP in the Emergency Department (ED) presents multiple challenges, including the efficient, cost-effective use of diagnostic tests, and, selecting the appropriate treatment. Due to these challenges, the World Health Organization (WHO), British Thoracic Society (BTS) and other health organizations have developed guidelines to help healthcare and non- healthcare personnel in the caring for pediatric patients presenting with pneumonia-like symptoms.[2] Particularly, diagnosis and management of CAP in pediatric patients who present to outpatient settings such as the Emergency Department (ED) presents multiple challenges, including the efficient and cost-effective use of diagnostic tests and treatment for the appropriate causal pathogen.

In the developed world, chest X-rays (CXR) are considered the standard diagnostic test for pneumonia in adult patients. However, the use of CXR for diagnosing pneumonia in children tends to be more conservative to reduce the lifetime exposure of children to radiation. Diagnosis depends on clinical presentation and physical examination. In the past decade, the WHO and other health organizations have developed guidelines to aim doctors in making the right decisions in choosing diagnostic tests and treatment options. Some of these guidelines are targeted for pediatric patients presenting with pneumonia symptoms in the inpatient and outpatient settings.[1] However, disparities in the utilization of these guidelines were reported among different ethnic groups.[3,4] Recent studies have shown that there are disparities in the effectiveness of healthcare received by ethnic populations, such as blacks and Hispanics, leading to economically inefficient healthcare.[5]

Assuming that adherence to established guidelines is considered a marker of adequate quality of care, we aimed to identify whether health care disparities existed among Hispanic/Latino and non-Hispanic/non-Latino pediatric patients when providing care for lower respiratory infections, particularly CAP. Being able to understand and identify potential racial and ethnic disparities could

help in the design of policies to decrease healthcare disparities and improve childhood health.

Methods

Design

We performed a secondary analysis of data from participants of the National Hospital Ambulatory Medical Care Survey (NHAMCS) from 2009 to 2015. The NHAMCS survey collects data on ambulatory care services in hospital emergency and outpatient departments, and in ambulatory surgery centers annually since 1992. Trained interviewers visited every location prior to participation to describe survey procedures and obtain eligibility. Each location was randomly assigned to a 4-week reporting period.

Sample Selection

The target population was all patients less than 18 years old that presented to the emergency department with suspicion of pneumonia. We made an assumption that neonates or premature infants would present less often to the emergency room, and instead may remain in the hospital from birth; additionally, the sample size of this subgroup was likely to be small. As such, we did not deem it necessary to exclude patients less than 1 month of age. To identify patients that presented with suspicion of pneumonia, we looked for pneumonia-based ICD-9 codes 480 through 487.

Due to the high-likelihood of having a CXR secondary to a previous diagnosis that predisposes to cardiothoracic pathology, children with a medical history of cancer, congestive heart failure, and HIV/AIDS were excluded from this study. The data available from before 2012 did not include diagnosis of cancer and thus data collected before 2012 may or may not have included children with a previous diagnosis of cancer. These might have affected our results if any specific group had a higher number of patients with the diagnosis.

Variables

To determine differences in quality care by ethnicity, our independent variable was the patients' ethnicity (Hispanic/Latino and Non-Hispanic/Latino) as self-reported. Our dependent variable was whether or not patients received a chest x-ray during the visit to the emergency department with suspicion of pneumonia, as recorded in the survey.

Potential confounders were the child's age at the time of visit (less than 1 year, between 1 and 4 years, and above 4 years), race ("White", "Black/African American", or "Other"), gender, region of residence ("Northeast", "Midwest", "South", and "West"), insurance type ("Private", "Government", "No insurance", or "Other"), presence of hypoxemia (measured by pulse oximetry and categorized as <93% and ≥93%), the child's temperature/fever at the ED arrival (<37.8°C and ≥37°.8C), and presentation severity (severe versus non-severe, assessed based on triage level from 1 to 5, using the Agency for Healthcare Research and Quality guidelines for Emergency Severity Index). Triage levels of 1, 2, or 3 were categorized as severe pneumonia, whereas triage levels of 4 and 5 were categorized as non-severe pneumonia. All data regarding confounders were retrieved from the dataset.

Statistical Analysis

Data analysis was conducted using Statistical Package of the Social Science (SPSS) v.20. First, descriptive analysis was conducted followed by bivariate analysis to assess the distribution of baseline characteristics among the two ethnic groups. Similarly, these tests assessed if ethnicity and covariates were associated with having a CXR during the visit in the ED. All variables were categorical, thus, chi-squared tests were used to assess statistical significance. Lastly, multivariate logistic regression analyses were used to assess the association between ethnicity and use of CXR while adjusting for potential confounders.

A number of patients in the study did not have information for ethnicity, the main exposure in our study, so they were excluded for the purpose of the primary analysis. Later we conducted a sensitivity analysis to determine if the results were robust, considering cases without data on ethnicity first as Hispanic/Latino and later as Non- Hispanic/Latino. We also conducted an analysis using an expanded inclusion criteria of "cough" as a presenting symptom, rather than differential diagnosis of pneumonia, to capture additional cases where CXRs were ordered based on initial presentation.

This study was based on analysis of de-identified data, thus, the IRB considered the study to be non-human subject research.

Results

Over the 6-year window of 2009 through 2015, 587 pediatric patients met the criteria of this study. Table 1 presents the characteristics of the sample. Hispanic/Latino patients predominantly identified as White (95.4%), were more likely to be located in the South (38.4%) and Western (38.4%) regions of the United States. They were also significantly more likely to have government insurance (80.6%) as opposed to private insurance when compared to their Non-Hispanic/Latino counterparts.

Table 2 shows the characteristics of subjects as it pertains to usage of chest X-rays during the same visits. Hispanic/Latino patients were slightly less likely to receive chest X-rays (80.8%) when compared to their Non- Hispanic/Latino counterparts (84.1%); however, this was not statistically significant. Age was the only baseline feature that showed a significant association with the use of X-rays, with younger patients having CXR less often than older children.

	Ethnicity Hispanic / Latino – N (%)		
Characteristics	**Yes**	**No**	**p-value**
Age (years)			0.579
<1	32 (16.3)	81 (21.0)	
1 to 4	88 (53.6)	197 (48.9)	
5 to 17	60 (30.1)	129 (30.1)	
Gender			0.676
Male	105 (54.4)	218 (56.8)	
Female	75 (45.6)	189 (43.2)	
Race			<0.001
White	105 (95.4)	229 (54.0)	
Black or African American	3 (2.51)	115 (37.9)	
Other	3 (2.1)	39 (8.1)	
Location			<0.001
Northeast	28 (9.2)	68 (13.9)	
Midwest	29 (14.0)	128 (31.9)	
South	50 (38.4)	136 (37.3)	
West	73 (38.4)	75 (16.9)	
Visit Day			0.614
Weekday	128 (69.4)	265 (66.0)	
Weekend	52 (30.6)	142 (34.0)	
Arrival Time			0.552
Day	79 (52.2)	193 (48.4)	
Night	99 (47.8)	210 (51.6)	
Triage Status			0.339
Severe	104 (60.5)	235 (66.3)	
Non-severe	54 (39.5)	131 (33.7)	
Temperature			0.846
Fever	100 (51.9)	208 (53.1)	
No Fever	80 (48.1)	189 (46.9)	
Oxygen Sat			0.257
<93%	10 (4.9)	31 (7.9)	
≥93%	170 (95.1)	376 (92.2)	
Insurance Type			<0.001
Private	23 (10.0)	158 (36.1)	
Government	140 (80.6)	208 (57.8)	
Other	4 (2.2)	4 (1.5)	
No Insurance	6 (7.2)	22 (4.6)	

Table 1. Characteristics of pediatric patients presenting to the emergency department by ethnicity, NHAMCS 2009-2014.

	Chest X-Ray – N (%)		
Characteristics	**Yes**	**No**	**p-value**
Ethnicity			0.5995
Hispanic/Latino	147 (80.8)	33 (19.2)	
Non- Hispanic/Latino	335 (84.1)	72 (15.9)	
Age (years)			0.0282
<1	95 (72.0)	33 (28.0)	
1 to 4	306 (84.5)	53 (15.5)	
5 to 17	185 (85.6)	43 (14.4)	
Gender			0.5806
Male	319 (81.7)	71 (18.3)	
Female	267 (83.6)	58 (16.4)	
Race			0.1734
White	312 (80.3)	77 (19.7)	
Black or African American	122 (86.2)	23 (13.8)	
Other	38 (92.9)	4 (7.1)	
Location			0.339
Northeast	90 (74.5)	32 (25.5)	
Midwest	160 (81.9)	30 (18.1)	
South	203 (86.9)	37 (13.1)	
West	133 (80.6)	30 (19.4)	
Visit Day			0.138
Weekday	375 (80.4	92 (19.6)	
Weekend	211 (86.3)	37 (13.7)	
Arrival Time			0.302
Day	269 (85.7)	50 (14.3)	
Night	313 (81.5)	70 (18.5)	
Triage Status			0.722
Severe	343 (83.9)	67 (16.1)	
Non-severe	179 (82.3)	44 (17.7)	
Temperature			0.753
Fever	306 (83.2)	64 (16.8)	
No Fever	208 (81.8)	65 (18.2)	
Oxygen Sat			0.528
<93%	53 (86.6)	6 (13.4)	
≥93%	533 (82.1)	123 (17.9)	
Insurance Type			0.847
Private	176 (80.5)	47 (19.5)	
Government	345 (83.4)	67 (16.6)	
Other	9 (72.2)	2 (27.8)	
No Insurance	32 (81.8)	4 (18.2)	

Table 2. Characteristics of pediatric patients presenting to the emergency department by use of chest X-Ray, NHAMCS 2009-2014

	Unadjusted		Adjusted	
Characteristics	**OR (95% CI)**	**p-value**	**OR (95% CI)**	**p-value**
Ethnicity				
Hispanic/Latino	0.8 (0.3-1.9)	0.600	0.8 (0.3-2.5)	0.744
Non- Hispanic/Latino	Ref		ref	
Age (years)				
<1	0.4 (0.2-0.9)	0.029	0.3 (0.1-0.6)	0.003
1 to 4	0.9 (0.5-1.7)	0.797	0.9 (0.4-1.8)	0.708
5 to 17	ref		ref	
Gender				
Male	ref			
Female	1.1 (0.7-1.8)	0.581	-	
Race				
White	ref		ref	
Black or African American	1.5 (0.7-3.1)	0.253	1.4 (0.6-3.1)	0.477
Other	3.1 (0.8-11.7)	0.079	-*	
Location				
Northeast	Ref		ref	
Midwest	1.5 (0.7-3.3)	0.251	1.2 (0.4-3.5)	0.804
South	2.2 (1.0-4.9)	0.038	2.2 (0.7-7.3)	0.197
West	1.4 (0.5-3.7)	0.470	2.1 (0.6-7.7)	0.261
Insurance Type				
Private	ref			
Government	1.2 (0.6-2.2)	0.539	1.1 (0.6-2.0)	0.796
Other	0.6 (0.1-3.6)	0.612	0.6 (0.1-6.2)	0.657
No Insurance	1.0 (0.3-3.8)	0.895	1.2 (0.1-13.9)	0.899
Visit Day				
Weekday (Mon-Fri)	ref		-	
Weekend (Sat-Sun)	1.5 (0.8-2.7)	0.140	-	
Arrival Time				
Day	ref		-	
Night	0.7 (0.4-1.3)	0.303	-	
Triage Status				
Severe	1.1 (0.5-2.1)	0.722	-	
Non-severe	Ref		-	
Temperature				
Fever	1.1 (0.5-2.0)	0.754	-	
No Fever	ref		-	
Oxygen Sat				
<93%	1.4 (0.4-4.0)	0.530	-	
≥93%	ref		-	

Table 3. Unadjusted and adjusted associations between ethnicity and use of chest X-Ray in pediatric patients presenting to the emergency department, NHAMCS 2009-2014.

Patients	Unadjusted OR (95% CI)	p-value	Adjusted[1] OR (95% CI)	p-value
Only those with data on Ethnicity	0.8 (0.3-1.9)	0.600	0.9 (0.3-2.6)	0.857
Counting all missing as Hispanic/Latino	0.8 (0.4-1.6)	0.502	1.0 (0.4-2.7)	0.921
Counting all missing as Non-Hispanic/Latino	0.9 (0.4-2.0)	0.710	0.7(0.2-1.9)	0.455

[1]: Adjusted for race, age, region, severity and health insurance

Table 4. Association between ethnicity (Hispanic/Latino vs Non- Hispanic/Latino) and use of X-rays - Sensitivity analysis for patients with and without information about ethnicity and sensitivity analysis with expanded inclusion criteria

	Ethnicity Information – N (%)		
Characteristics	**Yes**	**No**	**p-value**
Chest X-Ray			0.718
Yes	482 (83.0)	104 (80.6)	
No	105 (17.0)	24 (19.4)	
Age (years)			0.707
<1	113 (19.4)	15 (14.3)	
1 to 4	285 (50.5)	74 (55.9)	
5 to 17	189 (30.1)	39 (29.8)	
Race			0.158
White	334 (63.9)	55 (73.7)	
Black or African American	118 (29.5)	27 (26.3)	
Other	42 (6.7)	0	
Insurance Type			0.540
Private	181 (27.1)	42 (33.5)	
Government	348 (65.7)	64 (58.5)	
Other	8 (1.8)	3 (0.8)	
No Insurance	28 (5.5)	8 (7.2)	

Table 5. Characteristics of pediatric patients presenting to the emergency department who were included in the study (with ethnicity data) and those excluded from the study (no ethnicity data)

Before adjusting for potential confounders, we found an unadjusted odds ratio of 0.8 (95% CI 0.3-1.9) for Hispanic/Latino patients receiving chest X-rays. After adjusting for variables, the odds ratio remained unchanged (adjusted OR 0.8, 95% CI 0.3- 2.5) (Table 3). Younger patients (<1 year old) were again less likely to receive chest X-rays (adjusted OR 0.3; 95% CI 0.1 to 0.6). Gender, race, location, and insurance type did not yield significant differences on the use of X-rays.

One hundred-twenty eight patients in the study did not have information for ethnicity, the main exposure in our study. Sensitivity analysis based on an expanded inclusion criteria showed that unadjusted and adjusted odds ratios for the association between ethnicity and use of X-rays did not change significantly when assessing the two scenarios (counting all patients without data on ethnicity first as Hispanic/Latino and then as Not Hispanic/Latino) (Table 4). Table 5 shows the comparison for age, race, or insurance type between patients with and without information about ethnicity. There were no significant differences in major baseline characteristics between the two groups.

Sensitivity analysis showed that unadjusted and adjusted odds ratios for the association between ethnicity and use of X-rays did not change significantly whether or not these patients were included in the analysis (Table 4). There were no significant differences in major baseline characteristics (Table 5) such as age, race, or insurance type between patients with and without information about ethnicity.

Discussion

In this study, Hispanic/Latino ethnicity was not found to be significantly associated with a decreased quality of care in the ED diagnostic evaluation of pediatric pneumonia. Our findings are not in agreement with previous studies that found health care disparities in pediatric ED patients presenting with pain, asthma, or other conditions.[7,8,9] Hambrook found that in pediatric patients presenting with chest pain, Caucasians and those with private insurance were more likely to undergo testing compared to African Americans or those with public insurance (Medicaid).[7] Additionally, Jones et al. studied asthma pediatric patients in the ED and found that African Americans and Hispanics were 80 and 70% more likely to have used urgent care, respectfully, compared to their Caucasian counterparts.[8] Factors contributing to seeking urgent care include trouble getting care before the ED, symptom severity, and Medicaid enrollment. Guidelines are published on the management of CAP in children 3 months and older.[4] Specifically, decisions on CXRs are based on signs of respiratory distress, including tachypnea, dyspnea, retractions, grunting, nasal flaring, apnea, altered mental status, and pulse oximetry on room air. These guidelines are intended to make healthcare decisions non-biased, however, ordering CXRs or further tests are the decision of the healthcare provider and can be subjective. Although our study did not find an association between ethnicity and disparities in the pediatric population, Washington et al. found variations in patterns of care among different US ethnic/racial pediatric patients with pneumonia.[6] For example, minorities (African Americans, Hispanics, and Asians) were less likely to receive bronchoscopy or mechanical ventilation, as well as incurred higher charges during their stay in the hospital.

We further decided to investigate our inclusion criteria. We included patients based on differential diagnosis of pneumonia via ICD-9 codes. Other may have had CXRs ordered based on presenting symptoms even if pneumonia diagnosis was not provided, which may have narrowed the subset of our intended population. When we conducted an additional analysis to consider a presenting symptom of “cough” as the inclusion criteria, our results differed in terms of sample size and significance, while the odds ratio stayed the same. This suggests that an association may exist, yet we did not have enough power in the initial analysis to verify it. A possible limitation in our study design is the adjustment for triage level to classify severity of pneumonia symptoms. It is possible the triage staff had racial or ethnicity-related bias. A study of 78 million adult ED visits using NHAMCS found that Caucasians with chest pain were more likely to be triaged emergently than African Americans and Hispanics.[5] If Caucasian patients in our study were inappropriately assigned more urgent triage scores, our study results could underestimate the association between ethnicity and quality of care of pediatric pneumonia.

Another limitation of our study is the inability to explore English proficiency as a potential confounder. Language preference was not included in the NHAMCS surveys used, which may underestimate the association between ethnicity and quality of care. Finally, some hospitals may rely on self-reporting of race and ethnicity. Staff may assume a child or family is non-Hispanic if they are fluent English speakers. Inconsistent staff assignment of race and ethnicity could subject the study to misclassification bias, which could lead to falsely finding a lack of association.

While this study did not find an association between ethnicity and the management of pneumonia in pediatric ED patients, studies of other health problems documented clinically significant disparities. Additional research is necessary to investigate the circumstances where disparities exist, with the goal of improving patient care in vulnerable populations.

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CASE REPORT

A case report of dizygotic twin pregnancy concordant for non-syndromic cleft lip and palate with differing severity

Tiffany Beguiristain, Rolando De Leon, MD, Dr. Dibe Martin, MD

Herbert Wertheim College of Medicine, Florida International University, Miami, FL, USA

Corresponding Author: Tiffany Beguiristain, tbegu001@fiu.edu

Special Acknowledgements: Joseph Burns

Abstract

Introduction: Oral clefts are among the most common congenital malformations in the United States. The literature regarding oral clefts in twin gestations is limited. Concordance rates for cleft lip and palate in monozygotic and dizygotic twins have been reported in the literature, demonstrating 50% vs 8%, respectively. In this report, we present the case of a diamniotic, dichorionic twin gestation of male fetuses identified by ultrasound to have cleft lip (Baby A) and cleft lip and palate (Baby B).

Objective: To describe a unique case, in the absence of risk factors, of diamniotic, dichorionic twins concordant for nonsyndromic CL and CLP of differing severity.

Conclusion: With a multifactorial inheritance pattern, the etiology of this non-syndromic malformation may be due to unidentified genetic causes or environmental causes affecting the shared intrauterine environment of twin gestations. There is no increased risk of oral cleft associated for twins when compared to singletons. As in this case, early detection of this congenital malformation enables providers to adequately organize appropriate and specialized care for the duration of the gestation and for future surgical correction.

Key Words: oral clefts; cleft lip; palate; di-di twins; intrauterine diagnosis

Introduction

Non-syndromic orofacial clefts are among the most common congenital malformations.[1] Orofacial clefts may be divided into three distinct phenotypes: cleft lip (CL), cleft palate (CP) and cleft lip with cleft palate (CLP).[2] These birth defects arise due to failure of the normal fusion of facial structures during weeks 4-10 of embryologic development.[3] According to the Centers for Disease Control, approximately 2,650 babies are born each year in the United States with a cleft palate and 4,440 babies are born with a cleft lip with or without a cleft palate.[4] Prevalence depends on several factors including sex, maternal age, and race/ethnicity.[5] Of those affected, males demonstrate a higher prevalence of CL and CLP when compared to females, who more commonly have isolated CP.[5] Prevalence has also been shown to increase with maternal age ≥ 35 years.[5] Furthermore, American Blacks demonstrate the lowest prevalence (10.2/10,000 live births) while American Indian and Alaskan Natives demonstrate the highest prevalence (20.5/10,000 live births).[5]

Diagnosis of this congenital defect can be made during pregnancy via routine ultrasound or upon delivery and inspection of the newborn. Those affected initially face difficulties with feeding and will ultimately require multiple corrective surgical procedures. Despite surgical correction, patients may continue to face clinical problems related to speech, hearing, and dentition that require additional therapy.[1,6] It is important to identify these congenital malformations as early as possible to provide the opportunity to plan surgical correction and identify a syndromic etiology if present. While the literature provides information regarding oral clefts, studies concerning the risk of oral clefts in twins are limited due to small sample sizes. The purpose of this article is to describe a unique case, in the absence of the aforementioned risk factors, of diamniotic, dichorionic twins concordant for nonsyndromic cleft lip and palate with differing severity.

Case

A 33 year old gravida 3 para 1011 female with no significant past medical history presented for routine obstetrical care of a twin gestation conceived through in vitro fertilization (IVF) with preimplantation genetic screening. Other genetic testing included a karyotype of the patient demonstrating a 46, XX female with no chromosomal abnormalities identified. IVF was considered for this pregnancy due to male factor infertility of the partner. Testing during the pregnancy included first and second trimester screening tests for aneuploidy and neural tube defects, all of which were negative. Routine anatomical survey performed at 19 weeks gestation demonstrated a diamniotic, dichorionic twin pregnancy with no significant discordance. A cleft lip was identified in both twin A and twin B, with twin B's cleft appearing to extend into the palate. The remainder of the fetal anatomy ultrasound (US) identified no other anomalies. The patient's history identified no risk factors such as family history of cleft lip, cleft palate, or other birth defects. Both partners denied history of tobacco, alcohol, or substance use. Medications used during the pregnancy were limited to prenatal vitamins. Consultations with maternal fetal medicine (MFM), pediatric cardiology, and pediatric craniofacial surgical specialists were immediately organized. The MFM specialist recommended amniocentesis to further explore the possibility of fetal chromosomal abnormalities. The patient declined amniocentesis despite discussing the risks, benefits, and limitations of the testing. The pediatric cardiologist performed a complete fetal echocardiogram at 21 weeks gestation demonstrating normal cardiac anatomy in both fetuses. The pediatric craniofacial surgical specialists discussed management of children with facial clefts both before and after surgical repair. Upon further imaging via ultrasound Baby B was identified to have a bilateral cleft lip with extension into the palate as demonstrated in Figure 2B. The pregnancy remained uncomplicated. Serial growth ultrasounds were performed showing adequate growth of both twins with no significant discordance. Amniotic fluid volumes were within normal limits. Fetuses with cleft lip and/or palate can have difficulty swallowing, increasing their risk for polyhydramnios and preterm labor. For this reason, weekly biophysical profiles starting at 32 weeks were performed with consistently normal results.

The twins were delivered via an uncomplicated cesarean section at 37 weeks gestational age. Upon inspection, Baby A was identified to have a unilateral cleft lip as noted in the ultrasound and seen in Figure 1A. Baby B was identified to have a bilateral cleft lip and palate as depicted in Figure 2A. Following initial inspection, the infants were assessed for ability to feed and respire without complications. After 6 months, both underwent surgical repair by the pediatric craniofacial surgical specialists that had been following them since the initial diagnosis. Both babies were discharged home with their parents and are happy and healthy infants.

Discussion

Orofacial clefts arise from failure of the normal fusion of facial structures during embryologic development.[6] The basic morphology of the face is established between the fourth and tenth weeks of development by the joining of five facial prominences: frontonasal, two maxillary, and two mandibular prominences.[3] During the fifth week of development, paired maxillary prominences enlarge and grow ventromedially.[3] Simultaneously, a pair of nasal placodes form on the frontonasal prominence.[3] During the sixth week, the ectoderm found at the center of each of the nasal placodes invaginates to form a nasal pit, dividing the frontonasal prominence into the lateral and medial nasal processes.[3] During the sixth and seventh weeks of development, the lateral nasal processes fuse with the maxillary processes.[3] They then merge with the medial nasal process, forming the upper lip and primary palate.[3] Failure of the maxillary prominence to join with the medial nasal process results in a cleft lip.[3] The secondary palate begins development during the seventh week when the palatal shelves grow vertically alongside the tongue and later elevate to merge at the midline.[7] Failure of fusion of the two palatal shelves along the midline results in a cleft palate.[3]

While there are several theories for the etiology of orofacial clefts, among most infants the cause remains unknown. Studies have indicated that the etiology is multifactorial, including both genetic and environmental causes.[8] A genetic etiology for this congenital malformation was first suggested by Fogh-Anderson in 1942, as there was an increased frequency of cleft noted in relatives of patients with an orofacial cleft.[2] To date, the genetic cause of nonsyndromic cleft lip with or without cleft palate has not been fully identified. Progress continues to be made in identifying the genes and loci potentially responsible for these birth defects. Historically, interferon regulatory factor 6 (IRF6) was identified as the first causal gene for true nonsyndromic cleft lip with or without cleft palate.[8] More recently, a comprehensive review of the genetics in orofacial clefting by Mangold et al. discusses the introduction of genome-wide association studies (GWAS) and its contribution to the exploration of genetic loci possibly responsible for nonsyndromic orofacial clefts. There have been nine independent GWAS and two meta-analyses that have identified at least 25 genetic loci that contribute to the risk of orofacial clefts.[9] Proof of causality is still ultimately lacking, propagating the need for further investigation. Environmental risk factors associated with increased risks of isolated cleft lip and palate include maternal cigarette smoking, alcohol consumption, medication use, and folate deficiency.[10,11]

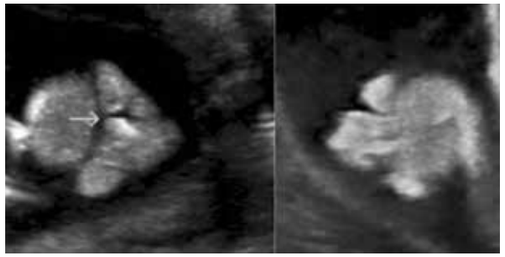
As mentioned previously, males demonstrate a higher prevalence of cleft lip with or without cleft palate. This apparent sexual dimorphism has been explored via a genome wide interaction study in the attempt to identify sex-specific risk alleles for nonsyndromic orofacial clefts. The results of this study supported observed dimorphism by finding a novel locus 10q21.1 with a genome-wide significant gene by sex interaction for multiple single nucleotide polymorphisms.[9]

Data regarding twins and the association to orofacial clefts is limited. Studies in the past have suggested a possible relationship between twinning and increased risk of oral clefts. However, a more recent study exploring the risk of oral clefts in twins by Grosen et al. suggested that there is no excess risk of oral clefts for twins compared to singletons.[12] This cohort study compared the oral cleft occurrence among singletons and twins using a 69-year Danish nationwide registry of isolated oral clefts.[12] Concordance rates for cleft lip and palate for monozygotic and dizygotic twins were identified demonstrating 50% vs 8%, respectively. Despite these results suggesting a strong genetic etiology, the incomplete concordance among monozygotic twins supports the theory that environmental exposures have an effect on oral cleft development.[2] In regards to dizygotic twins, recurrence risks among these types of clefts was demonstrated to be greater in dizygotic twins than in non-twin siblings.[12] This finding was postulated to be the result of a shared intrauterine environment.

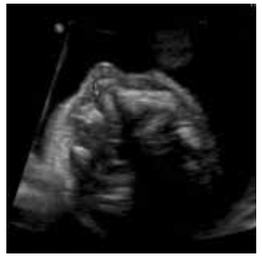
CASE REPORT

Baby A – Bilateral Cleft Lip and Palate

1A



1B



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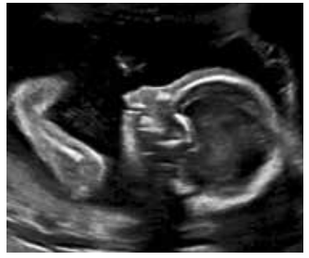
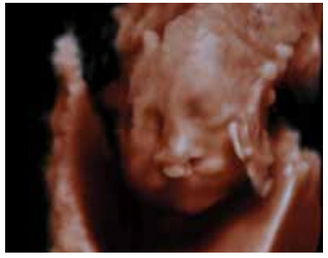


1D

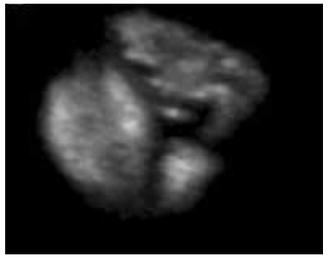


1E

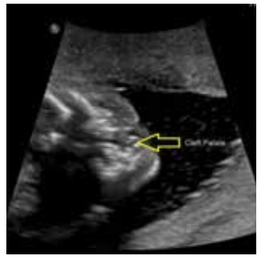
Figure 1A: Baby A with bilateral cleft lip and palate. **Figure 1B**: Both, 2D transabdominal ultrasound demonstrating coronal view of lips and nose. Imaging significant for bilateral cleft lip in Baby A. **Figure 1C**: 2D transabdominal ultrasound transverse view of upper lip and hard palate in Baby A. **Figure 1D**: 2D transabdominal ultrasonography depicting profile of Baby A. **Figure 1E**: 3D transabdominal ultrasonography at 26w6d demonstrating bilateral cleft lip in Baby A.

Baby B – Unilateral Cleft Lip and Palate

2A



2B



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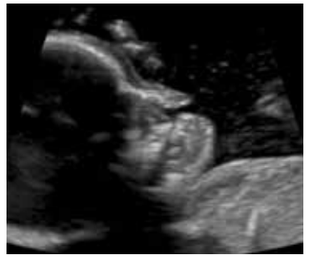
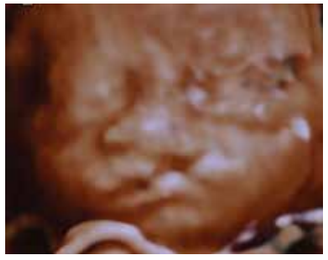


2D



2E

Figure 2A: Baby B with unilateral cleft lip and palate. **Figure 2B**: 2D transabdominal ultrasound demonstrating coronal view of lips and nose. Imaging significant for unilateral cleft lip in Baby B. **Figure 2C**: 2D transabdominal ultrasound transverse view of upper lip and cleft palate in Baby B. **Figure 2D**: 2D transabdominal ultrasonography depicting profile of Baby B. **Figure 2E**: 3D transabdominal ultrasonography at 26w6d demonstrating unilateral cleft lip in Baby B.

Assessment and treatment requires planning and coordination among an interdisciplinary team of specialists dedicated to the treatment of congenital anomalies. Wide use of routine ultrasonographic screenings can identify congenital anomalies such as orofacial clefts *in utero*. Despite the advancements in ultrasonography its accuracy at times may be limited. The sensitivity of routine transabdominal ultrasound at 20 weeks gestation may vary from 16% to 93%.[13] The variation in sensitivity may result from several factors such as experience of the ultrasonographer, maternal body habitus, fetal position, amount of amniotic fluid, and type of cleft.[13] When the diagnosis is made *in utero*, early access to prenatal coordination of care may be established. An accurate prenatal diagnosis ensures proper counseling with the parents when discussing prognosis and surgical planning.

Initial evaluation of the child is recommended within the first few days of life with attention focused on feeding and breathing. Those with palatal clefts cannot generate negative pressure while suckling.[14] As a result, a specialized nurser is needed to dispense milk into their mouths. Once adequate feeding and breathing are ensured, subsequent interval evaluations are conducted in order to assess the extent of the cleft anomaly and plan for surgical repair. In order to prepare for the first surgery at 3 to 6 months of age, attempts are made to reduce the deformity via a process known as pre-surgical infant orthopedics.[14] This serves to enhance the position of the maxillary alveolar segments.[15] It may also improve the nasolabial aesthetic outcomes prior to surgical closure of the cleft lip in some infants.[15] The goals of repair differ depending on the severity of the congenital malformation. For cleft lip, restoring normal function and anatomy is sufficient. For those with cleft palate, the goals of repair are slightly different as it aims to achieve normal function for speech and swallow.[15]

Conclusion

This case described a rare incidence of dizygotic twins identified *in utero* concordant for an orofacial cleft malformation with differing severities: unilateral cleft lip (Baby A) and bilateral cleft lip and palate (Baby B). While it is well known that oral clefts such as cleft lip and palate are among the most common congenital malformations, there is a paucity of information available regarding its association among dizygotic twins. Thus far, the literature fails to demonstrate an increased risk of oral cleft associated for twins when compared to singletons. With a multifactorial inheritance pattern, the etiology of this non-syndromic malformation may be due to unidentified genetic causes or environmental causes affecting the shared intrauterine environment of twin gestations. As demonstrated in this case, early detection of this type of congenital malformation enables providers to adequately organize appropriate and specialized care for the duration of the gestation and for future surgical correction.

To the best of our knowledge, this is the first reported case of concordant cleft lip and palate of differing severity in dichorionic diamniotic twins conceived by IVF.

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Go With the Flow: A Case Report of Trans-Transjugular Intrahepatic Portosystemic Shunt (TIPS) Complete Esophageal Variceal Embolization Using Liquid Embolic n-Butyl Cyanoacrylate Glue (nBCA)

Omosalewa Adenikinju MD[1], Elias Atri MS[2], David Wymer MD[1], Robert Beasley MD[1],
Timothy Yates MD[1], Brandon Olivieri MD[1]
[1]Department of Interventional Radiology, Mount Sinai Medical Center, Miami Beach, Florida, USA
[2]Herbert Wertheim College of Medicine, Florida International University, Miami, Florida, USA
Correspondence: Elias Atri, eatri001@fiu.edu

Abstract

Introduction: Variceal embolization during trans-jugular intrahepatic portosystemic shunt (TIPS) placement reduces the rate of post-TIPS hemorrhage. Embolic agents used for variceal embolization include metal coils or detachable plugs with or without additional sclerosing agents; however, these methods can result in lengthy procedural time and incomplete embolization. n-Butyl Cyanoacrylate (nBCA) glue, however, is a liquid embolic agent approved for the treatment of arteriovenous malformations. We present a case where post-TIPS nBCA embolization of extensive esophageal varices was performed using nBCA glue.

Methods: A 28-year-old male with alcoholic cirrhosis presented with bleeding esophageal varices refractory to repeat endoscopic interventions. Interventional Radiology consulted for TIPS placement. Persistent filling of an extensive esophageal variceal complex was noted after TIPS placement, despite a decrease in portosystemic gradient. Trans-TIPS access was obtained very distally into the variceal complex. A 1:2 nBCA: lipiodol glue mixture was instilled as the catheter was withdrawn back to the feeding left gastric vein achieving immediate, complete embolization of the entire extensive variceal complex.

Results: Successful TIPS with immediate, complete embolization of the entire esophageal variceal complex was obtained using nBCA glue.

Discussion/Conclusion: Post-TIPS variceal embolization with nBCA glue provided a highly controllable way to achieve immediate, complete cast-like embolization of extensive variceal complexes.

Keywords: Hemorrhage, n-BCA, TIPS, UGI Bleeding, Varices

Introduction

Transjugular intrahepatic portosystemic shunt (TIPS) creation is often successfully used to treat portal hypertension and its complications, including gastroesophageal variceal hemorrhage refractory to medical or endoscopic management.[1] TIPS has been shown to be effective in lowering portal pressures[2] and in the setting of variceal bleeding, embolization of varices during TIPS placement has been shown to reduce the rate of post-TIPS hemorrhage.[3] Embolic agents typically used for variceal embolization include metal coils or detachable plugs with or without additional sclerosing agents; however, these methods can result in lengthy procedural time, increased cost, and increased radiation exposure with potentially incomplete variceal embolization.[1]

n-Butyl Cyanoacrylate (nBCA) glue is a liquid embolic agent approved for the treatment of arteriovenous malformations. It is radio-opaque when mixed with lipiodol. The extent of embolization can be predicted based on vessel flow and glue polymerization rates. In experienced hands, glue embolization can be precisely deployed to create a complete plug of the target vessel, decreasing non-target embolization while conforming to the vessel framework.[4] Because of its liquid nature, nBCA glue embolization is particularly useful in the setting of coagulopathy as it is not reliant on intact coagulation cascade to obtain occlusion. It has been shown to be effective in failed coil embolization.[5-7]

Therefore, nBCA glue can provide a highly controllable way to achieve immediate, complete cast-like embolization of extensive variceal complexes. We present a case where post-TIPS nBCA embolization of extensive esophageal varices was performed resulting in immediate embolization of the entire variceal complex.

Case Presentation

A 28-year-old male with history of alcoholic cirrhosis and family history of cirrhosis (MELD 14; Child Pugh Class B) presented to our institution with hematemesis. On first admission, bedside esophagogastroduodenoscopy (EGD) was performed with banding of grade 3 esophageal varices.

Two days after discharge, the patient represented with recurrent hematemesis and underwent repeat EGD by gastroenterology with unsuccessful banding and sclerosis of the variceal complex.

A computed tomography (CT) scan demonstrated extensive esophageal and gastric varices, but no clear gastro-splenorenal shunt (Figure 1). Interventional radiology was consulted, and the patient was deemed a candidate for TIPS.

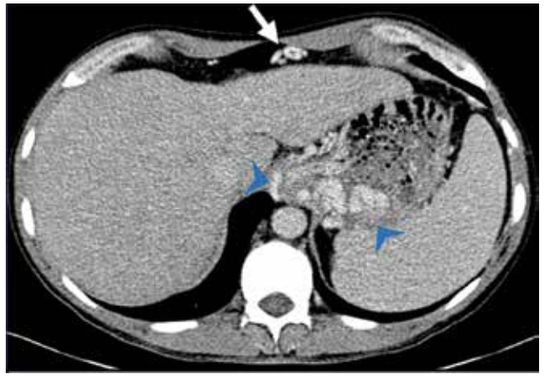

Figure 1: Axial contrast-enhanced CT image demonstrated sequela of portal hypertension with recanalized umbilical vein (white arrow) and a large gastroesophageal variceal complex (blue arrowheads).

Procedure

TIPS Creation:

A pre-TIPS portal venogram demonstrated contrast filling the extensive gastroesophageal variceal complex (Figure 2A). The right hepatic vein was catheterized via right internal jugular vein access. The portosystemic gradient was 14 mmHg. A right hepatic vein à right portal vein TIPS was created via right internal jugular vein access with 8-10 x 8 x 2 cm Viatorr stent graft deployed to 8mm, with a post TIPS portosystemic gradient of 10 mmHg.

Variceal Catheterization:

A portal venogram demonstrated persistent flow through an extensive gastroesophageal variceal complex. A 5 Fr 100cm angled glide catheter was used to select the left gastric vein. A 0.016" Fathom wire (Boston Scientific, Marlborough, MA) and a 2.4 Fr Progreat microcatheter (Terumo, Japan) were passed deep into the extensive, tortuous variceal complex.

Glue Embolization:

The glue mixture was prepared in a 1:2 nBCA: lipiodol ratio mixture (TRUFILL, DePuy Synthes, West Chester, PA). 3 mL of D5W were used to flush the microcatheter of ionic substances (blood, saline) to prevent intra-catheter glue polymerization. 1mL of glue mixture was then flushed through the microcatheter and a glue plug was allowed to form into a plug at the tip of the catheter to occlude the variceal outflow.

As the catheter was slowly withdrawn through the variceal complex feeding the left gastric vein, another 1mL of glue mixture was injected into the variceal complex. Once the feeding left gastric vein was reached, the catheter was flushed multiple times with

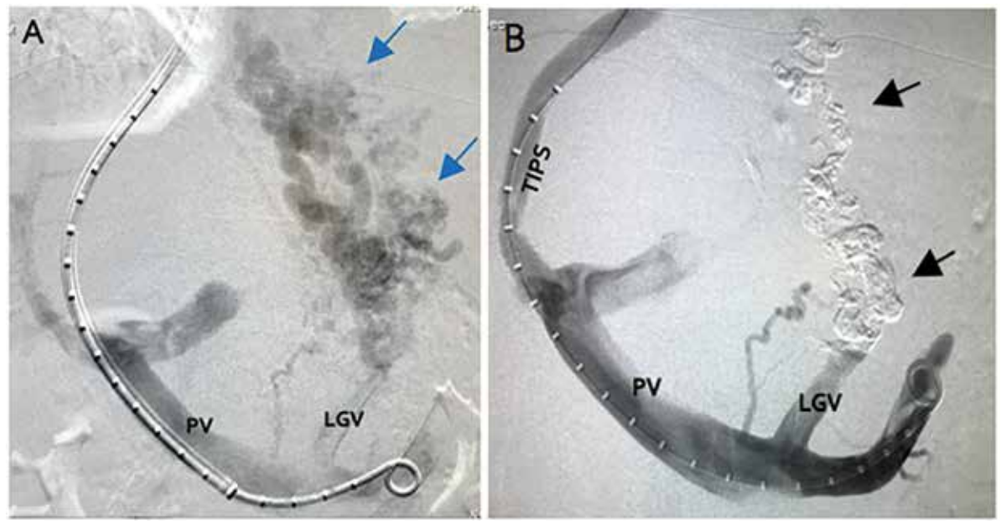

Figure 2: (A) Pre-TIPS portal venogram demonstrates contrast filling the extensive gastroesophageal variceal complex (blue arrows). (B) Portal venogram post-TIPS + embolization demonstrates no further variceal filling with complete embolization of variceal complex reflected by the glue cast (black arrows). PV = portal vein; LGV = left gastric vein.

D5W to clear the glue and then the catheter was removed.

Completion venography demonstrated no further variceal filling with complete cast-like embolization of the esophageal varices with a portosystemic gradient of 10 mmHg (Figure 2B). A post-procedural coronal CT image demonstrated the TIPS in place with the lipiodol: nBCA glue cast filling the gastroesophageal variceal complex (Figure 3).

Post-Procedure:

The patient tolerated the procedure well and was normotensive and hemodynamically stable after receiving 8 units of packed red blood cells and 2 units of fresh frozen plasma. He was subsequently transferred to the medical floor. The patient's hemoglobin began to drop and he became hypotensive, so he was transfused with an additional unit of packed red blood cells and fluid boluses and responded well. He did not have any signs of active bleeding. He also spiked low grade fevers and was tachycardic but no drainable ascitic fluid was found. He received intravenous antibiotics and his tachycardia resolved. After 24 hours of intravenous antibiotics, the patient remained afebrile, normotensive, and hemodynamically stable, his heart rate normalized, and he did not display any signs of active bleeding. He was discharged on postoperative day 5 and was referred to hepatology for further follow up.

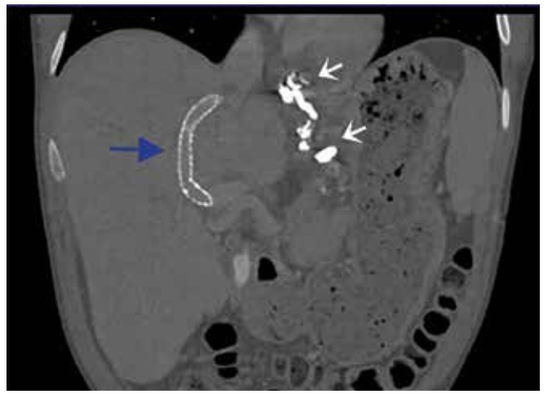

Figure 3: Post procedural coronal CT image demonstrates TIPS in place (blue arrow) with lipiodol: nBCA glue cast filling the gastroesophageal variceal complex (white arrows)

Discussion

The mortality rate of acute variceal bleeding in cirrhotic patients has been estimated to be 15-20% during the first episode.[8] This high mortality rate associated with variceal hemorrhage makes preoperative planning for maximizing therapy outcome imperative. Tesdal et al. compared TIPS alone and TIPS with adjunctive embolotherapy. After a mean follow-up time of 48.7 months, they found that 61% of patients with TIPS remained free of bleeding after 2 years and 53% after 4 years compared to 84% and 81% in patients who underwent both TIPS and embolotherapy.[9] Additionally, a meta-analysis conducted by Qi et al. found a significantly lower rate of rebleeding in adjunctive embolotherapy amongst six studies. They did, however, indicate the need for additional randomized controlled trials.[10] These findings suggest that adjunctive embolotherapy lowers the rate of rebleeding, and thus patient mortality.[9]

Classic use of nBCA in cerebral arteriovenous malformations[11], and pseudoaneurysms[4,12] has proven useful. Additionally, sclerotherapy with nBCA has been shown to be safe and effective in the control of bleeding and eradication of gastric varices[13]. Yi-Hsiu et al. evaluated the long-term efficacy and safety of endoscopic treatment of bleeding gastric varices with nBCA. The rate of hemostasis at one week was 94.4% and the rate of definitive hemostasis was 93.3% with minimal long term complications, such as mucosal defects; indicating that nBCA is highly effective without notable consequential complications.[14]

Yonemitsu et al. evaluated the outcome of transcatheter arterial embolization with gelatin sponge particles, microcoils, and nBCA, for acute hemorrhage in patients with coagulopathies. The microcoil group had a hemostatic rate of 80%, a recurrent hemorrhage rate of 0%, and a treatment time of 37 minutes ± 19. The nBCA group had a hemostatic rate of 100%, a recurrent hemorrhage rate of 0%, and a treatment time of 9 minutes ± 4, proving to be more effective in hemostasis and prevention of recurrent hemorrhage, with shorter treatment time, a value much coveted in a fee-for-service economy.[7]

In addition, nBCA has proven its high efficacy profile providing hemostasis of arterial bleeding when previous coil or particulate embolization has failed in complex patients,[6] like the case we presented here.

nBCA's success is partially due to its viscosity, which allows for the cast-like embolization, and its polymerization speed, which do not allow it to permeate to the capillary level.[6] Its dense radiopacity allows for precise embolization to be observed in real time by the operator.

Given the importance of post-TIPS variceal embolization due to the high mortality associated with hemorrhage, the effectiveness of adjunctive embolotherapy is vital. The safety, effectiveness, and shorter treatment time of nBCA makes it an optimal, perhaps, superior embolic choice for post-TIPS embolotherapy. It offers the interventionalist a powerful lifesaving agent in their arsenal to treat and decrease the mortality of these complex, sick patients.

Conclusion

In the presented case, post TIPS nBCA embolization of extensive esophageal varices was performed. This resulted in immediate, precise embolization of the esophageal variceal complex, providing a controllable and time effective treatment. We propose it should be considered in preoperative planning for all hemorrhagic etiologies, whether elective or emergent.

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A Case of Endovascular Management of Nutcracker Syndrome Presenting as Spontaneous Left Renal Vein Thrombosis: A New Age Interventional Approach to a Classic Ballad

Omosalewa Adenikinju MD[1], Elias Atri MS[2], Chase Parsons MD[1], Robert Beasley MD[1],
Timothy Yates MD[1], Brandon Olivieri MD[1]
[1]Department of Interventional Radiology, Mount Sinai Medical Center, Miami Beach, Florida
[2]Herbert Wertheim College of Medicine, Florida International University, Miami, Florida
Corresponding Author: Elias Atri, eatri001@fiu.edu

Abstract

Introduction: Nutcracker syndrome (NCS) is a condition that occurs when the left renal vein (LRV) is compressed, most commonly between the aorta and the superior mesenteric artery (SMA). NCS can predispose a person to left renal vein thrombosis (RVT). We present a case where successful aspiration thrombectomy was performed using the Penumbra Indigo CAT8 system, a mechanical thrombectomy device that uses an 8F catheter, to treat RVT in a patient with NCS.

Methods: A 20-year-old female with a past medical history of systemic lupus erythematosus (SLE) and lupus nephritis presented to the emergency department with acute flank and abdominal pain. The urinalysis was significant for proteinuria and hematuria. Contrast-enhanced CT of the abdomen and pelvis demonstrated isolated left RVT with compression of the vein between the SMA anteriorly and the aorta posteriorly, consistent with underlying NCS. Given the patient's age and severe pain, the decision was made to undergo pharmacomechanical aspiration thrombectomy with the Penumbra Indigo CAT8 system. The procedure was completed successfully.

Discussion/Conclusion: Spontaneous isolated RVT is a rare initial presentation of underlying NCS. Through a review of the literature, we aim to review the pathophysiology of this condition. We also introduce our successful use of the Penumbra Indigo CAT8 system for pharmacomechanical aspiration thrombectomy, a novel endovascular treatment regimen of this clinical entity.

Keywords: Nutcracker, Thrombosis, Pharmacomechanical Thrombectomy

Introduction

Nutcracker syndrome (NCS) is a condition that occurs when the left renal vein (LRV) is compressed, most commonly between the aorta and the superior mesenteric artery (SMA).[1] Without treatment, NCS can predispose a person to left renal vein thrombosis (RVT).[2] Advancements in biomedical engineering have expanded venous thromboembolism treatment beyond anticoagulation, specifically, catheter-directed pharmacologic thrombosis, mechanical and pharmacomechanical thrombectomy, and aspiration thrombectomy.[3]

Pharmacomechanical thrombectomy involves the combination of direct infusion of lytic agents into the thrombus and removal of the clot with an endovascular mechanical device via maceration or aspiration.[4] The Penumbra Indigo system for aspiration thrombectomy has catheter sizes of up to 8F. Power aspiration-based extraction of peripheral arterial thromboembolism with the Penumbra Indigo system has been shown to be safe and effective, both as a primary treatment and adjuvant therapy.[5]

We present a case where successful aspiration thrombectomy was performed using the Penumbra Indigo CAT8 system, a mechanical thrombectomy device that uses an 8F catheter, to treat RVT in a patient with NCS.

Case Presentation

A 20-year-old female with a past medical history of systemic lupus erythematous (SLE) complicated by lupus nephritis with no relevant family or social history presented to the emergency department with severe left flank and abdominal pain.

Contrast enhanced CT of the abdomen and pelvis demonstrated compression of the LRV as it coursed between the SMA and the abdominal aorta. Delayed left nephrogram indicated the presence of a left RVT. These findings were consistent with NCS. Further, extension of the thrombus into the left gonadal vein was noted (Figure 1).

Interventional Radiology was consulted for further evaluation and intervention. Given the patient's failed triple anticoagulation therapy, persistent severe pain, and signs of decreased renal perfusion on CT, the decision was made to perform a left renal venogram with possible LRV thrombolysis and possible stenting of the LRV.

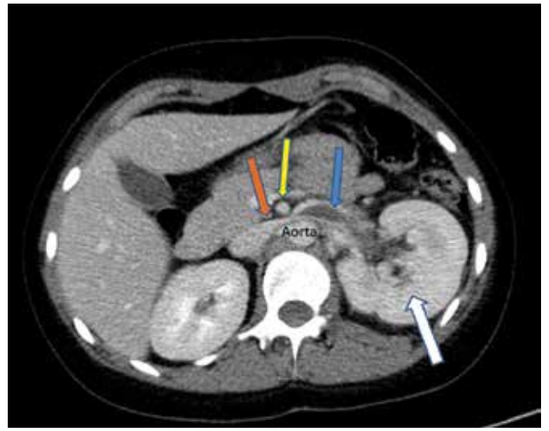

Figure 1: Marked compression of the LRV (orange arrow) as it courses between the SMA (yellow arrow) and the abdominal aorta (aortomesenteric angle 40 degrees, beak angle of 47 degrees), with resultant thrombosis of the LRV (blue arrow). Delayed venous nephrogram (white arrow) is noted. A filling defect in the left gonadal vein indicating thrombosis is not pictured.

Procedure

A left renal venogram demonstrated an expanded thrombus in the LRV and filling of distal collateral venous channels (Figure 2A). The thrombus was laced with 10 mg of tissue plasminogen activator (tPA) and allowed to dwell for 10 minutes. Subsequently, the Penumbra Indigo CAT8 system was used to perform aspiration thrombectomy of the LRV. Post thrombectomy intravascular ultrasound (IVUS) showed minimal residual thrombus within the LRV and a left renal venogram showed markedly improved vessel caliber (Figure 2B). However, severe compression of the LRV as it passed between the SMA and aorta was noted, consistent with NCS.

A systolic pressure gradient of 4 mmHg was measured in the post-stenotic LRV (18/14 mmHg) and inferior vena cava (14/12 mmHg). Given the non-significant pressure gradient across the region of stenosis (4mmHg) and the patient's young age, stent placement was deferred.

Post-operatively, the patient was started on Enoxaparin, a factor Xa inhibitor, and was switched to Apixaban, a different factor Xa inhibitor, for outpatient therapy.

Discussion

Similar to deep vein thrombosis or a pulmonary embolism, symptomatic RVT is initially treated with unfractionated or low molecular weight heparin (LMWH) followed by warfarin.[5] A study by Wu et al. reports successful treatment of RVT with LMWH in 3 patients with nephrotic syndrome, highlighting its safety, efficacy profile, and feasibility for outpatient treatment.[6] Lam et al. reported successful treatment of acute inferior vena cava thrombosis and unilateral RVT by local infusion of recombinant tPA. They recommend thrombolytic therapy as a second line treatment (after failed heparin therapy) in patients with bilateral involvement, acute renal failure, or severe flank pain, similar to our patient presentation.[7]

Percutaneous catheter-directed thrombectomy with or without fibrinolysis has been shown to restore renal function rapidly with a low incidence of morbidity due to pulmonary emboli or hemorrhagic complications in the treatment of RVT. Boosting the efficacy profile of percutaneous catheter directed thrombectomy, Kim et al. demonstrated no RVT recurrence after a median follow up time of 22.5 months.[8]

With a rare presentation of "complicated" NCS, where left RVT occurs, invasive treatment is indicated in patients who fail medical therapy or with persistent recurrence to preserve renal function. Endovascular stenting of the LRV, transposition of the SMA or LRV, and autotransplantation of the left kidney have all been described as successful therapies with some literature recommending stenting as first line when clinically indicated.[9,10]

Interventionalists, however, are reshaping traditional therapy. Based on the data above, treatment should first be initiated with anticoagulants, changing the site of coagulation cascade inhibition if therapy fails with subsequent targets being Vitamin K (Warfarin) and Factor Xa (Rivaroxaban). Angiography is considered for refractory cases with initial analysis encompassing pressure gradient measurements. Advancements in biomedical engineering have permitted venous thromboembolism disease to be treated with catheter directed thrombolysis and pharmacomechanical thrombectomy, with adjuvant stenting when indicated. We suggest the use of IVUS for precise endoluminal assessment pre and post treatment. The Penumbra Indigo CAT8 aspiration system allows for single session, prompt thrombectomy, decreasing radiation, procedure time, and complications compared with traditional lytic therapy.

In the case presented, given the patient's age, failed triple anticoagulation therapy, and considering thrombosis extension into the left gonadal vein, initial thrombolysis was performed, allowing for prompt and uncomplicated aspiration thrombectomy with no residual clot on IVUS. Adjuvant stenting was not deemed necessary secondary to lack of a significant pressure gradient. Preventative treatment with Apixaban was initiated after the procedure with no evidence of recurrence to date.

Conclusion

Venous thrombosis, a common disease elsewhere in the peripheral system, can present as a rare presentation of underlying NCS. The

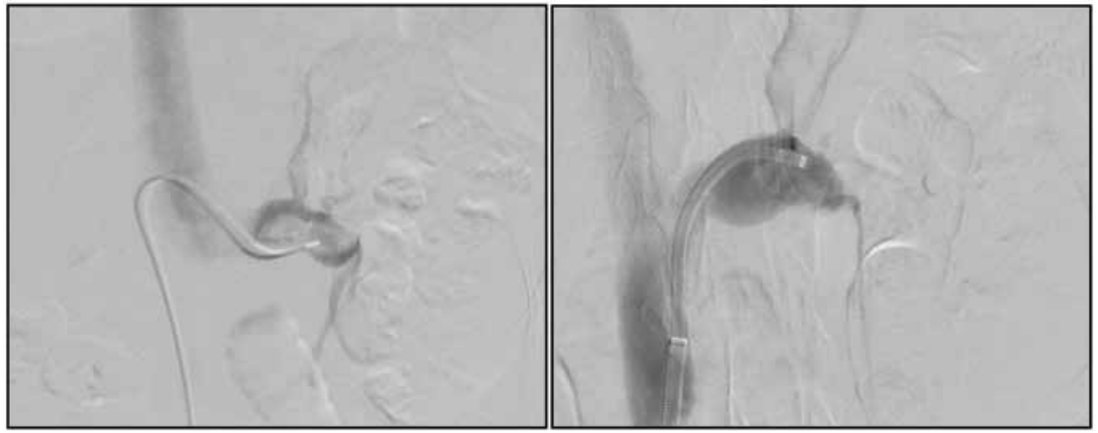

Figure 2: Initial venogram demonstrates extrinsic compression of the LRV with a large filling defect, concordant with thrombus (red arrow) seen on CT (left). Markedly improved vessel caliber (right) post-intervention with aspiration thrombectomy.

successful use of pharmacomechanical aspiration thrombectomy of the renal vein with the Penumbra Indigo CAT8 system allowed for optimal use of medical and minimally invasive therapy, placing the interventionalist at the cusp of modern, safe, and effective medicine.

Abbreviations

IVUS- Intravascular Ultrasound
LMWH- Low Molecular Weight Heparin
LRV- Left Renal Vein
NCS- Nutcracker Syndrome
RVT- Renal Vein Thrombosis
SLE- Systemic Lupus Erythematosus
SMA- Superior Mesenteric Artery
tPA- Tissue Plasminogen Activator

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Herpes Zoster: Case Review and Discussion

Reema Kola, Amalia Landa-Galindez MD

Herbert Wertheim College of Medicine, Florida International University, Miami, Florida, USA

Correspondence: Reema Kola, rkola004@fiu.edu

Abstract

We report a case of herpes zoster ophthalmicus complicated by post-herpetic neuralgia. A 63-year-old female with history of hypertension, anxiety, depressive disorder, and a recent traumatic fall presented to clinic with sudden onset of severe right frontal headache. Forty-eight hours later, her pain worsened and she developed a localized rash on the right upper eyelid. On physical exam, an erythematous eruption involving the right fronto-temporal and periorbital regions, and marked edema of the right upper eyelid were noted. A diagnosis of herpes zoster ophthalmicus was made. She was treated with oral valaciclovir, prednisone, and acetaminophen with codeine. After one week, eyelid edema resolved and most lesions had matured. At a four-week follow-up, she continued to have significant pain at the site of prior eruption. She was diagnosed with post-herpetic neuralgia and prescribed gabapentin. Five months after the diagnosis of herpes zoster ophthalmicus, she still reported significant pain and discomfort. Herpes Zoster and its sequalae are painful and debilitating, but are preventable with the zoster vaccine. It is critical for healthcare providers to counsel their patients regarding the importance of timely vaccination.

Keywords: Herpes zoster, herpes zoster ophthalmicus, post-herpetic neuralgia, vaccination

Introduction

The varicella-zoster virus belongs to the alpha-herpesvirus family. Primary infection causes varicella or “chicken pox,” which is usually a benign viral illness that presents in childhood as a generalized vesicular eruption with malaise and low-grade fever. In adults, illness can be more severe, and complications such as pneumonia or encephalitis may ensue. Reactivation of the varicella virus many years after primary illness can lead to herpes zoster or “shingles”. This reactivation is possible because after initial infection the virus establishes latency in the dorsal root ganglia and cranial nerve ganglia and is not completely eradicated.[1]

Herpes zoster presents as a painful rash in a dermatomal distribution. It can involve dermatomes in the head, chest and abdominal regions, and does not cross the midline. Involvement of the ophthalmic division of the trigeminal nerve is particularly painful, and is referred to as herpes zoster ophthalmicus[1]. Factors that have been associated with reactivation of the virus and resultant “shingles” later in life, include autoimmune disease, inflammatory bowel disease, immunodeficiency states, and depression.[2] Reactivation may also be related to the normal decline in immunity that occurs as individuals get older or after exposure to certain medications.[2] There are numerous complications from herpes zoster. The most common is post-herpetic neuralgia, a debilitating neuropathic pain that persists after the resolution of the rash.[3] Here we report a case of herpes zoster ophthalmicus with post-herpetic neuralgia, in the setting of recent physical trauma and depressed mood as risk factors.

Case Presentation

A 63-year-old female with a past medical history of hypertension, hypothyroidism, and depressive disorder presented to her physician with complaints of pain in the right forearm and left chest wall after a recent traumatic fall. She states that while at a wedding, she had gone to the bathroom to change her contact lenses for glasses due to eye discomfort. When she exited the bathroom, her vision was slightly blurred and she missed a step, falling on her left knee, left chest, and right wrist. She also bruised her forehead and her eyeglasses impacted the area lateral to her eyes. Her medications include levothyroxine 112 mcg daily, olmesartan 20 mg daily, and pravastatin 20 mg daily. Social history was significant for increased psychosocial stressors, with patient assuming primary caregiver duties for a terminally ill relative and the recent losses of her mother and cousin. On review of systems, patient had multiple painful sites from the trauma, fatigability, and a diminished mood. She denied any headache, blurred vision, dizziness, or chest pain. On physical exam, BMI was 32.07, temperature 98.4, pulse 78, respiratory rate 16, and blood pressure 118.84. HEENT examination was unremarkable. Musculoskeletal exam revealed a large eccymotic region in the right forearm and wrist with tenderness upon palpation and rotation. Left knee had patellar edema and tenderness, and there was tenderness in the left anterior/posterior chest wall upon light palpation, without crepitus. Neurologic examination was normal and patient had a normal mental status exam and affect. She was referred for chest, knee, forearm, and wrist x-rays and given an intramuscular injection of dexamethasone 10 mg mixed with triamcinolone 40 mg for acute muscular spasm and pain. She was started on oral cyclobenzaprine 10 mg tablets twice a day and acetaminophen with codeine 300-30 mg, one tablet three times a day as needed for severe pain. X-rays all came back negative, and patient had improved significantly within ten days.

CASE REPORT

Figure 1: 1) Day 1 of herpes zoster rash. 2) Day 5 of herpes zoster rash. 3) Day 8 of herpes zoster rash.

Two months later patient called with complaints of sudden onset of severe right frontal headache. She was advised to come to the clinic as potential etiologies that warranted further immediate evaluation included temporal arteritis and uncontrolled hypertension. Patient declined visit to the clinic. She started a regimen of acetaminophen alternating with ibuprofen for the headache and monitored her blood pressure, which she reported as normal. Forty-eight hours later, she developed increased pain and a localized rash involving the right upper eyelid (Figure 1) and presented to her ophthalmologist. Vital signs were as followed: afebrile, blood pressure 118/86, pulse 89, and respiratory rate 16. Physical examination showed an erythematous eruption involving the right fronto-temporal region and right periorbital region, with marked edema of the right upper eyelid and mild conjunctival erythema. Erythema of the skin extended to the right upper nasal region. The remainder of the physical examination was unremarkable.

Potential differential diagnoses considered included herpes simplex keratitis, impetigo, autoimmune blistering disorders, and drug reaction. Based on the classic history and physical exam findings the patient was given the diagnosis of herpes zoster ophthalmicus and referred for laboratory testing.

She was diagnosed with herpes zoster ophthalmicus and started on high dose oral valacyclovir 1000 mg every 8 hours for ten days. After the initial 24 hours of valacyclovir, a seven-day course of oral prednisone tablets (60 mg daily) was added. After 24 hours of treatment with steroids and valacyclovir, there was mild improvement in the eruption as seen by diminished erythema with a decrease in the affected area of eruption. After 72 hours eye pain completely resolved, but severe right frontal pain continued. After one week of treatment, the patient had almost complete resolution of eyelid edema. Most lesions had matured and turned brown, and the erythema had resolved. Repeat ophthalmic examination was normal, with no evidence of conjunctivitis, keratitis, or uveitis. Note that patient did not recall having had chickenpox as a child; but believes she had exposure, as she recalls one of her siblings having had the illness.

She was seen for follow up in the outpatient clinic after four weeks, and while skin lesions had resolved, she continued to have significant localized pain at the site of the prior eruption. Laboratory studies at that visit were similar to baseline labs, and showed glucose 90, HgA1C 5.6, WBC 5.2, hemoglobin 14.2, hematocrit 42.8, platelets 253, TSH 0.464, and vitamin D level of 21.3. Antinuclear antibody levels were negative. She was given the diagnosis of post-herpetic neuralgia and started on oral gabapentin (300 mg capsule twice a day) and vitamin D supplementation. Patient discontinued gabapentin after several days due to excessive somnolence, and pain was moderately controlled with alternating ibuprofen 600 mg and acetaminophen 500 mg twice a day. Stronger opioid therapy was avoided due to concerns for chemical dependency and respiratory depression. At follow-up several months later, she still had persistent moderate pain and numbness with paresthesias at the site of the previous eruption. She was started on duloxetine 30 mg daily by mouth to assist with both neuropathic pain as well as ongoing anxiety and depression.

At the time of her three-month follow up, patient did not show for her appointment and was contacted over the phone. She had improved, but still reported chronic discomfort in the right periorbital region, which she described as moderate pain with associated numbness. She reported improvement in her anxiety with duloxetine and family support. Patient was contacted via phone two months later after failing to attend her scheduled appointments. Several months later she was again contacted and reported some improvement in her pain and diminishing social stressors, though still experienced significant difficulty sleeping at night. Gabapentin 300 mg at bedtime was added to her medication regimen and she was scheduled for a follow-up appointment. Though she continues experiencing difficulties related to the post-herpetic neuralgia, she notes more effective coping with her medical and psychosocial situation.

Discussion

In the general population, the lifetime risk of developing herpes zoster is approximately 20% to 30%, and the risk increases up to 50% in those living beyond the age of 85.[3] In the United States, the Centers for Disease Control (CDC) estimates that there are 1 million cases of herpes zoster annually.[1] Almost half of all individuals with herpes zoster develop complications, with postherpetic neuralgia being the most common.[3] Postherpetic neuralgia is described as a neuropathic pain that persists more than thirty to sixty days after resolution of the rash and may last for more than one year in 30-50% of patients.[4] The pain can interfere with activities of daily living and consequently result in depression and loss of independent living.[5] Postherpetic neuralgia is the number one cause of suicide in patients with chronic pain over the age of 70[3].

Additional complications of herpes zoster include aseptic meningitis, bacterial superinfection, hearing impairment, Bell's palsy, Ramsay Hunt syndrome, motor neuropathy, transverse myelitis, vasculopathies, and herpes zoster ophthalmicus.[5] Among patients with herpes zoster, approximately 10 to 20% will have herpes zoster ophthalmicus.[3] Some of the manifestations of herpes zoster ophthalmicus include keratitis, episcleritis, iritis, and conjunctivitis, and neuritis.[3] These complications can decrease the quality of life and interfere with activities of daily living.

Studies have shown that multiple risk factors are associated with the risk of developing herpes zoster. The risk is higher among women, individuals with a family history, and immunocompromised individuals such as organ transplant recipients and those with leukemia, lymphoma, or human immunodeficiency virus infection.[5,6,7] A large study conducted in the United Kingdom by Forbes et al found that certain medical conditions were associated with an increased risk of herpes zoster. These high risk conditions included rheumatoid arthritis, systemic lupus erythematosus, inflammatory bowel disease, chronic obstructive pulmonary disease, asthma, kidney disease, type 1 diabetes, and depression.[8] A 2017 Danish study by Schmidt et al, reported similar risk factors, with the addition of type 2 diabetes, and the recent use of glucocorticoids.[6] A systematic review and meta-analysis by Kawai et al, reported that statin use and physical trauma were also independent risk factors for herpes zoster.[7] Kawai also found that smokers had a reduced risk of developing herpes zoster. Forbes et al found an increased risk for the development of postherpetic neuralgia in smokers.[7,9] In summary, risk factors for herpes zoster are varied, and include trauma and genetic, medical, psychosocial, iatrogenic factors.

Our patient's potential risk factors included recent physical trauma, recent steroid use, chronic statin use, and increased stressors. A patient history that explores risk factors is important for identification of high-risk patients and important when counseling patients about the importance of vaccination. The suffering due to herpes zoster and its serious long-term sequelae are completely preventable through vaccination. Providers should focus on identifying risk factors and prophylactically educate and offer vaccination to patients to decrease incidence of herpes zoster.

There are currently two vaccines available for the prevention of herpes zoster in adults. Zostavax, a live attenuated vaccine, has been in use since 2006.[10] Zostavax is similar to the varicella vaccine that is used in children to prevent chickenpox, but with an increased antiviral potency. Shingrix, a recombinant subunit vaccine, was recently approved for use in the United States by the Food and Drug Administration (FDA) in 2017.[10] Shingrix has greater effectiveness (90%) compared to 50-55% reported effectiveness for Zostavax. Shingrix offers greater protection against the post-herpetic neuralgia and a prolonged period of protection.[11] Shingrix has the disadvantage of requiring two doses given several months apart, compared to the single dose needed for Zostavax. Although immunocompromised individuals have an increased risk for the development of herpes zoster, live attenuated vaccines are contraindicated in this population; the Centers for Disease Control and Prevention (CDC) and the Advisory Committee on Immunization Practices (ACIP) does not recommend vaccination in this population.[12] Current recommendations from the AICP include vaccination of immunocompetent patients with Shingrix that can begin at age 50 as a two-dose vaccination series with the second dose given 2-6 months after the initial dose. Individuals who have previously received the Zostavax vaccine are encouraged to receive the additional two-dose Shingrix vaccine.[11] If Shingrix vaccine is unavailable in an area, then the CDC recommends vaccination with the Zostavax. There is no age limit as to when these vaccines can be given. As more that 99% of individuals living in the United States over the age of 40 have had exposure to chickenpox, vaccination is particularly important.[1] These CDC vaccination recommendations are supported by the U.S. Preventive Services Task Force.[12]

Conclusion

Our case demonstrates the classic presentation and course of herpes zoster, including the sequelae of chronic neuropathic pain. Herpes zoster is caused by reactivation of the varicella zoster virus. It presents as a painful dermatomal rash that may involve the head, thorax or abdominal regions. Herpes zoster affecting the ophthalmic division of the trigeminal nerve, known as herpes zoster opthalmicus, can cause severe and debilitating pain and affect the eye. The most common chronic complication of herpes zoster is post-herpetic neuralgia, which can have devastating consequences for patients especially those who are fragile or have underlying emotional disorders. Post-herpetic neuralgia negatively

affects quality of life and can lead to depression and even suicide. Identifying patients with risk factors can lead to more effective counseling regarding the benefits of vaccination. Given the serious sequelae and mental health concerns related to post-herpetic neuralgia, we strongly urge healthcare providers to counsel their patients proactively regarding the benefits of timely vaccination.

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The Impacts of Gender, Age, and Anatomical Location on Cutaneous Thickness Evaluated by Ultrasound: A Review of the Literature

Ali Rajabi-Estarabadi[1], Thomas Vazquez[1,2], Mahtab Forouzandeh[1], Isabella Camacho[1], Keyvan Nouri[1]

[1] Department of Dermatology and Cutaneous Surgery, University of Miami Miller School of Medicine, Miami, Florida, USA

[2] Herbert Wertheim College of Medicine, Florida International University, Miami, Florida, USA

Corresponding Author: Thomas Vazquez, tvazq020@med.fiu.edu

Abstract

Variability in skin thickness is an important consideration during dermatologic procedures, as it may have medical, cosmetic, and surgical implications. Thus, dermatologic surgeons may benefit greatly from a thorough understanding of the numerous factors that can affect skin thickness; these factors include age, gender, and the anatomical location of the skin. Ultrasound has proven to be a valuable tool in visualizing the skin layers, especially where precise interrogation of the skin's thickness and density is necessary. In this paper, we outline current literature to explore the factors that contribute to skin thickness variability and evaluate the utility of ultrasound to measure these changes.

Keywords: Skin thickness, aging, ultrasound

Introduction

In order to measure skin thickness, a variety of tools have been used and described in the literature. Scanning electron microscopy and light microscopy have both been used to measure thickness of skin in vitro.[1] To measure the thickness of the skin in vivo, a skin caliper instrument has been used, however, it is less commonly used today as it is not a precise measurement.[2] Interestingly, ultrasound scanning offers a more modern, noninvasive, and reliable method for direct in vivo measurement of epidermal and dermal thickness.[3] Two types of ultrasonography, including modes A and B, as well as different frequencies can be used. The dermis and hypodermis are measured well with 20MHz ultrasound; however, the epidermis is much thinner, indicating that high frequency ultrasonography (HFUS) up to 100MHz should be used to better visualize the epidermis.[4] The purpose of this review is to discuss the differences in skin thickness with respect to sex, anatomic location, and age as measured by ultrasound. This review also discusses the utility of ultrasound in measuring skin thickness when indicated for various clinical situations.

Factors influencing skin thickness and echo density

Skin thickness and echo density can be influenced by factors such as increasing age, gender, and the particular anatomical site on the body. Factors, such as sun exposure, medication use, atrophic skin diseases, and various other dermatoses should also be taken into consideration. Echo density can provide helpful information regarding the keratin and collagen status of the epidermis and dermis, respectively, as ultrasound of the skin demonstrates an entrance echo [1]. In particular, evidence suggests that skin thickness is typically higher in males than females, as opposed to echo density, which is typically higher in women.[1,5-7] Although age was not reported to significantly affect echo density,[1] it has a considerable impact on skin thickness. The dermis is often thinner in the elderly, with progressive loss of thickness with age.[1,5,6,8-10] In addition to its importance within a number of other clinical scenarios, information regarding the factors that influence skin thickness is particularly vital to the success of skin graft harvests and wound healing efforts.

Firooz et al. used HFUS to assess influencing factors such as gender, age, and the location on the skin to further determine how these variables affect skin thickness and echo density.[1] Epidermal entrance echo thickness, dermal thickness, and dermal echo density were measured in 30 individuals, 17 female and 13 male. With the use of 2D HFUS at 22 and 50MHz ultrasonic probes, five anatomic locations were measured, and healthy participants were placed into groups based on age. The age range was 24 – 61 years old; the young skin group consisted of subjects less than 35 years old and the old skin group consisted of subjects over 35 years old. Subjects were not included in the study if they met any of the following exclusion criteria: any skin disorders, application of corticosteroid drugs, BMI >30, chronic systemic diseases, constant sun exposure in previous 3 months, and/or hard physical activity.

The five skin locations measured included the cheek, neck, palm, sole, and dorsum of the foot. The study was done in the winter to avoid prior sun exposure in subjects over the previous 3 months due to the fact that sun exposed areas atrophy at a different rate than protected areas.[11]

Dermal Thickness

Firooz et al. found that dermal thickness was higher in males compared to females, showing statistical significance on the neck and dorsum of foot. Shuster et al. also showed that the thickness

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of the dermis in all ages was higher in men than in women on the forearm.[5] Furthermore, 25 MHz A-mode (amplitude mode) ultrasonography used to measure the ventral forearm of 54 men and 64 women between ages 0-90+ years of age showed that in all ages, the skin thickness of men was higher than women's ($p<0.001$).[6] Because different sites of the body were measured and different tools were utilized, the studies suggest that there is strong evidence that men have a thicker dermis than women do overall.

Epidermal Entrance Echo Thickness

Epidermal entrance echo thickness was also measured with the use of 2D HFUS, indicating that it is higher in men than women; however, it did not reach statistical significance in any site.[1] Echo thickness was almost equal in men and women on the dorsum of the foot. All of the information regarding epidermal entrance echo thickness is based on the findings of Firooz et al. There is a limited amount of information on epidermal entrance echo thickness, likely due to the fact that it may not be commonly measured.

Echo Density

Lastly, the echo density of the dermis was found to be higher in females on all sites, showing significance on the neck only.[1] Similar to epidermal entrance echo thickness, the echo density on the dorsum of the foot was almost equal in men and women. When comparing age groups, however, there was no significant difference in echo density.

Supporting these findings, Seidenari et al. concluded that the echo density of the dermis was higher in women than men using a 20MHz 2D scanner.[7] The skin thickness and echo density of the dermis was analyzed on six sites of 48 individuals divided into two groups each with 27 subjects, from 27-31 years of age and over 60 years of age respectively. This same study also concluded that skin thickness on the forehead, cheek, volar forearm, dorsal forearm, and upper abdomen was higher in males compared to females.[7]

Skin thickness variation by anatomic location

Different locations on the body also influence skin measurements. Taking the overall mean of all the sites measured, Firooz et al. reported that the palm had the thickest dermis, the sole had the highest epidermal entrance echo, and the neck showed the highest echo density of the dermis.[1] This may be a result of some sites receiving more sun exposure or mechanical stress than others. Additionally, Iyengar et al. showed that different locations of the face have varying thicknesses, further demonstrating the importance of considering anatomic location. This study also utilized ultrasound at 15.0 MHz for analysis of a depth of 1.5 cm to 2cm and 18.0 MHz for 0.8 cm. This methodology underscores the need to not only take into account skin thickness for procedures like skin surgery, but also for selecting the appropriate scanning technique for a certain region. As an effective tool for measuring skin thickness, ultrasound lends utility to managing inflammatory dermatoses as well as skin atrophy with steroid therapy.[12]L. O.</author><author>Takiwaki, H.</author><author>Serup, J.</author></authors></contributors><auth-address>Bioengineering and Skin Research Laboratory, Department of Dermatology, Bispebjerg University Hospital, Copenhagen, Denmark.</auth-address><titles><title>High-frequency ultrasound characterization of normal skin. Skin thickness and echographic density of 22 anatomical sites</title><secondary-title>Skin Res Technol</secondary-title><alt-title>Skin research and technology : official journal of International Society for Bioengineering and the Skin (ISBS In the study by Iyengar et al., the two different probes with unique frequencies each recorded significantly different measurements. This highlights the importance of probe consistency when making comparative measurements.[13]

Skin thickness variation by age

Comparison between the two age groups found that epidermal entrance echo thickness and dermal thickness in the younger age group was higher than the older age group.[1] Epidermal entrance echo thickness decreased with age on the palm, cheek, and dorsum of the foot; however, it was only significantly higher in young adults on the dorsum of the foot. It remained constant on the neck and sole. Thickness of the dermis was statistically higher in young adults on the sole.[1]

Furthermore, Branchet et al. concluded that in both men and women, epidermal thickness decreased with age after analyzing the skin of 34 women and 30 men between 20 – 80 years of age. The study showed that skin thickness in men decreased 7.2% per decade whereas in women there was a 5.7% decrease per decade, with the results being more significant in the male group.[8] Other studies suggest that age related thinning of the skin is more prominent in women.[6,9] Thinning of the skin can begin as early as the third and fourth decade of life.[8,9] Shuster et al. found that skin thickness in females was shown to be constant until the age of 40, and then begins decreasing with age ($p<0.001$). In men, skin thickness progressively decreases with aging and at all ages, without a period of constant skin thickness ($<p<0.001$).[5]

Using 25MHz 2D ultrasound, images were obtained from 142 women with 10-20 subjects in each decade of life from 0-90 years old. De Rigal et al. showed that the skin on the volar forearm of women mostly thinned after the eighth decade ($p<0.05$), without showing significant variations between the first and seventh decade of life ($p<0.001$) [10]. Conversely, Escoffier et al. showed that subjects under 15 years old had thinner skin, and their skin thickness actually increased between 0 and 20-30 years of age ($p<0.013$) with no variation between 15-65 years of age. Skin thickness was significantly thinner in subjects after 65 years of age.[6] Slight differences in the findings between De Rigal et al. and Escoffier et al. could be associated to the use of 2D and A-mode devices respectively.

However, other studies found no significant difference between age groups when evaluating skin from the back of the arm. Using 25MHz ultrasound and confocal microscopy, dermal thickness on the back of the arm was measured in females (16 women 18-25 years old and 18 women 62-69 years old). The thickness of the living epidermis was lower in aged subjects; however, there was no significant difference between the young group (15 ± 3 um) and aged group (17 ± 3um).[14] Sauerman et al. also found no correlation between whole skin thickness and age with the use of confocal microscopy.[15] The disregard for anatomical site, which can alter results, may explain this lack of change seen in skin thickness with age. For example, depending on the anatomical site, some skin may thicken with age whereas some sites may thin.

The images from HUFS include the epidermal entrance echo, dermal layer, and echogenic subcutaneous tissue. The echogenicity of the epidermis is affected by the content of fat lobules in the subcutaneous tissue, and the keratin and collagen content in the dermis.[16] Some studies suggest that echogenicity increases with age[17] while others report echogenicity of the dermis decreases with age.[18-21] These differences in results might be explained by the changes that occur with aging such as decreased elasticity of the skin, which may affect dermal echogenicity as well as skin thickness.[22,23]

Conclusion

Epidermal and dermal thickness varies depending on many factors such as age, gender, and anatomical location. Although some studies noted a change in cutaneous thickness with age and others did not, the discrepancies may be explained by differences in the anatomical location from which the skin was measured. For example, perhaps the skin found on the forearm changes in thickness with age, but the skin on the back of the upper arm is not as affected. However, further studies with larger samples sizes are needed to better describe the effects that age, gender, location, and environmental factors have on skin thickness. These effects should then be considered during dermatologic procedures and wound management, as well as during the harvesting of skin grafts. Lastly, it has been noted that high frequency ultrasonography is an accurate tool for skin thickness measurements, density, and echogenicity of the dermis. In addition to the need for larger sample sizes and standardized conditions, the use of ultrasonography for skin measurements could be a beneficial tool for future research.

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Wilms' Tumor: A Clinical Review of Doxorubicin Use in Pediatric Postoperative Treatment

Douglas Chung[1], Rechna Korula[2], Shawn Hyunh[3], Jiemin Li[4], Ian Gallicano[2]

[1]Herbert Wertheim College of Medicine, Florida International University, Miami, FL, USA

[2]Georgetown University School of Medicine, Georgetown University, Washington, D.C., USA

[3]Georgetown University Graduate School of Arts and Sciences, Georgetown University, Washington, D.C., USA

[4]Medical College of Georgia, Augusta University, Augusta, Georgia, USA

Correspondence: Douglas Chung, dchun011@fiu.edu

Abstract

Background: Wilms' tumor (WT) is a pediatric nephroblastoma commonly affecting children in the first few years of life. Advances in treatment have increased five-year survival rates from 5% in the early 1900s to presently over 90%. Doxorubicin is a common chemotherapeutic agent used both preoperatively and postoperatively in the treatment of WT. Though it has benefitted patient survival, it is also a known cardiotoxin that may predispose WT survivors to heart failure in later life. The purpose of this work is to investigate the literature on the clinical use of doxorubicin in the pediatric treatment of WT.

Methods: Comprehensive literature review on pre- and post-operative anthracycline use in WT patients due to staging based on the two main research groups, the Children's Oncology Group (COG and the International Society of Pediatric Oncology (SIOP).

Results: Green et al[1] found cumulative dosage of doxorubicin exceeding 300 mg/m^2 in the chemotherapeutic regimen of WT pediatric patients to be the most significant variable in increasing the likelihood of developing congestive heart failure later on in life. Pritchard-Jones et al[2] investigated 583 patients diagnosed with WT between the ages of 6 months and 18 years, which found that doxorubicin had a negligible benefit in the 5 year survival rates of stage II-III intermediate risk WT patients.

Discussion/Conclusion: With WT's excellent prognosis, the focus of treatment has shifted from maintaining high five-year survival rates to mitigating the long-term effects of chemotherapy. Investigation of multiple studies suggest alternative anthracyclines and accurate staging of WT to prevent overtreatment since cumulative dosage has been directly correlated to risk of developing congestive heart failure.

Keywords: Wilms Tumor, Pediatric Nephroblastoma, Anthracycline

Introduction

Wilms' tumor (WT) is the most common renal malignancy of early childhood, affecting one out of every 8,000-10,000 children each year in North America, typically presenting as a unilateral tumor.[3] WT occurs via loss of function mutations of tumor suppressor genes WT1 or WT2 on chromosome 11.[4]

WT is typically categorized into different stages based on the severity of the nephroblastoma. Staging is of particular importance in WT management due to variance in recommended chemotherapy and associated side effects. WT is typically diagnosed using imaging tests such as ultrasounds and computed tomography (CAT) scans. Once the diagnosis is made, the WT is surgically removed and histologically staged, and further evaluated by the surgeon and pathologist to determine postoperative chemotherapy treatment.[5]

Currently, treatment for WT at intermediate-risk Stage II and beyond involves partial to complete nephrectomy and the administration of chemotherapy, which involves the use of doxorubicin, vincristine, and actinomycin D. Doxorubicin belongs to the anthracycline family of antitumor agents and is one of the most effective cancer treatments.[6] While use of doxorubicin in postoperative chemotherapy is extremely effective, shown by the high survival rate of WT patients, there are growing concerns over the cardiotoxic effects of long-term anthracycline use.[1] Based on several recent studies, it appears possible to mitigate doxorubicin's cardiotoxic effects for all stages and its potential for excessive use secondary to over staging in intermediate-risk Stage II WT children.

Etiology

While a single cause of WT has yet to be found, there are several chromosomal mutations that appear in patients diagnosed with this malignancy. Currently, the most common mutation found in 30% of patients is the inactivation of the tumor suppressor *FAM123B* gene, which is located on the X chromosome that includes the gene *WT1*. When the *WT1* gene is suppressed by the inactivation of *FAM123B*, embryologic metanephric blastema fail to differentiate, leading to

Staging Systems	Stage I Tumor	Stage II Tumor	Stage III Tumor	Stage IV Tumor	Stage V Tumor
COG	• Limited to kidney • No penetration of renal capsule • No involvement of renal sinus vessels • Not ruptured or biopsied before complete resection	• Extends beyond the capsule of the kidney • Completely resected • No evidence of tumor at or beyond the margins of resection • Penetration of the renal capsule or invasion of the renal sinus vessels is possible	• Gross or microscopic residual tumor remains postoperatively • Ruptured or biopsied before removal	• Hematogenous metastases or lymph node metastases outside the abdomen	• Bilateral renal involvement at diagnosis • Each side staged individually
SIOP	• Limited to kidney or surrounded with a fibrous pseudocapsule if outside the normal contours of the kidney • Renal capsule or pseudocapsule may be infiltrated but does not reach the outer surface, • Is completely resected • May protrude into the pelvic system and ureter • Vessels of the renal sinus not involved • Intrarenal vessels may be involved.	• Extends beyond the kidney or penetrates through renal capsule or fibrous pseudocapsule • Is completely resected • Infiltrates the renal sinus or invades blood and lymphatic vessels • Infiltrates adjacent organs or the vena cava • Surgically biopsied before preoperative chemotherapy or surgery	• Gross or microscopic tumor remains postoperatively • Abdominal lymph nodes involved • Tumor rupture before or during surgery (irrespective of other criteria for staging). • Tumor penetrates the peritoneal surface. • Tumor thrombi present at resection • margins of vessels or ureter transected and removed	• Hematogenous metastases or lymph node metastases outside the abdominopelvic region	• Bilateral renal tumors diagnosis • Each side substaged according to classifications

Table I: Comparing COG and SIOP staging for Wilms' Tumor. Since Wilms' Tumor (WT) staging determines its subsequent treatment, accurate description and analysis allows for optimal treatment. Because the Children's Oncology Group (COG) and the International Society of Pediatric Oncology (SIOP) recommend chemotherapy at different stages of treatment, their staging of WT will evaluate different histological samples. Different guidelines summarizing the definition of each stage are presented below.[6,9]

patches in the pediatric kidney that are believed to be the cause of the nephroblastoma.[7-8]

Due to the location of *FAM123B* on the X chromosome, there appears to be a slightly higher incidence of WT in girls than in boys.[9] Several other studies have also shown a higher incidence in Africans and African Americans, possibly because of higher rates of a separate nephrotic syndrome focal segmental glomerulosclerosis (FSGS) and HIV-1 infection in these populations, both of which are strongly associated with *WT1*.[10] Despite the varied genetic origins of the nephroblastoma, the survival rate of WT has increased to approximately 90%, compared with 5% in the 1900s.[6]

STAGING OF WILMS' TUMOR

Treatment for WT will depend on patient age, tumor pathology, treatment efficacy, and tumor stage. Staging refers to the classification of the tumor based on its extent and magnitude.[9]

The two main WT research groups, the Children's Oncology Group (COG) and the International Society of Pediatric Oncology (SIOP), suggest different staging methods. However, both COG and SIOP describe stage II tumors as those extending beyond the kidney capsule but still completely resected during surgery. COG staging does not indicate renal blood vessel involvement, whereas SIOP staging includes blood, lymphatic, and nearby organ invasion as long the tumor is completely removed. For SIOP criteria, stage II tumors are also biopsied prior to preoperative chemotherapy or surgery. Stage III tumors in both cases involve residual tumor following surgery, abdominal and pelvic lymph node metastases, tumor thrombi during surgical resection, and tumor rupture prior to or during surgery.[6]

Considering the importance of proper WT staging, Borgstein et al. investigated the relative agreement between surgical and pathological level staging of WT patients. This study found 84% majority agreement in the WT staging between the surgical stage and pathological stage assessment of the tumor, citing one of the difficulties of accurate WT staging occurring when histological tissue samples are collected during surgery. Occasionally, the sampled tissue does not encompass the area of greatest risk of rupture, which can lead to understaging of the tumor to stage II.[5]

General Treatments for Wilm's Tumor

In general, all the stages of WT are treated with nephrectomy (partial or radical) and chemotherapy. In terms of surgical procedure, radical nephrectomy remains the primary treatment for unilateral WT.[6,11] Here the surgeon removes the entire affected kidney, samples suspected lymph nodes, and evaluates for tumor metastases to determine accurate tumor stage.

In addition to surgery, chemotherapy may be used preoperatively or postoperatively, depending on COG or SIOP recommendations. The two most commonly administered are vincristine and actinomycin D. Depending on the tumor's severity and associated risks, such as in intermediate-risk stage II-III WT, doxorubicin may be included in treatment.[6]

Preoperative chemotherapy typically includes doxorubicin in addition to vincristine and actinomycin D.[6] The benefit of preoperative chemotherapy includes reduction of tumor size and its vascular supply, which may subsequently reduce the risk of surgical complications.[12]

Recommended postoperative chemotherapy regimens for WT include Regimen EE-4A (vincristine, actinomycin D for 18 weeks postnephrectomy) for lower stages of WT and Regimen DD-4A (vincristine, actinomycin D, doxorubicin for 24 weeks with baseline nephrectomy or biopsy with subsequent nephrectomy) for higher stages of WT.[6] The key distinction between the two regimens is the inclusion of doxorubicin.

Dosage dependence of Doxorubicin

Doxorubicin has been an important antineoplastic used in the treatment of more aggressive stages of WT for the last three decades, despite its long-term cardiotoxic effects. Studies since the early 1990s have shown the cardiotoxic nature of anthracyclines, which includes doxorubicin.[13] However, the efficacy of anthracyclines in increasing pediatric survival rates was thought to outweigh its adverse effects. In 2001, Green et al[1] looked into the development of congestive heart failure (CHF) as a consequence of the long-term cardiotoxic effect found in patients with WT treated with doxorubicin. Although there is a high survival rate of WT using doxorubicin, a significant cardiotoxic risk occurs at higher doses.[1]

In the study there were two cohorts: Cohort 1 comprised of patients who received doxorubicin as part of their initial treatment plan for WT; Cohort 2 comprised of patients who were not given doxorubicin in their initial therapy, but were treated with a higher cumulative dose of doxorubicin compared to Cohort 1 after a relapse of WT. Patients were monitored for up to twenty years from diagnosis of WT to development of CHF.

Relative risk (RR) analysis revealed that the incidence of developing CHF in Cohort 1 was 4.4% and 17.4% in Cohort 2. The study analyzed several characteristics of the thirty-five patients that developed CHF of the 2,710 monitored patients. Females were four and a half times more likely to develop CHF as males; patients receiving lung radiation and left abdominal radiation had a two-fold increase in RR of CHF compared to those treated without radiotherapy.

However, the study states that "cumulative doxorubicin dose was the most important risk factor for the occurrence of CHF".[1] Patients receiving a cumulative dose of ≥300 mg/m^2 doxorubicin showed a six-fold increase in RR. Interestingly, those receiving a cumulative dose of 1-199 mg/m^2 saw no increase RR and those receiving 200-299 mg/m^2 of cumulative doxorubicin were only 50% more susceptible to CHF.

Finally, the study found that RR increased three-fold for every 100 mg/m^2 of doxorubicin given to patients who also had radiation therapy.[1]

The higher RR seen in Cohort 2 can be attributed to the increased amount of lung radiation and higher dose of doxorubicin used in conjunction to combat a relapsed WT. Gender and radiation both affect the RR of WT, but overall using ≥ 300 mg/m^2 doxorubicin was the most significant variable in increasing the likelihood of developing CHF. Because the median dose of doxorubicin given to patients in the study was 302 mg/m^2, at least half the patients received a dose of doxorubicin above the threshold of greatest RR.[1]

Overuse of Doxorubicin

A large study by Dr. Pritchard-Jones was conducted on behalf of the SIOP Renal Tumors Study Group. This study found that doxorubicin offered no significant difference in 2-year and 5-year survival rates of intermediate-risk stage II-III WT patients, bringing into question the chemotherapeutic value of doxorubicin and whether its benefit on short-term survival outweighs its known long-term risks of cardiotoxicity.

In this study 583 patients had been diagnosed with WT between the ages of 6 months and 18 years, ascertained from 251 hospitals in 26 countries, following these children carefully to investigate the "effects of placebo controlled omission of doxorubicin from their postoperative chemotherapy".[2] Doxorubicin had negligible benefit in the 5-year survival rates of stage II-III intermediate risk WT patients when "histological assessment of tumour response is positively received during in preoperative chemotherapy".[2]

Doxorubicin was the only omitted chemotherapeutic agent from the standard regimen of doxorubicin, actinomycin D, and vincristine. All patients received the same timing and quantity of dosage of actinomycin D and vincristine with a median study follow-up of 60.8 months. Of the 291 children receiving treatment including doxorubicin, there were 24 cases of tumor relapse. From the group of 292 children receiving treatment without doxorubicin, there were

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36 incidents of tumor relapse, suggesting that the difference in number of tumor relapses between the two groups is statistically insignificant.[2]

Alternative Anthracyclines

Doxorubicin and daunorubicin are the two most commonly used anthracyclines in cancer treatment. Past studies have not extensively compared their cardiotoxicities.[13] Feijen et al[14] evaluated data from four cohorts with approximately 16,000 childhood cancer survivors. Patients were followed for an average of twenty years – with an upper limit at forty years of age for follow up. Of the 271 recorded diagnoses of heart failure (HF) seen in the study, more than two-thirds of patients were treated with only doxorubicin, and less than 10% were treated with only daunorubicin. The median dose for treatment of doxorubicin was approximately twice as high as for daunorubicin. The two anthracyclines were compared at an equivalence ratio of 1:1 per each mg/m^2 and a bootstrap method with 1000 replications was used to determine the hazard ratio (HR) of daunorubicin to doxorubicin.

Primary analysis of the data was restricted to those patients treated with either daunorubicin or doxorubicin. Only patients with a minimum survival of five years from diagnosis of cancer were included. Of all these patients, the cumulative incidence of HF was 3.2% by the age of forty, and the primary model determined that the HF risk of daunorubicin to doxorubicin with all stipulations factored was 0.45. Therefore, it was concluded that daunorubicin was less cardiotoxic than doxorubicin.[14]

Discussion

As WT prognosis continues to improve, the focus of treatment has shifted from maintaining high five-year survival rates to mitigating the long-term effects of chemotherapy.

Ultimately, the cumulative dosage of doxorubicin ≥300 mg/m^2 leads to a six-fold increase in the relative risk of developing heart failure later on in life. Borgstein et al[5] found small discrepancies between surgical and pathological staging that could offer a reduction in doxorubicin exposure. Additionally, Pritchard-Jones et al[2] found that with accurate staging, doxorubicin's established risk of cardiotoxicity could be avoided in intermediate-risk stage II-III WT patients. This raises the interesting question of whether daunorubicin, as proposed by Feijen et al[14], could be used instead as an alternative to doxorubicin in WT treatment.

These studies show that in specific cases of intermediate-risk stage II-III WT, doxorubicin may not provide sufficient benefit to warrant its associated risks. Minimizing the cumulative dosage of doxorubicin in postoperative treatment can lead to a better quality of life for childhood WT survivors by decreasing their relative risk for developing heart failure as young to middle-aged adults.

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French Huguenots in the medical development of sixteenth century Spanish St. Augustine, Florida

John D. Ehrhardt Jr. and J. Patrick O'Leary, M.D., F.A.C.S.

Herbert Wertheim College of Medicine, Florida International University, Miami, Florida, USA

Corresponding author: John D. Ehrhardt Jr.; jehrh002@med.fiu.edu

Abstract

In 1564, French colonists led by René Laudonnière erected Fort Caroline, a riverside settlement in Timucua tribe territory near modern-day Jacksonville. French-Timucuan relations in northeast Florida undoubtedly served as a foundation for the Spanish who conquered in 1565 and controlled the region from their nearby fort at St. Augustine. French Huguenots lived with native Timucua at Fort Caroline through disease, famine, hostility, and supply shortages. Challenging times introduced French settlers to novel Timucua treatments, a catalyst for colonial medical progress. After the Spanish destroyed Fort Caroline, French surgeons cared for Spaniards and Timucua alike at St. Augustine. French collaboration with Timucuan healers and later surgical support at the Spanish fort influenced the formation and persistence of St. Augustine, today the oldest city in the continental United States.

Keywords: Huguenots; Fort Caroline; St. Augustine; Timucuan medicine; colonial medicine

Historical Background

Spanish forces led by Pedro Menéndez de Avilés established a colony at St. Augustine in 1565 that predated the famous British settlements at Jamestown, Virginia in 1607 and Plymouth, Massachusetts in 1620. Menéndez de Avilés' became Florida's founding colonial governor after forty years of conquistador voyages sponsored by the Spanish crown. From 1513 to 1559, the militia of Ponce de Léon, Narváez, De Soto, Cáncer, and De Luna confronted Florida natives in an effort to expand the Spanish empire.[1-5] Conquistador caravans marched the peninsula in search of resources. Some brigades adhered closely to the coast, others trudged through interior wetlands, but all retreated without planting a viable colony.

Many conquistador voyages to Florida were riddled with sequelae from trauma and infectious disease. In 1521, Ponce de Léon's second voyage drew to an abrupt close shortly after landfall in southwest Florida when he suffered a shot in the groin from a native Calusa arrow. The voyage "mediciner," who likely learned the craft by assisting a Caribbean surgeon and held no certification from the royal medical licensing *protomedicato*[6], rose to Ponce de Léon's side to operate on the lodged arrow. With successful hemorrhage control and foreign body removal, their leader survived the first surgical operation in the history of Florida.[7] His fleet retreated to Cuba where complications from sepsis killed Ponce de Léon three days after their arrival to Havana. Similarly, Hernando De Soto's grueling three-year expedition came to a grinding halt in 1542 when he contracted a debilitating fever in the remote western reaches of the Florida territory.[8] He died soon thereafter with Florida remaining a wild, unclaimed frontier. The deaths of Ponce de Léon and Hernando De Soto highlighted limitations that prevented early Spanish efforts at Florida colonization.

Frequent food and medical supply shortages also hastened the deterioration of Spanish militia in precolonial Florida. Without adequate food or potable water, health dwindled and fevers became endemic among Hernando De Soto's men. At one point during their trek, De Soto's men fled from the natives into the Gulf of Mexico. His soldiers ate their horses as a last ditch effort to provide them the nutrition and strength to escape alive. Conquistador expeditions often lasted for several years on uncharted land, adding a dimension of logistic complexity that afforded few opportunities for supply reinforcements. Native tribes understood that medical supplies were scarce, crucial for survival, and conspired on several occasions to burn Spanish surgical supplies in retaliation for conquistador brutality.[9]

Conquistador fleets often explored the interior of Florida with few surgeons and no nursing personnel.[10] One extant narrative from the De Soto expedition noted, "There was not in the whole army more than one doctor, and he was not so skillful and diligent as was needed; on the contrary, he was stupid and practically useless."[11] Later, the expedition scribe described a surgeon who the soldiers distrusted. In reference to one soldier's experience with the expedition surgeon, he became, "…Enraged at the clumsiness of that gentleman's hands, [and] most insultingly told him that even though he knew himself to be dying, he would never call upon [the surgeon] again."[11] When medical attention was nowhere to be found, some Spanish soldiers entrusted native women with combat wound care. After one battle during the De Soto expedition, Spaniards "took the women and divided them among the most seriously wounded, in order that they [the women] might nurse them [Spanish soldiers]."[12] It remains unclear if the conquistadors enslaved, employed, or exchanged goods for nursing services from the native women.

FLORIDA MEDICAL HISTORY REVIEW

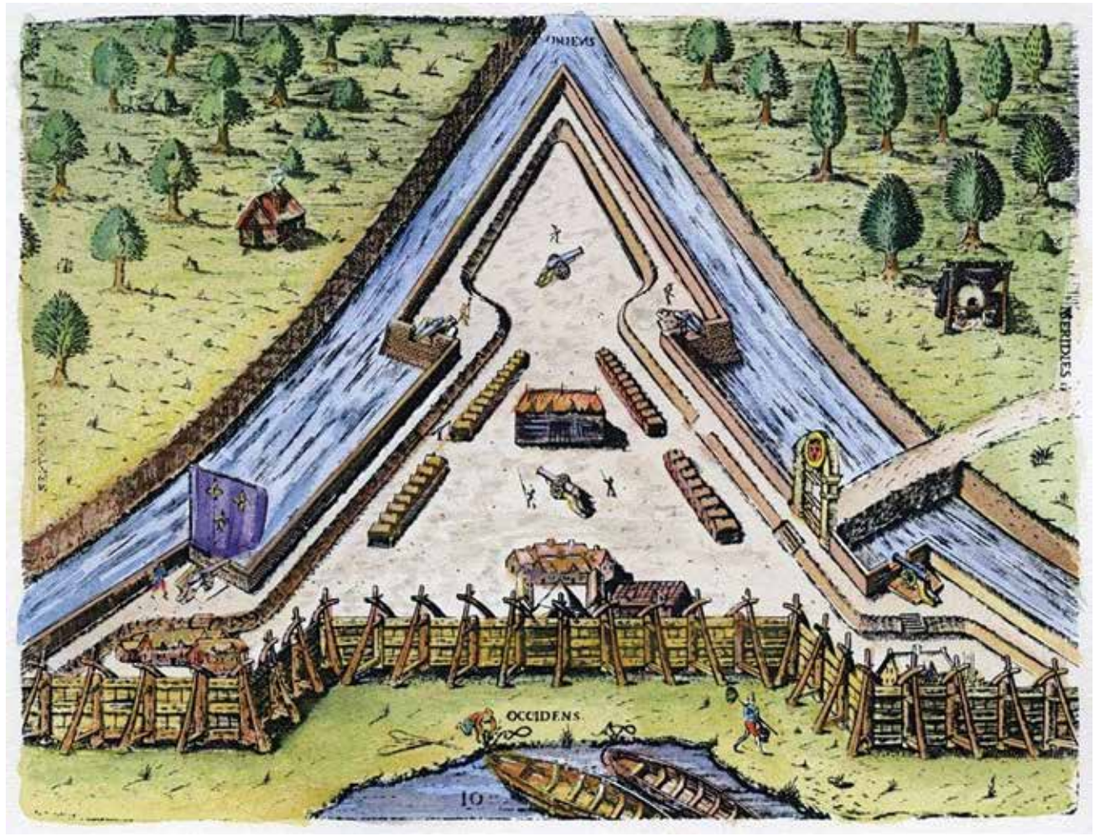


Figure 1: Fort Caroline, Le Floride.[19]

Firsthand accounts of trauma, contagious disease, starvation, and lackluster medical care trickled back to the Spanish crown. In 1561, King Philip II of Spain decided that settling Florida was no longer worthwhile and suspended all plans for future conquistador expeditions.[13] Spain temporarily abandoned Florida, yet remained active in the New World with successful missions flourishing across the Caribbean, Central America, and South America.

Without Spanish occupation, other Europeans began to express imperial interest in the Florida peninsula. In June 1564, French fleets made remarkable colonial progress along the unsettled northeastern coast of Florida under the guidance of René Laudonnière. His voyage led a French Protestant group collectively known as Huguenots in constructing and populating a fort near the mouth of a river many historians place at the St. John's River near modern-day Jacksonville. They christened the settlement as Fort Caroline (Figure 1), making the first fortified European settlement in the continental United States a French entity.[14]

French-Timucuan Medical Exchange at Fort Caroline

Fort Caroline blossomed as the French forged amicable relationships with the native Timucua tribe. The French were far less military-centric than Spanish conquistadors and satisfied with living free of religious persecution in Florida. French colonists did not strive to conquer the entire peninsula, nor did they take efforts to enslave and religiously convert natives. The friendly disposition of the French earned them access to native food supplies.

Timucua healers went to great lengths to instruct the Huguenots at Fort Caroline on methods for using local plants to make medicinal treatments for their ill settlers. One of the most important herbal medications introduced to the French was derived from the sassafras plant (Figure 2). The natives taught the French to take sassafras roots and brew medicinal teas. They used sassafras for nearly every ailment, believing in its ability to renew a person's strength and help them overcome periods of illness. Fevers and dysentery weakened European settlers in the New World, leaving

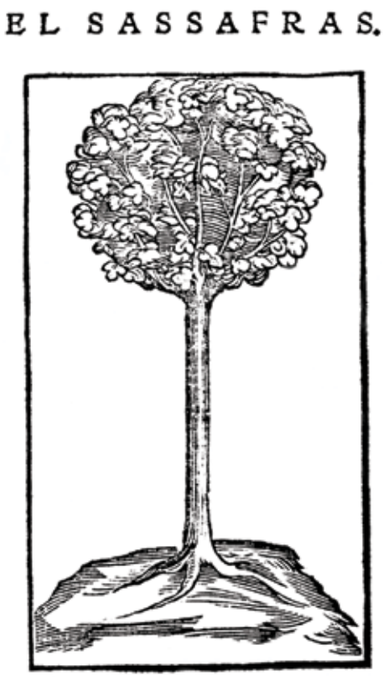


Figure 2: Sassafras plant, drawn by Spanish physician Nicolás Monardes.[20]

them without an appetite and vulnerable to further disease. Sassafras administered as a tea seemed to stimulate their appetite and ultimately restore vitality. The act of brewing sassafras roots also killed most of the microbes in the water supply, thereby reducing the risk of water-borne illnesses. Enamored by the wondrous drug, colonists at Fort Caroline shipped several loads of sassafras roots back to France. As time went on, sassafras gained popularity in both the New World and across Europe.[15]

While sassafras became the paramount plant for treating illnesses, the Timucua shared another tea known as *casina* that gained popularity among French settlers as a medicinal supplement for daily consumption.[16] The potent, highly caffeinated "black drink" had the power to suppress the appetite and fortify the constitution of those who drank it. The *casina* elixir enabled settlers to continue laboring, scavenging, and skip meals when food became scarce. Without these Timucuan medications, illness and starvation might have led the French to abandon Fort Caroline.

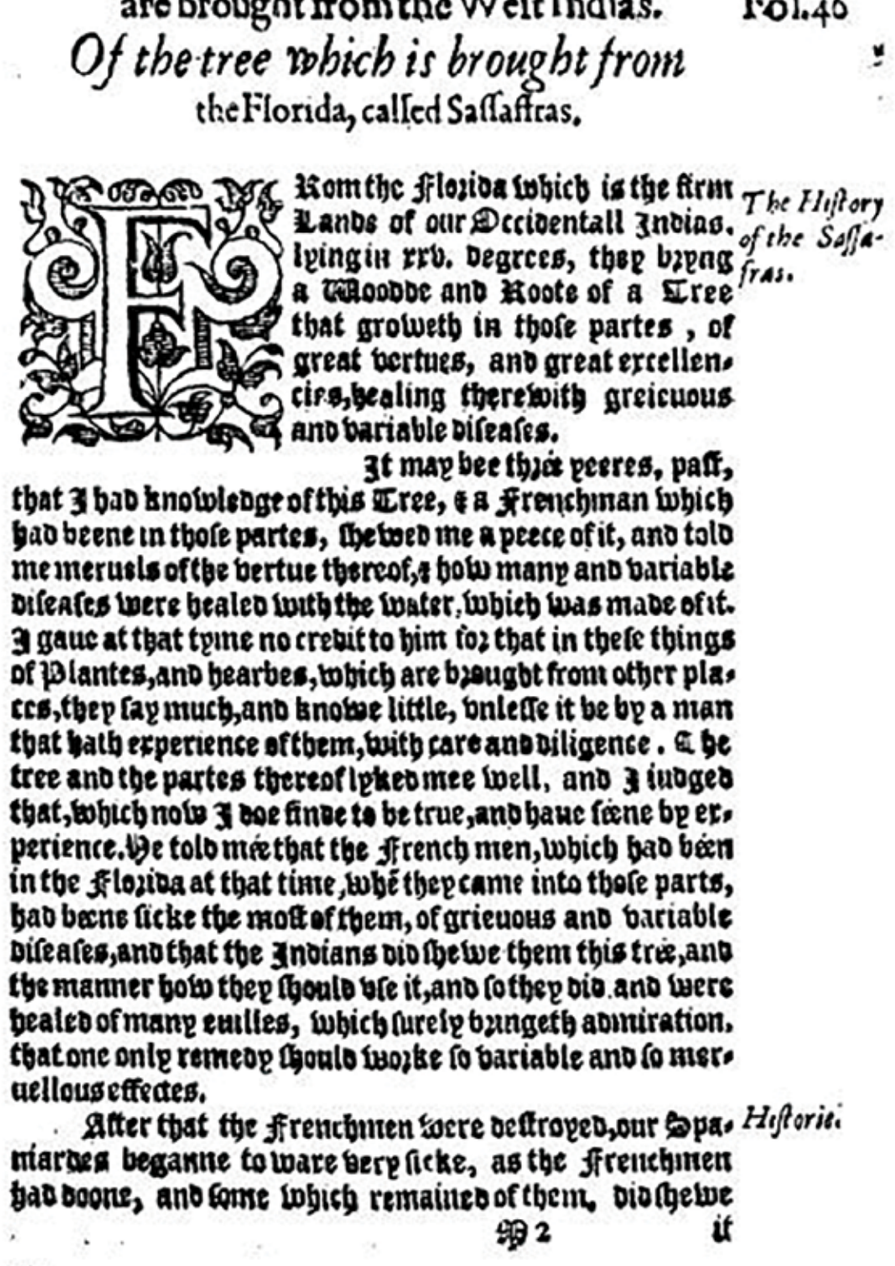
In addition to the new medications acquired at Fort Caroline, the French brought an essential member of the healthcare team that the Spanish conquistadors before them did not emphasize. Captain Laudonnière brought a handmaid who served as a nurse in Florida. He mentioned in his journals she was, "a nurse for the soldiers in their sickness as well as my own sickness." He discussed her instrumental role in life at Fort Caroline where she was "esteemed by each of the men" for her nursing. In little more than one year, the French created a settlement that integrated a European surgeon and nurse with Timucuan health beliefs and practices.[17-18]

Huguenot survival and integration with the Timucua gained attention from the Spanish and swayed them to reconsider their laissez-faire stance on Florida the following year. On August 28, 1565, the feast day for St. Augustine of Hippo, a fleet of Spanish galleon directed by Pedro Menéndez de Avilés approached the Florida coast and made plans for invasion. Their raid on Fort Caroline resulted in French massacre, sparing only a few Huguenots who remained in custody of Spanish militia. The surviving French played an essential role in relaying information to the Spanish regarding nutrition, medicinal plants, treatment methods, and health rituals they learned from the Timucua at Fort Caroline.[19]

Following Menéndez de Avilés' massacre at Fort Caroline, the remaining French became medical liaisons who enlightened the Spanish militia at St. Augustine with their knowledge of local pharmaceutical plants and health rituals. A noteworthy 1565 medical tome published in Spain alluded to the French influence on medicine in St. Augustine. Spanish physician Nicolás Monardes wrote a monograph entitled *Historia medicinal de las cosas que se traen de nuestras Indias Occidentales* (Medical study of the products imported from our West Indian possessions) that became famous as the first comprehensive book about medicines from the New World (Figure 3). Within his work, a twenty-page discussion on sassafras revealed, "a Frenchman which had been in those parts [Florida], showed me a piece of it, and told me of its virtue thereof." He went on to say that "After the Frenchmen were destroyed, our Spaniards began to ware very sick, as the Frenchmen had been, and some of which [French] remained, did show it [sassafras] to our Spaniards, and how they had cured themselves with the water of this marvelous tree… Our Spaniards began to cure themselves with the water of this tree, and it wrought in them great effects that are almost incredible." Given the imperial rivalry between the Spanish and French, it was remarkable for a Spanish physician to credit the French with passing New World medical wisdom of Frenchmen during this period.[20]

A similar series of events transpired for the utilization of "black drink" in St. Augustine. Throughout Florida's colonial period, there were continual references to the habitual use of *casina* as a health supplement. A 1595 report from Florida noted that the Spaniards drank *casina* every day. A later account commented with satire that the only local products used by Spanish families in Florida were corn and *casina*. The Spanish revered the potent tea to the extent that they sent two native Florida Timucua back to Spain to cure the Canon of Seville of urinary tract disease, likely secondary to ureteral and bladder stones, with the diuretic *casina*.[21]

FLORIDA MEDICAL HISTORY REVIEW



are brought from the West Indias. Fol.46

Of the tree which is brought from the Florida, called Sassafras.

FRom the Florida which is the firm Lands of our Occidentall Indias, lying in xxv. degrees, they bryng a Woodde and Roote of a Tree that groweth in those partes, of great vertues, and great excellencies, healing therewith greicuous and variable diseases. *The History of the Sassafras.*

It may bee thyrty yeeres, passt, that I had knowledge of this Tree, & a Frenchman which had beene in those partes, shewed me a peece of it, and told me merueils of the vertue thereof, & how many and variable diseases were healed with the water, which was made of it. I gaue at that tyme no credit to him for that in these things of Plantes, and hearbes, which are brought from other places, they say much, and knowe little, vnlesse it be by a man that hath experience of them, with care and diligence. The tree and the partes thereof lyked mee well, and I iudged that, which now I doe finde to be true, and haue seene by experience. He told mée that the French men, which had béen in the Florida at that time, whē they came into those parts, had beene sicke the most of them, of grieuous and variable diseases, and that the Indians did shewe them this trée, and the manner how they should vse it, and so they did, and were healed of many euilles, which surely bringeth admiration, that one only remedy should worke so variable and so merueilous effectes.

After that the Frenchmen were destroyed, our Spa- *Historia.*
niardes beganne to ware very sicke, as the Frenchmen had doone, and some which remained of them, did shewe

Figure 3: Folio within Nicolás Monardes' 1565 monograph referencing the French acquisition of sassafras at Fort Caroline.[20]

French Surgeons in Early St. Augustine

Medications were not the only French marks on medicine in sixteenth century St. Augustine. Spanish authorities took the liberty to import French surgeons to their fledgling military town. Spanish ship surgeons passed through St. Augustine, but their presence was often transient and short-lived. No salary or benefits package was large enough to keep a Spanish doctor stationed in the rural, dirt road, tidal marshland of St. Augustine. Spaniards addressed their doctor shortage in part by capturing French doctors and holding them as prisoners who then provided healthcare for the community.[22]

After the demise of Fort Caroline, the French continued efforts to become stakeholders once again along the Atlantic coast of the Florida territory. By the 1570s, the coast became peppered with Spanish and native outposts, but French ships spied upon unclaimed land in coastal estuaries where they could settle and rebuild. One severe storm in the winter of 1576 blew a French ship named *Le Prince* ashore near Santa Elena, a Spanish post in modern-day South Carolina. Natives killed many of their crew and enslaved those who remained. Forty prisoners from the shipwreck lived and worked for the local tribe. In August of 1579, Florida governor Menéndez Marqués commanded an army that raided their village. Spanish forces kidnapped the native chieftain's mother, wife, and sister and later released them in exchange for sixteen French prisoners. Spanish authorities charged the French with piracy in Florida waters and proceeded to execute most of them. Menéndez Marqués commanded they spare a handful of the prisoners: one *cirujano* and three boys who could interpret the native language.[23]

The French surgeon among their group of prisoners was Jean de Le Compte (named in Spanish letters at Juan de Leconte). Spanish authorities sent him to their post at Santa Elena for a brief period until they realized his extensive medical knowledge would be invaluable further south at St. Augustine. Upon Le Compte's arrival in late 1579, he continued his prison sentence for a grueling seven-year period during which he met the medical needs of Spanish and Timucua throughout the community. His good deeds awarded him a job as chief surgeon at the military fort in 1586, a position that came with a salary of four ducats monthly. Because St. Augustine began as a military town, the natural majority of his patients were soldiers at the fort. Over the course of his tenure as their surgeon leader, the colony grew and expanded his clinical responsibilities to a diverse spectrum of patients.[24]

Le Compte was the only permanent medical figure in Florida for over two decades. After twenty-three years' service, he declared that he was "old and tired and cannot support himself with the four ducats." He requested a return trip to Europe if the royal authorities were unwilling to negotiate a higher salary. Spanish authorities declined his highball request for a ten-fold salary increase to forty ducats. Florida Governor Gonzalo Méndez de Canço urged him to draft a formal address to the King of Spain regarding his salary and benefits as the only resident doctor of the colony. As a testament of his faith and reliance upon his colony's only physician, Governor Méndez de Canço affixed a letter of recommendation to the surgeon's appeal for a higher salary. The monarch returned the twenty-ducat request with an offer for ten ducats, still two-and-a-half times Le Compte's original salary.

Le Compte's work in St. Augustine represented a great deal of irony. The Spanish were not allies with France, but they were unable to recruit a competent doctor to their new Florida colony. It speaks volumes that Spanish authorities needed to capture a surgeon and hold him as prisoner in order to keep a resident doctor in St. Augustine. He did not practice medicine exclusively alone, but his support system of assistant surgeons and apothecaries were not as skilled. In an August 1583 letter Governor Menéndez Marqués wrote to the Crown, he mentioned Le Compte as the Frenchman who is "a surgeon, of which there are none Spanish in this land who are worth anything." Not only was their medical competence questionable, but they came and went with each new breeze that brought ships through the mouth of the Matanzas River. The King wanted French prisoners like Le Compte sent to Spain, presumably for trial, but Governor Menéndez Marqués would not relinquish Florida's only doctor. He believed that if Le Compte left St. Augustine, "he would be very much missed, and so I determined this time to leave him here."[25]

Three other unnamed French surgeons appeared in letters during the latter half of the sixteenth century, demonstrating St. Augustine's reliance on their training to meet their town's healthcare needs as well as the demands of Spanish medical regulations that called for the provision of a surgeon at each Spanish military fort.

Conclusion

St. Augustine's resilience through numerous fever epidemics and periods of famine speaks volumes of their community's ability to overcome forces of disease with limited resources. Although the Spanish Empire oversaw an unparalleled system of regulated healthcare in their Caribbean settlements, delivering care on Florida's peninsula presented unique challenges. The development of sustainable healthcare hinged on the difficult order of having medications available and recruiting surgeons to the nascent coastal colony. Shipments of medications and surgeons were unpredictable, forcing the Spanish to rely on native remedies passed along through the few French Huguenots who remained after the Fort Caroline massacre. During their short occupation of northeast Florida, they endeavored to understand Timucuan methods for medicine and healing, which included novel sassafras and casina medicinal teas, as well guiding them towards many other medicaments already introduced to Europeans elsewhere in the New World. To remedy the doctor shortage, a few French surgeons were held as prisoners during the early days of St. Augustine, notably Jean de Le Compte who garnered respect as the only competent doctor in the colony during the last two decades of the sixteenth century. Huguenot-Timucua medical exchange as well as the service of French surgeons contributed to the health and success of St. Augustine in becoming the oldest city in the continental United States.

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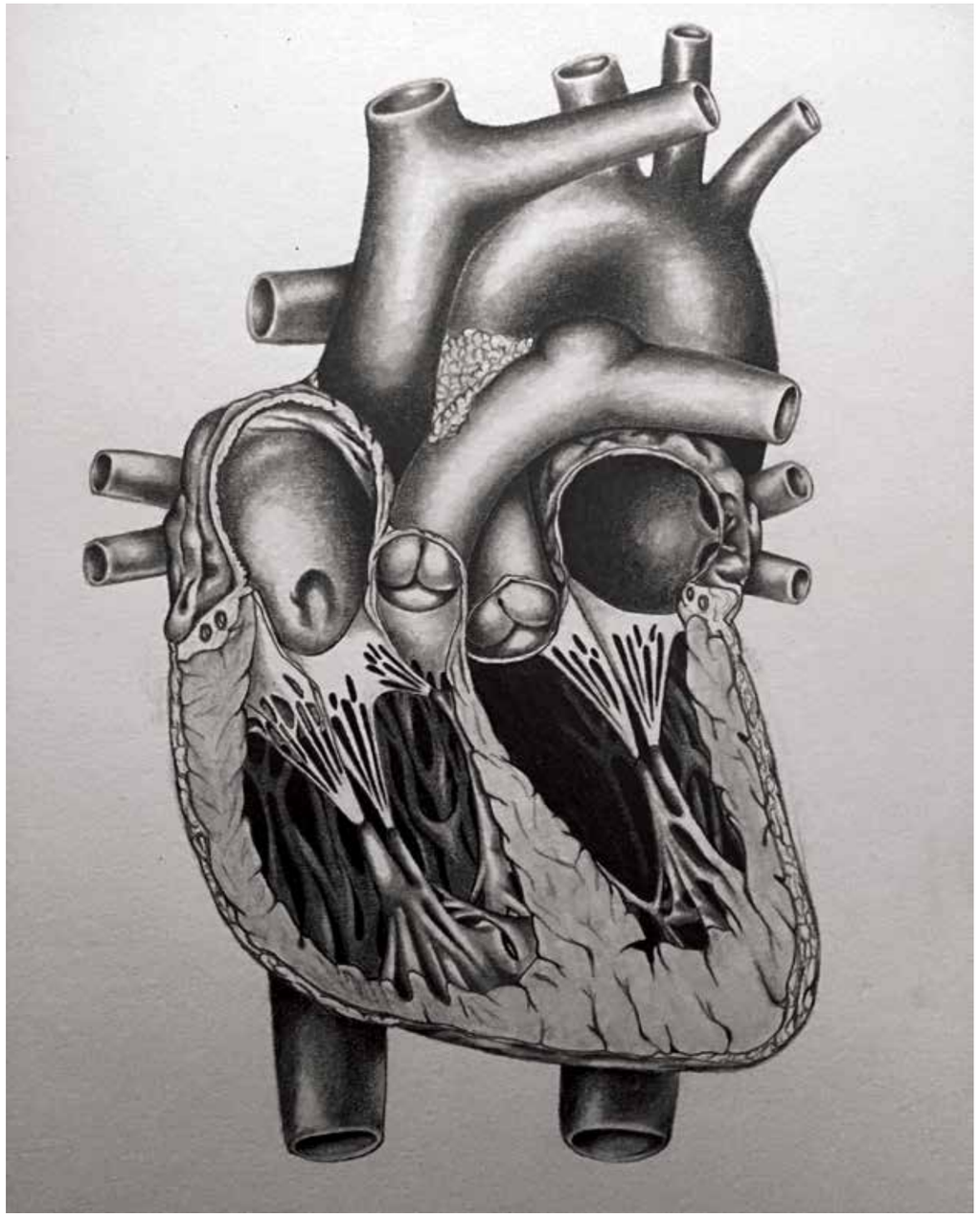

"Heart No. 1" by Emily Geisler
M.D. Candidate, Class of 2020
Florida International University
Cross published in *Eloquor*, 2016

Proceedings of the 2019 FIU Herbert Wertheim College of Medicine Research Symposium & Awards Ceremony

Friday, April 26, 2019 Student Academic Success Center

TIME	EVENT	LOCATION
7:30 - 8:30 a.m.	**Registration Opens**	**SASC 100**
8:30 - 8:45 a.m.	**Welcome Remarks** Robert Sackstein, M.D., Ph.D. *Dean and Senior Vice President for Health Affairs*	**SASC 160**
8:45 - 10:15 a.m.	**Oral Presentations I**	**SASC 160**
10:30 a.m. - 12:00 p.m.	**Oral Presentations II**	**SASC 160**
12:00 - 1:30 p.m.	**Open Poster Session** (Lunch Served)	**SASC 100**
1:30 - 3:00 p.m.	**Oral Presentations III**	**SASC 160**
3:00 - 3:15 p.m.	**Break**	
3:15 - 4:00 p.m.	**AOA Speaker** Robert Sackstein, M.D., Ph.D. *Dean and Senior Vice President for Health Affairs*	**SASC 160**
4:00 - 4:15 p.m.	**Break**	
4:00 - 5:00 p.m.	**Awards Ceremony**	**SASC 160**

ROBERT SACKSTEIN, M.D., Ph.D.

Robert Sackstein, M.D., Ph.D., is Dean of the Herbert Wertheim College of Medicine and Senior Vice-President for Health Affairs at Florida International University. He is a Professor Emeritus at the Harvard Medical School, where he continues to serve as the Director of the Harvard Career Development Program in Translational Glycobiology. Dr. Sackstein's clinical expertise is bone marrow transplantation, and he is a widely recognized for his contributions to cell-based therapeutics. His scientific research efforts have defined the molecular processes that regulate the movement of cells in blood flow into different tissues throughout the body, and clinical applications of his research findings have led to improved outcomes for patients undergoing bone marrow transplantation, and for patients suffering from a variety of illnesses including cancer, autoimmune conditions, and osteoporosis.

Dr. Sackstein was born in Cuba and immigrated to Miami with his family in 1960. He attended Dade County public schools, and received his undergraduate degree in Biology from Harvard College, Summa cum Laude. Dr. Sackstein then obtained both his M.D. and Ph.D. degrees from the Harvard Medical School, where, upon graduation, he received the James Tolbert Shipley Prize for outstanding research. Dr. Sackstein was bestowed the Young Investigator Award from the International Society of Experimental Hematology for his pioneering work in identifying how blood-forming stem cells enter the bone marrow, the critical first hurdle in the success of bone marrow transplantation. These efforts placed him at the forefront of the field known as of "translational glycobiology" and he is widely recognized for inventing a platform glycoengineering technology (known as "GPS") that pilots the movement of blood-borne cells to sites of tissue injury. Based on his contributions to medicine and to medical science, Dr. Sackstein was elected as a member of the prestigious Association of American Physicians for his "pursuit of medical knowledge, and the advancement through experimentation and discovery of basic and clinical science and their application to clinical medicine". Recently, he was awarded an honorary doctorate from the University of Murcia (Spain) for "improving the efficacy and safety of cell-based therapies, thereby enabling curative-intent treatments for a wide range of disabling and life-threatening diseases."

A VERY SPECIAL THANK YOU

On behalf of the directors and participants of the Fifth Annual FIU Herbert Wertheim College of Medicine Research Symposium and the Department of Medical and Population Health Sciences Research, we would like to extend a warm thank you to the amazing judges and reviewers who have worked tirelessly to support and recognize FIU research. We are tremendously appreciative of their selfless involvement in this process and are particularly grateful for their help in continuing and improving the Second Annual Research Symposium Awards.

This symposium would not have been possible if it were not for their generosity with their time and expertise. They completed more than 240 abstract reviews and were tasked with judging the quality of more than 70 final presentations. Because of their efforts and support, this year's symposium has proven to be the most successful to date.

Working together, we are preparing students for their future careers and driving FIU research to new heights. We hope that their generosity will inspire others to follow in their footsteps and volunteer their time and effort to support our FIU student researchers and the Herbert Wertheim College of Medicine community at large. Please join us once again in thanking these incredible women and men.

Oral Presentations I

Friday, April 26, 2019
8:45 a.m. – 10:15 a.m. | SASC 160

AUTHORS	TITLE	FIELD	ABSTRACT ID
Kenneth Chang, Hyunseo Jung, Kihyun Kwon	Race and prevalence of end-stage renal disease among U.S. type 2 diabetic patients with renal manifestations	Health Disparities	O1
Farouk Farouk, Zaid Sheikh, Omar Viqar	The association between race and survival among pediatric patients with neuroblastoma in the US between 1973 and 2015	Health Disparities	O2
Rahil H. Shah, Pooja Gurnani, Elan Baskir	Prescriptions of potentially inappropriate medications in older adults in the US: Results from the NAMCS 2013-2014	Health Disparities	O3
Christina Carr, Schuyler Hodge, David Liepa	Association between prepregnancy BMI and breastfeeding outcomes: Effect modification by household income level and race/ethnicity	Health Disparities	O4
Thomas Cowan, Pamela Duarte, Franklin Zheng	Lost in translation: The effect of interpreter use on colorectal cancer screening in North Miami-Dade	Health Services Research	O5

Oral Presentations II

Friday, April 26, 2019
10:30 a.m. – 12:00 p.m. | SASC 160

AUTHORS	TITLE	FIELD	ABSTRACT ID
Naiya Patel, Moneba Anees, Reema Kola	Association between knowledge of zika transmission and preventative measures among Latinas of childbearing age in farm working communities in South Florida	Infectious Disease	O6
Thomas Weppelmann, Marcelo Farias, Zakaria Abdulla	Seroepidemiology of Burkholderia pseudomallei, etiologic agent of melioidosis, in the Ouest and Sud-Est Departments of Haiti	Infectious Disease	O7
Matthew Alfonso, Zachary Pryor	Maternal education level and human papillomavirus (HPV) vaccination series initiation in adolescent females	Infectious Disease	O8
Jonathan Dahan, Calvin Strehl, Sonia Majid	Exploratory study of the association between selected demographic and socioeconomic factors and influenza vaccine uptake in U.S. adults	Infectious Disease	O9
Leah Cohen, Elnara Muradova, Nikhil Khushalani	Pseudo-progression of merkel cell carcinoma after avelumab therapy	Dermatology	O10
Oren Cohen, Laura Valente	Race/ethnicity and the primary anatomical location of cutaneous melanoma in Florida patients	Dermatology	O11

Oral Presentations III

Friday, April 26, 2019
1:30 p.m. – 3:00 p.m. | SASC 160

AUTHORS	TITLE	FIELD	ABSTRACT ID
Alejandra Figueroa, Ryan Bricknel, Cristobal Ducaud,	The association between e-cigarette use and stroke	Neurology	O12
Keneil Brown, Ottavia Green	The association between heavy alcohol consumption and morbidity and mortality in ischemic stroke patients: Does t-PA administration modify this association?	Neurology	O13
Nikita Bodoukhin, Benjamin Hellman	Male urinary incontinence and depression: A longitudinal analysis	Mental Health	O14
Ha Tran, Natalia Shringarpure, Natalie Ceballos	Impact of high BMI on outcomes of laparoscopic hysterectomy	Obstetrics & Gynecology	O15
Alixandra Garic, Tamlyn Hall, Eric Tano	Breastfeeding duration and its association with acute care visits for illness at age 6	Pediatrics	O16
Antoun Bouz, Gene K. Lee, David P. Perrault, Austin J. Pourmoussa, Roy Yu, Daniel Gardner, Maxwell Johnson, Sun Young Park, Athanasiois Bramos, Eun Kyung Park, Young Jin N. Seong, Sunju Lee, Lia E. Jung, Dongwon Choi, Young-Kwon Hong, Alex K. Wong	Continuous 9-Cis retinoic acid treatment improves lymphatic clearance and prevents secondary lymphedema	Basic Science	O17

Poster Presentations

Friday, April 26, 2019
12:00 p.m. – 1:30 p.m. | SASC 100

AUTHORS	TITLE	FIELD	ABSTRACT ID
Caroline Finn, Kai McKinstry	IL-21 is a necessary component for optimal heterosubtypic immunity against influenza virus	Basic Science	P1
Bianca Nguyen, Lia Gao, Abeer Almiman, Shirley Tang. Kathleen Dotts, Miguel A. Villalona-Calero, Wenrui Duan	Investigation of fanconi anemia pathway downstream genes	Basic Science	P2
Dana T. Shively, Cedric R. Uytingco, Kirill Ukhanov, Jeffrey R. Martens	Morphological constancy of olfactory sensory neuron cilia in rodents	Basic Science	P3
Kunal Dhume, Joanne Tejero, Caroline Finn, Ayushi Singh, Karl Kai Mckinstry	Determining differential effects of Interleukin-2 on immune cells in lymphoid organs and the gastrointestinal tract	Basic Science	P4
Antoun Bouz, David P. Perrault, Gene K. Lee, Cynthia Sung, Roy Yu, Austin J. Pourmoussa, Sun Young Park, Wan Jiao, Ketan M. Patel, Young-Kwon Hong, Alex K. Wong	Vascularized lymph nodes flap ischemia results in upregulation of CXCL1/GRO-alpha	Basic Science	P5
Christopher A. Febres-Aldana, Lydia Howard, Kritika Krishnamurthy, Robert Poppiti, Nicholas Kuritzky	Neoadjuvant chemotherapy is associated with therapy-induced senescence of non-neoplastic cells and loss of P16INK4a expression in residual stem cell-like (CD44+) hormone-receptor-negative breast cancer	Basic Science	P6
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Oral Abstracts

O1

Race and prevalence of end-stage renal disease among U.S. type 2 diabetic patients with renal manifestations

Kenneth Chang. Hyunseo Jung. Kihyun Kwon. Grettel Castro, MPH. Pura Rodriguez de la Vega, MPH. Amalia Galindez, MD. Juan G. Ruiz, MD, MMedSci.

Herbert Wertheim College of Medicine, Florida International University, Miami, FL

Keywords: ESRD, Race, Type 2 Diabetes Mellitus

Introduction and Objectives: Patients with Type 2 Diabetes Mellitus (T2DM) are at increased risk of developing microvascular disease, including chronic kidney disease (CKD). End-stage renal disease (ESRD) is a major cause of mortality among T2DM patients. Racial disparity in complications, especially ESRD, has been an ongoing issue and could be an important prognostic factor in these patients. Objective: To explore if there is an association between race and prevalence of ESRD among T2DM patients between age 15 and 64, with diabetic nephropathy.

Methods: We conducted a cross-sectional study (secondary analysis of National Hospital Discharge Survey (NHDS) data from 2010). Study population consisted of patients of age 15-64 from non-federal short-stay hospitals with confirmed diagnosis of T2DM and diabetic nephropathy. Our independent variable was race (white and non-white) and the outcome was prevalence of ESRD. We performed customary descriptive statistics and bivariate comparisons of distributions of control variables according to race and according to ESRD status. Both unadjusted and adjusted (multiple logistic regression) for potential confounders odds ratios (OR) and 95% confidence intervals between race and ESRD were computed.

Results: A total of 397 patients were included. With the exception of region of origin of cases there were no differences in the distribution of any control variables according to race nor according to ESRD status. There was no statistically significant relationship between race and the diagnosis of ESRD, and this estimation didn't change even after adjusting for age (adjusted OR 0.95, 95% CI 0.53-1.76). Adjusted analysis also found a mildly elevated risk of ESRD in patients from age 40-54 years (adjusted OR 2.09, 95% CI 0.59-7.46), compared to patients between 15-39 and 55-64 years old.

Conclusions-Implications: We didn't find evidence of a significant association between race and the prevalence of ESRD in T2DM patients with diabetic nephropathy. Due to insufficient statistical power and potential for selection bias, such an association cannot be ruled out. Further research with prospective collection of data, which allows for computing incidence rather than prevalence of ESRD is needed.

O2

The association between race and survival among pediatric patients with neuroblastoma in the US between 1973 and 2015

Farouk Farouk, MS. Zaid Sheikh, MS. Omar Viqar, MS. Grettel Castro, MPH. Grettel Castro, MPH. Noël C. Barengo, MD, MPH, PhD.

Herbert Wertheim College of Medicine, Florida International University, Miami, FL

Keywords: Cancer, Child Health, Neuroblastoma

Introduction and Objectives: Neuroblastoma is the most common childhood cancer diagnosed during the first year of life and the third most commonly diagnosed childhood cancer overall. Information regarding the influence of race on survival among neuroblastoma patients is limited compared to other childhood cancers. This study investigates the association between race and 5-year cause-specific survival in pediatric patients diagnosed with neuroblastoma in the US between 1973 and 2015.

Methods: This was a retrospective cohort study using the Surveillance, Epidemiology, and End Result (SEER) database. Patients aged 17 and younger of Black, White or Asian Pacific Islander (API) race diagnosed with neuroblastoma from 1973-2015 were included (n=2,119). Those who had missing information and/or were diagnosed at autopsy were excluded. The exposure variable was race (White, Black, API), and the outcome variable was 5-year cause-specific survival. Covariates included age (<1 years, 1-4 years, 5-17 years), gender, ethnicity (Hispanic, Non-Hispanic), stage (localized, regional, distant, unstaged/unknown), tumor site (adrenal, non-adrenal), and year of diagnosis (1973-1999, 2000-2004, 2005-2015). Cox proportional hazard models were used to calculate unadjusted and adjusted hazard ratios with their corresponding 95% confidence intervals.

Results: After adjusting for potential confounders, there was not a statistically significant difference in the hazard of survival for blacks (HR 0.93; 95% confidence interval (CI) 0.74-1.16) or API (HR 1.02; 95% CI 0.76-1.37) compared with whites. In addition, patients diagnosed between 2000-2004 (HR 0.46; 95% CI 0.36-0.59) and 2005-2015 (HR 0.33; 95% CI 0.26-0.41) had decreased hazards of death when compared to patients treated during 1973 to 1999. Finally, patients with adrenal neuroblastoma were not found to have different survival when compared to those with a non-adrenal neuroblastoma (HR 1.16; 95% CI 0.99-1.36).

Conclusions-Implications: Our study did not find an association between race and 5-year survival among pediatrics patients diagnosed with neuroblastoma. However, survival improved among all patients treated during 2000-2004 and 2005-2015, respectively, when compared with neuroblastoma patients treated before the year 2000. Future research that takes socioeconomic status, genetic factors, and changes in treatment into account should be conducted to further explore possible disparities by race.

O3

Prescriptions of potentially inappropriate medications in older adults in the US: Results from the NAMCS 2013-2014

Rahil H. Shah, BS. Pooja Gurnani, BS. Elan Baskir, BA. Marcia H. Varella, MD, PhD, MHS. Pura Rodriguez de la Vega, MPH. Grettel Castro, MPH. Jorge C. Mora, MD.

Herbert Wertheim College of Medicine, Florida International University, Miami, FL

Keywords: Violence, Childhood, Depression

Keywords: Beers List, Potentially Inappropriate Medications, Geriatric, Polypharmacy

Introduction and Objectives: The American Geriatrics Society (AGS) developed Beers Criteria for potentially inappropriate medications (PIMs), in which the risks outweigh the benefits in the elderly population. Yet, studies have shown that 42% of elderly American adults from 2006-2010 were prescribed at least one medication on Beers List. Objective: To assess the frequency of PIM use, and to determine if selected patient characteristics are associated with PIM prescriptions in adults 65 years or older in the United States.

Methods: We analyzed cross-sectional data from the 2013 and 2014 National Ambulatory Medical Care Surveys (NAMCS). All patients 65 years and older were included (n=26,506). We assessed the association of being prescribed a PIM with the following patient characteristics: polypharmacy (use of ≥5 medications), race/ethnicity, age, gender, source of payment, and physician type. In this study, we narrowed our definition of PIMs to only include medications on Beers List with a "strong" strength of recommendation, "high" quality of evidence and recommendation to "avoid". Multivariable logistic regression analysis was conducted to determine the independent association of selected patient characteristics and PIM prescriptions.

Results: We found that 14% of patients in our study received PIMs. The PIM categories prescribed were related to central nervous system (73%), cardiovascular (18%), endocrine (6%), and pain (3%) medications. Patient characteristics found to be independently associated with prescription of PIMs were: polypharmacy use [adjusted Odds Ratio (aOR)=4.0; 95% Confidence Interval (CI)= 3.4-4.7], females (aOR=1.4; 95% CI=1.2-1.5), Non-Hispanic Blacks (aOR=0.7, 95% CI=0.5-0.9, compared to Non-Hispanic Whites), and self-pay insurance status (aOR=2.7; 95% CI=1.1-6.4, compared to private insurance).

Conclusions-Implications: Of public health concern, 14% of older adults in ambulatory care settings received potentially inappropriate medications, with a strong recommendation to avoid. CNS-related PIMs were most frequently prescribed. Initiatives to decrease PIM prescriptions should be developed, giving special attention to patients with the characteristics identified to be significant in this study.

O4

Association between prepregnancy BMI and breastfeeding outcomes: Effect modification by household income level and race/ethnicity

Christina Carr, BA*. Schuyler Hodge, MS*. David Liepa, MS*. Grettel Castro, MPH. Juan M. Lozano, MD, MSc. Marcia H. Varella, MD, PhD, MHS.

Herbert Wertheim College of Medicine, Florida International University, Miami, FL

Keywords: Breastfeeding, Pregnancy, Body Mass Index (BMI), Income, Socioeconomic Status

Introduction and Objectives: Maternal obesity has been consistently correlated with decreased incidence and duration of breastfeeding. Social determinants of health, including socioeconomic status and race/ethnicity also play a role in breastfeeding practices; however, the interaction between these factors and obesity regarding breastfeeding practices is less well explored. Aim: To assess if household income or race/ethnicity modify the association between maternal prepregnancy BMI and initiation and duration of breastfeeding.

Methods: We utilized data from the US Infant Feeding Practices Study 2 (IFPS 2, 2005-2007). Our independent variables were maternal prepregnancy BMI and the dependent variables were ever breastfeeding and duration of breastfeeding in weeks. Effect modifiers explored include household income as % of poverty line (≤100%, >100% to ≤200%, >200% to ≤400%, >400%) and maternal race/ethnicity (white, black, Hispanic, other). Independent associations were assessed using multivariate logistic regression for the outcome ever breastfeeding and cox proportional hazard model logistic regression.

Results: Being obese was associated with decreased odds of initiation of breastfeeding (OR= 0.74, 95% CI=0.56-0.98) and with higher hazard of breastfeeding cessation (HR=1.17, 95% CI=1.05-1.3) compared to normal weight women. At lower levels of maternal income, obese women had a higher hazard of breastfeeding cessation compared to normal weight women (HR=1.56, 95% CI=1.15-2.12 at ≤100% poverty line). At higher income levels, there was no difference in cessation of breastfeeding (HR= 0.93, 95% CI=0.71-1.23 at >400% poverty line). Obese or overweight black women had higher hazards of breastfeeding cessation than those of white women (HR=2.8, 95% CI=1.46-5.36 for black overweight, HR=2.21 95% CI=1.04-4.7 for black obese, and HR=1.13, 95% CI=1.01-1.27 for white overweight, HR=1.19, 95% CI=1.05-1.35 for white obese).

Conclusions-Implications: Higher maternal prepregnancy BMI negatively impacts breastfeeding practices, and the impact is highest for the lowest income and black women. Health care providers and policy implementers can target these at risk populations to improve breastfeeding rates and reduce disparities. KEYWORDS: breastfeeding, breastfed, pregnant, pregnancy, body mass index (BMI), prepregnancy BMI, obesity, income, socioeconomic status, education, race, ethnicity.

O5

Lost in translation: The effect of interpreter use on colorectal cancer screening in North Miami-Dade

Thomas Cowan, BS. Pamela Duarte, BS. Franklin Zheng, BS. Marcia H. Varella MD, PhD, MHS. Juan G. Ruiz, MD, MMedSci. Grettel Castro, MPH. Melissa Ward-Peterson, MPH, PhD. Pura Rodriguez de la Vega, MPH.

Herbert Wertheim College of Medicine, Florida International University, Miami, FL

Keywords: Colorectal Cancer Screening, Interpreter, Translator, Language, North Miami

Introduction and Objectives: In the United States, colorectal cancer (CRC) is the second leading cause of cancer death. The USPSTF recommends screening in persons aged 50–75 years. Yet, screening rates are suboptimal in the Hispanic population, with only 50% of eligible Hispanic patients reporting adherence to screening guidelines in the National Health Interview Survey in 2015. Language has been proposed to be a crucial determinant of the utilization and quality of health services delivered to patients with limited English proficiency. Aim: To determine if interpreter use by North Miami-Dade households whose primary language was not English was associated with ever receiving CRC screening.

Methods: We performed a secondary analysis of data from the North Miami Benchmark Survey conducted between 2009 and 2010. This was a cross-sectional study of a representative sample of households (survey response was 79%). We included all households who reported a language other than English as their primary language and had at least one household member 50 years of age or older. The exposure variable was self-reported interpreter use in a medical visit. The outcome was CRC screening at any point in a household member's life. The independent association between interpreter use and CRC screening was assessed using multivariate logistic regression via SPSS software v.20 at an alpha level = 0.05.

Results: Of the 1,845 households who completed the survey, 309 were eligible for this study. Approximately 40% of eligible households reported CRC screening. About 10% (n=31) used interpreters. The screening frequency was 35.5% for households who used interpreter and 40.7% for households who did not use interpreter (p=0.578). The unadjusted odds ratio (OR) between CRC screening and interpreter use was 0.80 (95% CI=0.37-1.74). After adjusting for socioeconomic status, education, and insurance status, the adjusted OR was 1.02 (95% CI=0.31-3.35). Households reporting a gap in insurance coverage within the last 12 months had borderline significantly for less CRC screenings (adjusted OR 0.52, 95% CI = 0.25-1.06).

Conclusions-Implications: Interpreter use was not found to be associated with CRC screening in households from North Miami. Further studies need to be conducted assessing standardized trained healthcare interpreters to confirm the results. Keywords: colorectal cancer screening, colorectal cancer, CRC, colonoscopy, sigmoidoscopy, fecal occult blood testing (FOBT), interpreter, translator, language, communication barriers, limited English proficiency, language discordance, North Miami, Miami-Dade County, and South Florida.

O6

Association between knowledge of zika transmission and preventative measures among Latinas of childbearing age in farm working communities in South Florida

Naiya Patel. Moneba Anees. Reema Kola. Grettel Castro, MPH. Pura Rodriguez de la Vega, MPH. Juan G. Ruiz, MD, MMedSci. Juan M. Acuña, MD, MSc, FACOG. Patria Rojas, PhD, MPH, MSW.

Herbert Wertheim College of Medicine, Florida International University, Miami, FL

Keywords: Latinas, Knowledge, Transmission, Prevention

Introduction and Objectives: Zika virus is a public health problem because the virus causes birth defects and is difficult to track since those carrying Zika are usually asymptomatic. Currently, there is no vaccine; therefore, use of personal preventative measures is the only method of avoiding transmission of Zika virus. The aim of this study was to evaluate the association between knowledge of Zika transmission and the use of preventative measures taken among Latinas of childbearing age who lived in or near farm working communities in South Florida.

Methods: A secondary data analysis was performed on a cross-sectional study, carried out on a convenience sample of 100 Latina women aged 18-50 years who lived in or near farm working communities of South Florida. Three women who declared not having ever heard about Zika were excluded. It was hypothesized that there would be an association between level of knowledge of Zika transmission and quality of preventive measures taken. Exposure variable was knowledge about preventative measures obtained from answers to specific questions about mode of transmission, and categorized as no knowledge, low and high level of knowledge. The outcome was the reported use of practices for preventing Zika infection categorized as poor or good. Control variables included demographics and socioeconomic status, English proficiency and perception of Zika related risk. Both crude and adjusted for confounders (multivariable logistic regression) ORs and confidence intervals were computed.

Results: In total, 69% participants demonstrated a high degree of knowledge of Zika transmission and 68% were categorized as taking good preventative measures. After adjusting for confounders and as compared with women with no knowledge about Zika transmission, women with high knowledge had 5.86 higher odds to take good preventative measures (p-value = 0.05).

Conclusions-Implications: Knowledge is associated with higher use of preventative measures. Therefore, it is essential to further investigate the relationship between the knowledge of transmission of Zika virus and the preventative measures taken in order to develop effective public health interventions for this population. Keywords: Latinas, Zika, knowledge, transmission, prevention Word count: 335 *All three authors contributed equally to this manuscript.

O7

Seroepidemiology of Burkholderia pseudomallei, etiologic agent of melioidosis, in the Ouest and Sud-Est Departments of Haiti

Thomas Weppelmann, PhD, MPH. Marcelo Farias. Zakaria Abdulla. Marcia H. Varella, MD, PhD, MHS.

Herbert Wertheim College of Medicine, Florida International University, Miami, FL

Keywords: Haiti, Melioidosis, Seroepidemiology, Burkholderia Pseudomallei

Introduction and Objectives: Burkholderia pseudomallei, the etiological agent of melioidosis, has been hypothesized to be endemic throughout the Caribbean, including the impoverished nation of Haiti. However, due to the protean clinical manifestations, presence of asymptomatic infections, and limited medical diagnostic capacity, the identification of active melioidosis cases remains challenging. The objective of this study was to use a serological data collected from a large sample of native Haitians to provide evidence of undiagnosed human melioidosis in Haiti.

Methods: A cross-sectional, seroepidemiological study was conducted using data previously generated with an enzyme-linked immunosorbent assay (ELISA) to detect antibodies toward B. pseudomallei in the native population. Serum originated from asymptomatic population members (n=756) from three clinics in the Ouest Department of Haiti and was screened for polyvalent (IgM/IgG/IgA) and monoclonal (IgG or IgM) immunoglobulins. Seropositive population members were defined by a threshold absorbance value three standard deviations above the sample population average. The number of IgG and IgM positives were tabulated by location, gender, and age-group. Simple logistic regression was used to determine the associated between seroprevalence and demographic factors; multiple logistic regression was used to adjust for potential confounding and included all variables.

Results: The population seroprevalence was 11.5% (95% CI: 9.2, 13.8) for polyvalent immunoglobulins, 10.1% (95% CI: 7.7, 11.9) for IgG, and 1.7% (95% CI: 0.8, 2.6%) for IgM. The seroprevalence was not significantly different by gender (P =0.173), but increased significantly (P <0.001) with age (OR 1.03; 95% CI 1.01, 1.05). All IgM positive samples originated from Gressier; and the prevalence of IgG was higher in Jacmel than Gressier or Chabin, even after adjustment for age and gender (OR 1.72, 95% CI 1.05, 2.94 P=0.04).

Conclusions-Implications: The detection of both recent (IgM+) and previous (IgG+) exposure to B. pseudomallei provides serological evidence that melioidosis is endemic in Haiti and supports the hypothesis that B. pseudomallei is present throughout the Caribbean. These findings should encourage environmental sampling efforts and increase the level of clinical suspicion for melioidosis cases in Haiti.

O8

Maternal education level and human papillomavirus (HPV) vaccination series initiation in adolescent females

Matthew Alfonso. Zachary Pryor. Grettel Castro, MPH. Juan M. Lozano, MD, MSc. Noël C. Barengo, MD, MPH, PhD.

Herbert Wertheim College of Medicine, Florida International University, Miami, FL

Keywords: Adolescents/Female, Papillomavirus Vaccines/Administration and Dosage, Health, Knowledge, Attitudes, Practice, Uterine Cervical Neoplasms/Prevention and Control, Patient Compliance/Statistics and Numerical Data

Introduction and Objectives: Rates of vaccination against human papillomavirus lag behind those of other readily available vaccinations in the United States. The current scientific evidence in regards to an association between maternal education and HPV vaccination is inconsistent. The aim of the study was to determine the association between maternal education and human papillomavirus (HPV) vaccination series initiation in adolescent females.

Methods: This cross-sectional study analysis used data provided by the Center of Disease Control's National Immunization Survey (NIS-Teen) years 2008-2014. NIS-Teen is a random-digit-dialing survey conducted in the United States and Puerto Rico consisting of an initial telephone interview with parents of adolescents. Inclusion criteria were female sex, age 13-17 years-old and participation in NIS-Teen. Exclusion criteria were non-completion of telephone survey and participating as part of non-state estimation areas. The exposure variable of the study was maternal education (measured in years). The main outcome variable was HPV vaccination initiation, defined as having received at least one injection of the complete three-injection HPV vaccine. Covariates included in the study were income, race/ethnicity, adolescent's age, region, respondent type, maternal age, and marital status. Unadjusted and adjusted logistic regression models were used to study the association between maternal education and HPV vaccination. Odds ratios (OR) and 95% confidence intervals (CI) were calculated.

Results: A total of 9,445 respondents were included. Respondents with mothers who graduated college did not have increased odds of to be vaccinated than the reference group (OR 1.17; 95% CI 0.92-1.50). Participants with mothers who did not complete high school were equally likely to be vaccinated as compared to those with higher education (OR 1.21, 95% CI 0.86-1.70). The group with mothers who completed some college yielded similar results (OR 1.17, 95% CI 0.92-1.50). Fathers who responded to the survey had higher odds to report that their child had not completed their vaccinations (OR 0.78, 95% CI 0.64-0.96) than mother respondents.

Conclusions-Implications: Further study should assess whether mothers of different education status have difference reasons for not vaccinating their daughter, and whether maternal education is associated with completion of the HPV vaccine.

O9

Exploratory study of the association between selected demographic and socioeconomic factors and influenza vaccine uptake in U.S. adults

Jonathan Dahan. Calvin Strehl. Sonia Majid, MPH. Grettel Castro, MPH. David Brown, MD. Frederick Anderson, MD. Marcia H. Varella, MD, PhD, MHS.

Herbert Wertheim College of Medicine, Florida International University, Miami, FL

Keywords: Influenza Vaccination, Vaccination Review, Social Determinants of Health, Cross-Sectional, Demographics

Introduction and Objectives: Influenza vaccinations prevent hospitalizations and mortality due to flu. However, the rates of flu vaccination in the U.S. continues to fall below the Healthy People 2020 goal of 70%. Objective: To evaluate whether selected demographic, socioeconomic, and health-related factors were associated with influenza vaccination uptake among U.S. adults.

Methods: We studied adult participants of the 2017 Behavioral Risk Factor Surveillance System (BRFSS). The main independent variables included demographic (age, gender, and race/Hispanic ethnicity) and socioeconomic (education status, income) factors. Health-related characteristics (insurance, self-perceived health, comorbidities) were accounted for. The outcome was influenza vaccination uptake in the past year. Multivariate logistic regression analysis was be performed to assess potential independent associations.

Results: Of the 404,582 participants studied, 46.5% received the flu vaccine in the past year. Factors independently associated with higher odds of flu vaccine uptake were age 65 years or older [odds ratio (OR)=2.2, 95% confidence interval (CI) 2.1-2.3], being female (OR=1.2, 95% CI=1.2-1.2) and Asian/Pacific Islander (OR=1.1, 95% CI=1.0-1.2 compared to Whites, higher education (OR 1.1, 95% CI= 1.0-1.1 and OR=1.5, 95% CI=1.5-1.6 for more than high school and college graduates , respectively, compared to high school graduates) and comorbidities (strongest association found for prevalent diabetes, OR=1.5, 95% CI=1.5-1.6). Lower independent odds of vaccine uptake were found for Black race (OR=0.7, 95% CI=0.7-0.8 compared to Whites) and "Other" race (OR=0.6, 95% CI=0.8-0.9 compared to Whites), yearly income lower than $25,000 (OR=0.9, 95% CI=0.8-1.0 for the group of income between $15,000 and $25,000 compared to income between $35,000 and $50,000), not having health insurance (0.6, 95% CI=0.5-0.6), and longer intervals since last health check-up (OR=0.3, 95% CI=0.3-0.3 for check-up within >5 years compared to those who did check-up in past year).

Conclusions-Implications: The results suggest that groups traditionally targeted for influenza vaccination including the elderly and those with comorbidities continue to have higher odds of being vaccinated. Additionally, women and those with highest income and educational level have higher odds of vaccination. Groups with the lowest odds of vaccination include those with the greater than a year since last health check-up, those without health insurance, those of Black or "Other" race, and those without a college or technical school degree. This provides preliminary data that can be used to design interventions for at-risk populations identified.

O10

Pseudo-progression of merkel cell carcinoma after avelumab therapy

Leah Cohen, BA[1]. Elnara Muradova, MS[2]. Nikhil Khushalani, MD[3].

[1]*Herbert Wertheim College of Medicine, Florida International University, Miami, FL*

[2]*University of South Florida, Morsani College of Medicine*

[3]*Moffitt Cancer Center, Department of Cutaneous Oncology*

Keywords: Merkel Cell Carcinoma, Pseudo-Progression, Immunotherapy, Avelumab, Immune-Related Response Criteria

Introduction and Objectives: The introduction of immunotherapies for the treatment of cancer has required the development of immune-related response criteria to categorize their unique response patterns. Pseudo-progression involves the development of new or enlarging lesions after treatment initiation, mimicking tumor progression, followed by an eventual decrease in total tumor burden. Currently no valid biochemical or radiologic marker exists to differentiate pseudo-progression from true progression. This case report describes a patient with Merkel cell carcinoma (MCC) treated with Avelumab (anti-PD-L1 monoclonal antibody) who initially experienced an alarming increase in the size of his tumor followed by a near-complete response.

Case Presentation: The patient is a 69-year-old man who developed a painful erythematous cutaneous nodule underlying a forearm cast at the base of the right thumb. The lesion was excised and pathology was consistent with MCC. A PET/CT demonstrated a suspicious hypermetabolic lymph node in the right axilla which, after biopsy, was confirmed MCC. The patient was not a surgical candidate, so therapy with Avelumab was initiated. After three doses the nodule had increased in prominence. Repeat PET/CT demonstrated increased metabolic activity around the lesion, as well as in two right axillary lymph nodes. Avelumab was held and surgery was planned pending cardiac clearance. Two days prior to surgery there was dramatic near-complete resolution of the lesion and significantly decreased axillary lymphadenopathy on exam. The decision was made to postpone surgery and reinstate Avelumab.

Conclusions-Implications: With recent FDA approval for the use of immunotherapies in MCC, data and clinical anecdote regarding their responses in MCC are limited. Currently, no literature exists describing a pseudo-progression response to Avelumab or any other immunotherapies in patients with MCC. Because the incidence of pseudo-progression is relatively low and most cases of disease progression are true progression, it is important for physicians to become familiar with the unique and rare response patterns of immunotherapies. Future studies investigating biochemical or radiologic markers to differentiate pseudo-progression from true progression are needed.

O11

Race/ethnicity and the primary anatomical location of cutaneous melanoma in Florida patients

Oren Cohen. Laura Valente. Juan M. Acuña, MD, MSc, FACOG. Grettel Castro, MPH. Pura Rodriguez de da Vega, MPH. Marcia H. Varella, MD, PhD, MHS.

Herbert Wertheim College of Medicine, Florida International University, Miami, FL

Keywords: Melanoma, Dermatology, Ethnicity, Skin Cancer, Sun Protection

Introduction and Objectives: Melanoma is responsible for the majority of skin cancer deaths. Florida ranks second among US states for incidence of melanoma cases. Melanoma has been found to differ by anatomical location depending on patients' race or ethnicity. With Florida's ethnically diverse population, we sought out to compare the incidence of melanoma by anatomical location amongst the different race/ethnicities.

Methods: We used data from adult patients with melanoma from the Florida Cancer Data System years 1998-2014. The independent variable was race/ethnicity [White Non-Hispanic (WNH), White Hispanic (WH), and Black Non-Hispanic (BNH)]. The dependent variable was the primary anatomical location of the melanoma (Face, Neck/Scalp, Upper Limbs, Trunk, and Lower Limbs). Multivariate multinomial logistic regression was used to determine the independent associations.

Results: We studied 96,713 melanoma cases. About 97% of patients were White Non-Hispanics (WNH), 3% were White Hispanics (WH), and less than 1% were Black Non-Hispanics (BNH). About 8% of WNH and WH had melanoma on the face, compared to 3% BNH. About 16% of WNH and 23% of WH had melanoma on the lower limb and hips compared to 62.1% in BNH (p-value <0.001). We found independent associations between race and the anatomical locations of lower limbs and hips (versus face) after adjusting for age, gender, stage at diagnosis, marital status, and health insurance status. As compared to White Non-Hispanics, BNH had 9.95 times higher odds of having melanoma in the lower limbs and hips [odds ratio (OR)= 9.9, 99% confidence interval (CI)= 5.1-19.5)] and White Hispanics had 21% decreased odds of presenting melanoma in the trunk, and 29% lower odds of presenting melanoma in the regions of upper limbs and shoulder (OR = 0.8, 99% CI= 0.6-1.0 and OR= 0.7, 99% CI= 0.8-0.9, respectively). Additionally, White Hispanics had higher odds of presenting melanoma on the lower limbs and hips as compared to Whites Non-Hispanics (adjusted OR=1.3, 99% CI= 1.0-1.6).

Conclusions-Implications: We found differences in the location of melanoma according to race/ethnicity. Physicians should tailor skin exams when screening for melanomas in otherwise low-risk anatomical locations depending on the patient's race. Keywords: melanoma, primary cutaneous melanoma, anatomical location, race, ethnicity, Hispanic, Non-Hispanic White, Non-Hispanic Black, Florida

O12

The association between e-cigarette use and stroke

Alejandra Figueroa. Ryan Bricknel, BS. Cristobal Ducaud, BS., Noël C. Barengo, MD, MPH, PhD. Juan C. Zevallos, MD.

Herbert Wertheim College of Medicine, Florida International University, Miami, FL

Keywords: E-Cigarettes, Stroke, Smoking, Vaping

Introduction and Objectives: Electronic cigarette use in the United States has steadily become more common, with 3-5% of the population today reporting daily use. There is a relative scarcity of population-based studies investigating long term health implications of E-cigarette use. Stroke is associated with conventional cigarette smoking and is an important health outcome in the U.S., causing significant long-term disability and contributing to 1 out of every 20 deaths. Our study aims to measure the association between e-cigarette use and a history of stroke.

Methods: We utilized the 2016 Behavioral Risk Factor Surveillance System to conduct a cross-sectional analysis comparing E-cigarette use and history of stroke. Individuals who answered "yes" or "no" to questions regarding electronic cigarette use and history of stroke were included in the study. Multivariate logistic regression statistics were used to determine adjusted odds ratios (AOR).

Results: Of the 486,303 total participants, 465,594 met inclusion criteria. Current daily and someday E-cigarette use was independently associated with increased odds of having had a stroke (AOR 1.6, 95% CI 1.2-2.3 and OR 1.28, 95% CI 1.02-1.61, respectively). Other independently associated factors include age >65 yr (AOR 7.3; 95% CI 5.7-9.3), female sex (AOR 1.2; 95% CI 1.1-1.3), aggregate non-White race (AOR 1.17; 95% CI 1.08-1.28). Daily (AOR 2.1; 95% CI 1.9 - 2.4), some day (AOR 1.8; 95% CI 1.6-2.1), and former (AOR 1.3; 1.2-1.4) conventional cigarette smoking were also independently associated with increased odds of having had a stroke. Independently associated comorbidities included coronary artery disease (AOR 4.3; 95% CI 3.8-4.6), chronic kidney disease (AOR 2.1; 95% CI 1.8 - 2.3), diabetes (AOR 1.8; 95% CI 1.6-1.9) and conventional cigarette smoking. Of note, over half (55.9%) of current daily E-cigarette smokers are former conventional cigarette smokers.

Conclusions-Implications: Daily and some-day use of electronic cigarette use is independently associated with increased odds of having had a stroke. Further research is needed to investigate the temporal association of the relationship between stroke and E-cigarette use.

O13

The association between heavy alcohol consumption and morbidity and mortality in ischemic stroke patients: Does t-PA administration modify this association?

Keneil Brown, BA. Ottavia Green, BS. Noël C. Barengo, MD, MPH, PhD. Marcia H. Varella, MD, PhD, MHS. Grettel Castro, MPH. Pura Rodriguez de la Vega, MPH.

Herbert Wertheim College of Medicine, Florida International University, Miami, FL

Keywords: Stroke, Tissue-Type Plasminogen Activator, Thrombolysis, Heavy Alcohol, Cerebrovascular Accident

Introduction and Objectives: Stroke is a leading cause of death and long-term disability in the United States. Heavy alcohol consumption is risk factor for stroke and has been shown to increases morbidity and mortality. But, in patients with an ischemic stroke, evidence is scarce. Also, it is uncertain if the efficacy of tPA - the standard of care for ischemic stroke - is altered in patients with heavy alcohol consumption. The aim is to investigate the association between heavy alcohol consumption and morbidity and mortality in patients with an ischemic stroke, and to assess if t-PA modifies this association.

Methods: We performed secondary analysis of data from the Florida Hospital Discharge Database for Stroke. Participants 19 years and older who suffered an ischemic stroke and admitted between 2008-2012 were included. The independent variable was heavy alcohol consumption (>7 drinks and >14 drinks per week for females and males, respectively). The dependent variables were presence of selected morbidities (post-stroke complications including dysphasia, hemiparesis, disability, and length of hospitalizations >5 days) and in-hospital mortality. Multivariate logistic regression was performed, and interaction terms were tested to assess the potential effect modification by tPA treatment.

Results: We studied 194,414 stroke participants. About 1.6% were heavy alcohol users. About 3% died in -hospital and 37.3% developed at least one comorbidity after the stroke. Heavy alcohol use was not associated with mortality [unadjusted odds ratio (OR)= 0.82, 95% confidence interval (CI)= 0.65-1.02, adjusted odds ratio (OR)= 1.16, CI= 0.92-1.46]. However, heavy alcohol use increased the odds of morbidity (OR=1.39, 95% CI=1.30-1.50 and OR=1.43, CI =1.33-1.54). tPA administration was associated with an increased odds of mortality (OR=5.10, CI=4.37-5.94 and OR=5.92, CI=5.05-6.93), but there was no evidence for effect modification of tPA use and the associations tested (p= 0.756 and p=0.431 for interaction for mortality and morbidity, respectively).

Conclusions-Implications: Heavy alcohol consumption increased the risk of morbidity but not mortality in adult patients with ischemic stroke and this association was not modified by tPA exposure.

O14

Male urinary incontinence and depression: A longitudinal analysis

Nikita Bodoukhin, BSc. Benjamin Hellman, BA. Grettel Castro, MPH. Carlos Salgado, MD. Juan G. Ruiz, MD, MMedSci.

Herbert Wertheim College of Medicine, Florida International University, Miami, FL

Keywords: Urinary Incontinence, Depression, Geriatric, Retirement, Males

Introduction and Objectives: Urinary incontinence (UI) has been demonstrated as a significant risk factor for developing depression in elderly females. In elderly males, urinary incontinence is a prevalent problem that has long been suspected to have significant social consequences and has been given relatively little attention. We set out to elucidate a temporal relationship between UI and depression.

Methods: A secondary data analysis was performed on the Health and Retirement Study cohort, an ongoing study of adults 51-61 years at recruitment when the first wave in 1992; all participants were followed up every two years. Data from biennial follow up of men from 1996 to 2014 was used. Men with probable depression at baseline were excluded from analysis. Variables: The outcome of interest was probable depression, defined as a score of ≥3 on the 8-item Center for Epidemiologic Studies-Depression scale. UI was defined based on questions about experience urine loss. Statistical Analysis: We fit Cox regression models to this data, adjusting for estimates of baseline demographic, psychosocial and health status variables found to confound the association between UI and the outcome of interest. As a test of our methodology, we ran the previously described analysis using a female sample and were able to replicate a previously reported association between UI and developing depression.

Results: Our final model included 8,897 men. Notable baseline characteristics of the study population include 8% of men reporting incontinence in the past year. Additionally, 0.6% were living in a nursing home at entry into the study. A history of psychiatric disease was reported by 7%.Time-dependent recurrent event survival analysis by Cox regression employing the counting process approach yielded an unadjusted hazard ratio of 1.9 (95% CI: 1.7, 2.0). Adjusting for these confounders in a time-dependent fashion yielded a hazard ratio of 1.3, (95% CI: 1.1, 1.4).

Conclusions-Implications: Urinary incontinence is positively associated with incident depression in previously non-depressed retirement-age men. Increased awareness on the part of treating physicians to the benefit of patient's psychosocial welfare is warranted.

O15

Impact of high BMI on outcomes of laparoscopic hysterectomy

Ha Tran, BS. Natalia Shringarpure, BS. Natalie Ceballos, BS. Jaime Rodriguez, MD, FACS. Pura Rodriguez de la Vega, MPH. Grettel Castro, MPH. Noël C. Barengo, MD, MPH, PhD.

Herbert Wertheim College of Medicine, Florida International University, Miami, FL

Keywords: Obesity, Overweight, Hysterectomy, Complications

Introduction and Objectives: In 2017, nearly 40% of American adults were found to be obese. Though obesity is a known risk factor for increased surgical morbidity, and hysterectomy is a common gynecologic operation, the effects of obesity on hysterectomy complications are yet to be determined. The objective of this study was to investigate the association between obesity and intra/postoperative complications of total laparoscopic hysterectomy.

Methods: A retrospective cohort study was conducted from data provided by the American College of Surgeons National Surgical Quality Improvement Program, which comprised of 21,356 patients that underwent a total laparoscopic hysterectomy in 2016. Medical records were reviewed for patient demographics, history of chronic conditions, and presence of intra/postoperative complications. The main independent variable, body mass index, was stratified into groups according to the current WHO BMI classification (normal: 18.5-24.9 kg/m2, overweight: 25.0-29.9 kg/m2, obese I: 30-34.9 kg/m2, obese II: 35-39.9 kg/m2, obese III: >40kg/m2). The primary outcome was measured by the presence of intra/postoperative complications. Unadjusted and adjusted logistic regression models were used to calculate odds ratios (OR) and 95% confidence intervals (CI).

Results: There was a decrease in odds of complications in Obese I patients compared with normal weight patients (OR 0.8; 95% CI 0.7-0.9). The percentage of complications was highest among patients in the obese III category. The subpopulations with increased odds of complications were those that were postmenopausal (OR 1.3; 95% CI 1.1-1.4), black (OR 1.4; 95% CI 1.2-1.6), or had a chronic hypertension (OR 1.3; 95% CI 1.2-1.5), COPD (OR 1.9; 95% CI 1.3-2.8), disseminated cancer (OR 2.8; 95% CI 1.8-4.2), and bleeding disorders (OR 4.2; 95% CI 3.0-5.9).

Conclusions-Implications: While morbid obesity is a risk factor for developing comorbid conditions and increased surgical morbidity, it appears that a moderately high BMI may be protective in recovery. These findings support the "obesity paradox" suggesting a counterintuitive benefit to excess adipose tissue when undergoing physiologic stress. Future studies should categorize complications into intraoperative, medical, and surgical to compare type among BMI categories.

O16

Breastfeeding duration and its association with acute care visits for illness at age 6

Alixandra Garic, BS. Tamlyn Hall, BS. Eric Tano, BS. Marcia H. Varella, MD, PhD, MHS. Grettel Castro, MPH. Pura Rodriguez de la Vega, MPH. Juan G. Ruiz, MD, MMedSci.

Herbert Wertheim College of Medicine, Florida International University, Miami, FL

Keywords: Breast Fed, Formula Fed, Sick Visit, Emergency Room

Introduction and Objectives: Breastfeeding has been studied extensively for its benefits during infancy. Few studies have investigated long-lasting effects. Using the same dataset as the present study, Li et al. found a protective, dose-response association between breastfeeding and maternal reports of infection and sick visits in the past year among 6-year-olds.1 However, they did not include ER visits for acute illness. Therefore, we examined the association between breastfeeding duration, and total acute care visits for illness (sick visits + ER visits) during the same time period.

Methods: A historical cohort was assembled using data from the CDC's 'Infant Feeding Practices Study and its Year Six Follow-Up' dataset. Records from mother-infant dyads who provided information on variables of interest at the Year 6 Follow-Up survey were included. Exposure was breastfeeding during the first year of age (never breastfed, breastfeeding for less than or equal to 6 months, and more than 6 months breastfeeding). Outcomes of interest at the age of six were: a) total number of acute care visits in the preceding year (sick visits + ER visits for acute illness) and b) ER visits for acute illness. By fitting multivariate binomial regression models, crude and adjusted measures of association (incidence rate ratios and 95% confidence intervals) were computed.

Results: Our sample included 1,444 mother-child dyads. After adjusting for potential confounding factors (zero-inflated negative binomial regression for total visits, and Poisson regression for ER visits) we found that when comparing children who were breastfed for 6 months or more and those who were never breastfed, incidence rates of total visits for both acute care and emergency room care decreased by 17% (IRR: 0.83, p: 0.045) and by 47% (IRR: 0.53, p: 0.008) respectively.

Conclusions-Implications: The rates of total acute care visits and ER visits are significantly lower among children of mothers who breastfed for more than 6 months when compared to mothers who never breastfed. We did not find evidence for effects of breastfeeding for 6 months or less as compared to never breastfeeding, but we cannot rule out such an effect. This highlights the importance of breastfeeding past 6 months for proven long-term health benefits. This may be due, in part, to the impact of extended breastfeeding on immune development. Future research with higher power should test whether there is some effect of shorter breastfeeding duration on long-term immune system. The final objective in this line of research is to reduce child morbidity and the associated burden on the healthcare system.

O17

Continuous 9-Cis retinoic acid treatment improves lymphatic clearance and prevents secondary lymphedema

Antoun Bouz, BS[1]. Gene K. Lee, MD[2]. David P. Perrault, MD[3]. Austin J. Pourmoussa, MS[1]. Roy Yu, BS[2]. Daniel Gardner, MD[2]. Maxwell Johnson, MD[2]. Sun Young Park, MS[2]. Athanasiois Bramos, MD[2]. Eun Kyung Park, MS[2]. Young Jin N. Seong, BS[2]. Sunju Lee, PhD[2]. Lia E. Jung, MS[2]. Dongwon Choi, PhD[2]. Young-Kwon Hong, PhD[2]. Alex K. Wong, MD[2].

[1]*Herbert Wertheim College of Medicine, Florida International University, Miami, FL*

[2]*Keck School of Medicine of USC*

[3]*Stanford University School of Medicine*

Keywords: Lymphedema, 9-Cis Retinoic Acid, Lymphangiogenesis

Introduction and Objectives: Secondary lymphedema, a common sequelae of breast cancer therapy, affects up to 200 million people worldwide and 3 million people in the United States. There is currently no curative treatment. Previous studies have demonstrated the efficacy of 9-cis Retinoic Acid, a vitamin A metabolite, in the prevention of secondary lymphedema through its pro-lymphangiogenic properties. The purpose of this study was to determine the minimal effective dosing regimen of 9-cis Retinoic Acid for clinical and functional improvement of postsurgical lymphedema.

Methods: Lymphedema was induced in the tails of 50 C57BL/6 mice through a circumferential skin incision followed by microsurgical ablation of deep lymphatic vessels. The mice received daily intraperitoneal injections of either 100 µL vehicle solution (90 µL sunflower seed oil/10 µL 100% ethanol) or 0.8 mg/kg 9-cis Retinoic Acid (9-cis RA) dissolved in 100 µL of vehicle solution. The animals were randomly assigned to one of five groups following surgery: control (vehicle for 45 days following surgery), 7 day (9-cis RA for 7 days), 14 day (9-cis RA for 14 days), 45 day (9-cis RA for 45 days), and delay (9-cis RA for 7 days beginning one week after surgery). All interventions were administered on postoperative day (POD) one. On POD 45, indocyanine green (ICG) lymphangiography was performed. Lymphatic fluid clearance was quantified over time using ImageJ, and student-t tests were calculated between each group at various time points using GraphPad Prism 7. Animals were photographed every 7 days, and tail diameter was measured using ImageJ. Tail volume was then calculated using a truncated cone formula, and percent change in tail volume was recorded. Animals were sacrificed on POD 47. Tail specimen were harvested, sectioned, and stained with hematoxylin and eosin. Dermal and epidermal thicknesses were measured using ImageJ. All measurements were taken by a blinded researcher and all statistical analyses were performed using GraphPad Prism 7.

Results: At day 42, tail volume was significantly lower in the 45-day ($p<0.0001$) and delay ($p<0.05$) groups compared to control. ICG lymphangiography demonstrated improved lymphatic fluid clearance in the 14-day, 45-day, and delay groups compared to control ($p<0.05$). A thinner dermal layer was observed in the 14-day ($p<0.0001$), 45-day ($p<0.05$), and delay ($p<0.05$) groups compared to control. A thinner epidermal layer was also observed in the 7-day ($p<0.05$), 14-day ($p<0.0001$), 45-day ($p<0.001$), and delay ($p<0.0001$) groups.

Conclusions-Implications: Consistent with our previous studies, 9-cis Retinoic Acid treatment for 45 days resulted in significantly decreased tail volume and improved lymphatic function, as demonstrated by the significantly improved indocyanine green clearance. These results suggest that a dosing regimen involving continuous post-operative 9-cis Retinoic Acid administration may be a useful and efficacious treatment to prevent secondary lymphedema.

Poster Abstracts

P1

IL-21 is a necessary component for optimal heterosubtypic immunity against influenza virus

Caroline Finn, BA. Kai McKinstry, PhD.

University of Central Florida, Orlando, FL

Keywords: Immunology, Influenza, Interleukin 21

Introduction and Objectives: The aim of current influenza A virus (IAV) vaccines is to induce neutralizing antibodies against surface proteins of circulating IAV strains. This type of protection, known as 'homotypic' immunity, is only effective against IAV subtypes recognized by these neutralizing antibodies, and fails to protect if the vaccine does not match circulating IAV strains. However, it is well established that T cells can also provide immunity against IAV and, unlike antibodies, T cells can recognize internal viral proteins shared across diverse IAV subtypes. This form of protection is known as 'heterosubtypic' immunity. The cytokine interleukin 21 (IL-21) is best known to aid in optimal immunity by stimulating development of antibody responses. However, IL-21 also plays diverse roles in some models of infection in the function and survival of anti-viral T cells. Here, we examine the role of IL-21 in murine models of homotypic and heterosubtypic immunity against IAV.

Methods: Wild type (WT) or IL-21 receptor knock-out (IL-21r-/-) C56BL/6 mice were primed with a sub-lethal dose of the mouse-adapted IAV strain A/PR8 (H1N1) and challenged 28 days later with a lethal dose of A/PR8, or of the heterosubtypic IAV strain A/Philippines (H3N2). After challenge, mice were monitored for weight loss and morbidity. In addition, to model current intranasal vaccine strategies, mice were primed with the cold-adapted, attenuated vaccine strain A/Alaska (H3N2) and challenged after 28 days with a lethal dose of A/PR8/ or A/Philippines. To directly asses the role of IL-21 in viral clearance, pulmonary IAV titers were determined after heterosubtypic challenge by quantitation of viral copy number.

Results: We saw no impact of IL-21 on weight loss or recovery during priming of WT and IL-21r-/- mice. Similarly, primed IL-21r-/- mice were equally protected when challenge with a lethal dose of homotypic IAV compared to WT controls. However, following heterosubtypic challenge, IL-21r-/- mice showed increased weight loss and mortality versus WT controls. Similar patterns were seen after heterosubtypic challenge of mice primed with PR8 or vaccinated with A/Alaska. Finally, decreased protection in the primed IL-21r-/- mice correlated with increased viral titers compared to WT mice.

Conclusions-Implications: Surprisingly, although IL-21 is best known in supporting maximal antibody responses, IL-21r-/- mice showed no defects in homotypic immunity against IAV. Unexpectedly, the primed IL-21r-/- mice displayed increased weight loss and death following heterosubtypic challenge. These studies indicate that IL-21 may contribute more to mechanisms associated with heterosubtypic rather than homotypic immunity. Understanding how to best stimulate T cell-dependent heterosubtypic immunity may aid in the development of improved IAV vaccines. Therefore, our future studies will examine how IL-21 signals impact the generation and function of protective heterosubtypic CD8 and CD4 T cells responses against IAV.

P2

Investigation of fanconi anemia pathway downstream genes

Bianca Nguyen[1]. Lia Gao[1]. Abeer Almiman, PhD[1]. Shirley Tang[2]. Kathleen Dotts[2]. Miguel A. Villalona-Calero, MD[3]. Wenrui Duan, PhD[1].

[1]*Herbert Wertheim College of Medicine, Florida International University, Miami, FL*

[2]*Comprehensive Cancer Center at the Ohio State University College of Medicine and Public Health*

[3]*Miami Cancer Institute*

Keywords: DNA Repair, Lung Cancer, Fanconi Anemia, Homologous Recombination, Oncogene

Introduction and Objectives: A key response mechanism to DNA damage is the Fanconi Anemia repair pathway (FA), which involves homologous recombination DNA repair and is activated through mono-ubiquitination of FANCD2. Impaired regulation of DNA repair results in genomic instability. FANCD2 is considered to promote cell growth through interactions with cell proliferation pathways. We hypothesize that FA deficient tumors have a low growth rate and reduced ability for DNA repair compared to FA functioning tumor cells. We aim to explore the association between the FA repair pathways and downstream genes involving in cell cycle regulation that influence tumor growth.

Methods: To generate FANCD2 knockdown cells, human lung cancer cell lines A549 and H1299 were transduced with FANCD2-specific short hairpin RNA (shRNA) expressing and puromycin-resistant lentiviral particles or control shRNA lentiviral particles. The cells were cultured in growth medium, and successful FANCD2 knockdown was confirmed by western immunoblot analysis. RNA deep sequencing was completed with Illumina RNA-Seq. We compared gene expression between knockdown FANCD2 and control samples across three cell lines and ranked significant gene expression changes, defined as a five-fold change in upregulation or downregulation. The fold change was calculated by dividing FANCD2 deficient expression by FANCD2 efficient expression.

Results: 13436 genes were evaluated across three cell lines and 17 genes demonstrated gene expression change by at least 5-fold with FANCD2 knockdown in all three cell lines. FANCD2 knockdown resulted in 14 downregulated genes and 3 upregulated genes. The downregulated genes RP11-618G20.1, RP5-1021I20.4, RP11-219A15.1, XXbac-BPG32J3.20, and BMS1P17 demonstrated significant expression change across three cell lines. Of the 14 downregulated genes, 13 genes had literature supporting oncogenic function. Each upregulated gene had literature supporting oncogenic function.

Conclusions-Implications: As FANCD2 is considered to promote cell proliferation, downregulation of oncogenic genes expression was expected with FANCD2 knockdown. However, the literature suggested that the 3 upregulated genes with FANCD2 knockdown also have oncogenic function. These genes may have other functioning beyond the scope of carcinogenesis which may explain

gene upregulation with FANCD2 knockdown. Pinpointing genes related to the functional deficiency of the FA pathway may lead to a better understanding of genetic and epigenetic phenomena that drive cancer in these patients. Our results provide a starting point for developing targets to specific downstream genes associated with FA deficient tumors. Further investigation is needed to determine how FANCD2 interacts with these genes to promote cell proliferation.

P3

Morphological constancy of olfactory sensory neuron cilia in rodents

Dana T. Shively, BS. Cedric R. Uytingco, PhD. Kirill Ukhanov, PhD. Jeffrey R. Martens, PhD.

University of Florida

Keywords: Olfaction, Cilia, Therapy

Introduction and Objectives: Olfaction allows perception of our chemosensory environment. All odorant receptors and signal transduction molecules are compartmentalized in the cilia of olfactory sensory neurons (OSNs). Shortening or loss of olfactory cilia as the result of disease impairs odor detection illustrating their critical role in olfactory function. Although our understanding of olfactory cilia has grown, it remains unclear whether ciliary morphology changes under varying conditions. Utilizing adenoviral ectopic expression and live confocal en face imaging, we thoroughly analyzed cilia length and number in olfactory epithelium under various conditions. Overall expanding our knowledge of the structural features of olfactory cilia will provide us with a reference to understand structure-function relationship between cilia morphology and odorant detection.

Methods: En Face. Mice were anesthetized, decapitated, and split along the cranial midline. The olfactory epithelium was isolated and placed turbinate surface down in a bath of 1x PBS in the imaging chamber. Samples were imaged on a Nikon TiE-PFS-A1R confocal microscope. Cilium Measurements. The turbinates were identified through the eyepiece (10x) under epifluorescence. Individual OSNs with intact cilia were identified based on AV-mediated ectopic expression of MyrPalmGFP or MyrPalm-mCherry. Confocal z stack images of OSNs were collected at 60x. Cilium length and count measurements were performed on ImageJ.

Results: Mean cilia length and number per OSN showed no significant difference across all regions ($F(7,137)=2.111$, $p=0.0463$); ($F(7,137)=2.789$, $p=0.0096$). Data displays reduced mean OSN cilia lengths and number in 24 hour 4% PFA drop fixed OEs compared to en face visualization ($p<0.0001$). Mean cilia length per OSN, showed no significant difference across the different age groups ($F(3,468)=0.736$, $p=0.531$). Data of the mean cilia number per OSN, showed a significant difference between the 3-5 week old mice and other ages ($F(3,467)=22.70$, $p<0.0001$). Data of the mean cilia length and number per OSN showed no significant difference between male and females ($t(136)= 1.39$); ($t(136)= 1.87$). The mean cilia length and number per OSN showed a significant difference among the various strains ($F(3, 505)= 26.45$, $p=<0.0001$); ($F(3, 504)=40.46$, $p< 0.0001$).

Conclusions-Implications: Ectopic expression of lipid-anchored fluorescent probes allowed us to examine the endogenous structure of OSN cilia allowing us to determine that OSN cilia lengths and numbers were uniform throughout the septal and turbinate regions of the OE. OSN cilia lengths and numbers were also consistent across ages and gender but differed across the various strains of animals. In addition, paraformaldehyde fixation can disrupt endogenous cilia structure. By accurately classifying OSN cilia morphology, we hope to gain insight regarding the processing of olfactory input, and cilia regulation as their presence in the OE is crucial for odor detection.

P4

Determining differential effects of Interleukin-2 on immune cells in lymphoid organs and the gastrointestinal tract

Kunal Dhume, MS. Joanne Tejero, BS. Caroline Finn, BA. Ayushi Singh. Karl Kai Mckinstry, PhD.

University of Central Florida, Orlando, FL

Keywords: IL-2, Crohns Disease, GI Tract, Immune Cells

Introduction and Objectives: Interleukin-2 (IL-2) is a pleiotropic cytokine demonstrated to be effective in treating some cancers. However, clinical use of IL-2 can be associated with severe side effects including gastrointestinal toxicity (GT). Similar GT symptoms are observed in inflammatory disease states such as Crohn's disease (CD). Interestingly, mounting evidence indicates a role for IL-2 in CD, but the underlying mechanisms are unknown. Indeed, studies concentrating on the in-vivo activities of IL-2 have mostly focused on secondary lymphoid organs and immune cells associated with them. Very few studies have addressed how IL-2 signals impact populations of immune cells in the gut. Here, we aim to identify and compare the effects of systemic IL-2 administration on six major leukocyte populations in gut associated lymphoid tissues versus the secondary lymphoid organs.

Methods: Complexing recombinant IL-2 protein with certain neutralizing monoclonal antibodies increases the bioavailability of IL-2 and can be used to selectively target IL-2 to different cellular subsets. Thus, we injected wild-type C57BL/6 mice (in the steady state condition) intraperitoneally for three days with IL-2 complexes or treated control mice with phosphate buffer saline (PBS) alone. On the fourth day we assessed the cellular composition in the gut associated lymphoid tissues (Mesenteric lymph nodes, Peyer's Patches, lamina propria, intraepithelial cells) and systemic secondary lymphoid tissues (spleen and peripheral lymph nodes). In addition, the lungs were taken as another control, as they comprises a complex immune system in a non-GT mucosal site. Single cell suspensions were analyzed via multicolor flow cytometry to determine the frequency and numbers of individual cell populations. In this manner, we directly compared the impact of IL-2 signals on immune cell subsets within each organ compared to the PBS treated mice.

Results: While we confirmed previously observed changes in specific immune cell populations in secondary lymphoid organs driven by IL-2 complexes, very few changes were seen in the gut and gut- associated lymphoid tissues. Unexpectedly, a sharp decline was seen in B cells, most notably in Peyer's Patches. Our data furthermore indicates that B cells in IL-2 treated mice undergo enhanced apoptosis in Peyer's Patches.

Conclusions-Implications: These studies demonstrate a differential impact of IL-2 on immune cell subsets in secondary lymphoid organs versus gut associated lymphoid tissues. Our future goals are to determine if IL-2 acts directly on B cells and if it impacts only certain B cell subsets in Peyer's Patches, as some studies suggest that changes in B cells may contribute to development of CD. Thus, this study may aid in defining new ways in which IL-2 can contribute to disease etiology, and also lead to novel treatments for CD.

P5

Vascularized lymph nodes flap ischemia results in upregulation of CXCL1/GRO-alpha

Antoun Bouz, BS[1]. David P. Perrault, MD[2]. Gene K. Lee, MD[3]. Cynthia Sung, BS[3]. Roy Yu, BS[3]. Austin J. Pourmoussa, MS[1]. Sun Young Park, MS[3]. Wan Jiao, MD, PhD[3]. Ketan M. Patel, MD[3]. Young-Kwon Hong, PhD[3]. Alex K. Wong, MD[3].

[1]Herbert Wertheim College of Medicine, Florida International University, Miami, FL

[2]Stanford University School of Medicine

[3]Keck School of Medicine of USC

Keywords: Lymphatics, Ischemia, Reperfusion, Flap

Introduction and Objectives: Free vascularized lymph node transfer (VLNT) has been shown to be an effective treatment modality for lymphedema. While limited flap ischemia is inevitable, prolonged ischemia induces a cascade of deleterious effects that can negatively affect outcomes. To date, the physiologic response of lymphatic tissue to ischemia and reperfusion has not been well studied. The development of the Prox-1 GFP lymphatic reporter rat (PRAT) has enabled easy visualization of lymphatic tissue (green florescence) from surrounding fat in real time. Although the critical ischemia time and physiologic response to ischemia for various flap tissue types such as muscle and skin have been previously studied, lymphatic tissue ischemia has yet to be well characterized. Thus, the purpose of this study is to explore the physiologic and transcriptional response of lymphatic tissue to ischemic injury.

Methods: The PRAT groin lymph node (LN) flap ischemia model based on the superficial epigastric artery/vein was utilized for this study. For each time point (n=5), LN flaps were elevated, islandized, and subjected to ischemia using an Aclund clamp for 1, 2, 4, and 8 hours. Flaps were harvested at 0 hours, 24 hours, or 5 days after reperfusion. Animals were randomly assigned to each group. GFP-positive LN were dissected free from the surrounding adipose tissue and LN RNA was isolated using standard methods. qRT-PCR was used to quantify expression of a panel of genes related to lymphatic biology or ischemia including: platelet endothelial cell adhesion molecule (PECAM-1), CXCL1/GRO-alpha, tumor necrosis factor-alpha (TNF-alpha), and Mucin-1 (MUC1). qRT-PCR results were recorded and analyzed using GraphPad Prism 7.

Results: While some changes in gene expression were observed after 1 hour of ischemia, they did not become statistically significant until after 2 hours: CXCL1/GRO-alpha (40x increase, $p<0.001$), MUC1 (5x increase, $p<0.05$), and PECAM-1 (3x increase, $p<0.05$). TNF-alpha was upregulated after 4 hours (4x increase, $p<0.05$). Ischemia followed by reperfusion for 5 days, demonstrated that the ischemia induced CXCL1/GRO-alpha upregulation returned to baseline levels whereas levels of MUC1, PECAM-1, and TNF-alpha remained elevated.

Conclusions-Implications: In lymphatic tissue, ischemia induces significant changes in gene expression after as little as 2 hours of ischemia. Ischemia results in a 40-fold transient increase in CXCL1/GRO-alpha, and reperfusion returns expression levels of CXCL1/GRO-alpha back to baseline. In VLNT, surgeons should aim to keep ischemia time less than 2 hours. CXCL1/GRO-alpha may be a useful bio-marker to monitor ischemia in LN flaps.

P6

Neoadjuvant chemotherapy is associated with therapy-induced senescence of non-neoplastic cells and loss of P16INK4a expression in residual stem cell-like (CD44+) hormone-receptor-negative breast cancer

Christopher A. Febres-Aldana[1]. Lydia Howard[1,2]. Kritika Krishnamurthy[1]. Robert Poppiti[1,2]. Nicholas Kuritzky[3].

[1]A.M. Rywlin, MD Department of Pathology, Mount Sinai Medical Center, Miami Beach, FL

[2]Herbert Wertheim College of Medicine, Florida International University, Miami, FL

[3]Department of Radiation Oncology, Mount Sinai Medical Center, Miami Beach, FL

Keywords: Senescence, Breast Cancer, P16, CD-44, Chemotherapy

Introduction and Objectives: Cellular senescence is a stress response associated with P16-mediated cell arrest and the acquisition of a secretory phenotype that can promote tumor progression. Hormone-receptor-negative breast cancers (HRNBCs) can show aberrant expression of P16. We aimed to assess the impact of neoadjuvant chemotherapy (Ct) on P16-mediated senescence in breast cancer specimens.

Methods: P16 and CD-44 (stem cell marker) were evaluated by immunohistochemistry in breast biopsies and subsequent post-Ct excision in a cohort of 21 women with HRNBCs. P16 positivity was estimated by calculating cellular densities on hotspots using ImageJ 1.51t (National Institutes of Health, USA).

Results: All pre-Ct HRNBCs (n=18) showed nuclear and cytoplasmic P16 expression in variable proportions. There were no significant differences in pre-Ct CD-44 and p16 expression between HRNBCs with complete (n=10) versus incomplete (n=8) pathologic response. Residual HRNBCs were likely to lose the expression of P16 (5/8, $P<0.05$) while CD-44 expression (6/8, $P<0.05$) increased after Ct. Post-Ct changes correlated with pre-Ct tumor positivity ($r=0.27$ for P16; $r=-0.87$ for CD-44). There was accumulation of senescent

(P16+) cells in non-neoplastic ductal and lobular epithelium (n=18, P<0.05), which correlated with cases showing a complete response to Ct (r=0.86). Adipose tissue, peri-ductal and –lobular stroma but not the peritumoral stroma exhibited mildly increased numbers of P16+-cells after Ct.

Conclusions-Implications: Neoadjuvant Ct treatments lead to the accumulation of senescent cells in non-neoplastic breast tissue. P16(-/low) and CD-44(+/high) expression in HRNBC is compatible with a residual Ct-resistant phenotype. P16 as a marker of senescence in cancer cells should be further studied.

P7

A long noncoding RNA of lung epithelial cells in cigarette smoke-associated COPD

C. Long[1]. D. Devadoss[1]. G. Daly[2]. N. Baumlin[3]. G. Borchert[2]. M. Nair[1]. M. Salathe[3]. R. Langley[2]. H.S. Chand[1].

[1]Department of Immunology and Nano-Medicine, Herbert Wertheim College of Medicine, Florida International University, Miami, FL

[2]Department of Pharmacology, University of South Alabama, Mobile, AL

[3]Department of Internal Medicine, University of Kansas Medical School, Kansas City, KS

Keywords: COPD, Non-Coding RNA, Airway Epithelial Cells, Mucous, Cigarette Smoke

Introduction and Objectives: Airway epithelial cells (AECs) are crucial for lung innate immunity and any dysregulation in AECs can lead to hyperreactive mucous response that is often observed in chronic obstructive pulmonary disease (COPD). Therefore, studies were conducted to help understand the molecular mechanisms responsible for the cigarette smoke (CS)-associated lung pathologies of the COPD patients.

Methods: RNA-seq analyses of AECs was conducted to identify mucous-associated long non-coding RNA (lncRNA) species. The RNA-seq data was validated by qRT-PCR analysis of air-liquid interface cultured AECs that were exposed to CS extract (CSE). The age- and gender-matched lung tissues (Lung Tissue Research Consortium, NIH) from COPD smokers with varying disease severity of GOLD (Global initiative of COPD) stage 1, 2, 3 or 4 were analyzed for airway mucous and lncRNA expression. Mucous was analyzed by Alcian blue histochemical staining and by qPCR analysis for a secretory mucin MUC5AC levels. Fluorescence In-Situ Hybridization (FISH) analysis by RNAScope® was performed to assess airway distribution of the lncRNA in COPD subjects.

Results: The newly identified putative lncRNA AC05 was more than 6-fold upregulated in human AECs showing induced mucous levels compared to the non-treated controls. The in-silico sequencing and annotation analysis revealed that this lncRNA is 32.4 kb long with 3 exons and 2 introns and has several splicing sites. This lncRNA had the negligible protein coding potential with a Fickett Testcode score of 0.273 with coding probability 0.198. Both exon I and exon II of this lncRNA showed induced expression whereas there was no significant induction in exon III transcript, indicative of existence of the splice variants. CSE treatment of AECs showed an increase in MUC5AC mucin levels with correlative increase in lncRNA AC05 exon II levels. Most importantly, airway sections from GOLD stage-2 and -3 COPD that had increased mucous expression in airways also showed higher expression of lncRNA AC05 exon II transcripts. FISH analysis using the RNAScope® technology demonstrated predominantly cytosolic localization of lncRNA AC05 in the airway epithelium of the GOLD stage-3 COPD patients.

Conclusions-Implications: Here, we report that a novel AEC-specific lncRNA could be responsible for the CS-associated mucous hyperreactivity in COPD patients. Studies are underway to investigate whether the hyperreactive mucous response of COPD AECs can be regulated by modulating this lncRNA using gain- or loss-of-function strategies. These studies will thus provide a key foundation toward understanding the molecular mechanisms by which lncRNAs modulate airway epithelial responses and COPD pathogenesis.

P8

Isolation and characterization of slow-cycling tumor initiation cells in mouse model of hGBM

Bhavya Sheth, BS[1]. Loic P. Deleyrolle, PhD[2].

[1]Florida International University, Miami, FL

[2]University of Florida

Keywords: Immunotherapy, Glioblastoma, Cancer-Stem Cell, KR158

Introduction and Objectives: Glioblastoma (GBM) is an aggressive primary malignant brain tumor that carries a fatal prognosis in almost all cases. Despite the poor one and five-year survival rates (36.5% and 5% respectively) what is most alarming is the stagnant nature of advancements in treatment therapies in the past 40 years. However, recently the efficacy of immunological targeting has been promising in treating cancers but there are very few immunocompetent animal models of slow-cycling hGBM that can be used for determining immunotherapeutic treatment efficacy. Our focus is to identify and characterize a slow-cycling cancer stem cell model in an immunocompetent mouse model of glioma to test different immunological targeting approaches in subsequent animal studies.

Methods: We identified a potential murine cell line which accurately reciprocates what is observed in human cell models of GBM. Using FACS based on CellTrace Violet (CTV) retention, we separated the slow and fast cycling KR158B-Luciferase cells. Then we determined the slow cycling cells are far more resistant to temozolomide (TMZ) than fast cycling cells through multiple proliferation assays: MTT, CyQyant, Sphere forming assay, and propidium iodide incorporation. Finally, in-vivo animal studies were done to compare tumorigenic potential of each cell subtype.

Results: All proliferation assays produced statistically significant differences between slow-cycling cells (SCC) and fast-cycling cells (FCC): MTT ($p<0.01$, $n = 12$), CyQyant ($p<0.01$, $n = 12$), Sphere forming assay ($p<0.01$, $n = 120$), and PI incorporation ($p<0.001$). The EC50 dose of TMZ for the KR158 cell line was estimated to be 3x the EC50 dose for hGBM cell culture (1mM vs 0.3mM, respectively). Further, we show the slow-cycling cells are also more tumorigenic both in vitro and in vivo suggesting they are principle the tumor initiating cells which is the observation in human models.

Conclusions-Implications: We concluded that the KR158B-Luciferase cell line is an adequate murine cell model of slow cycling GBM cells. Further, we determined these slow cycling cells are more resistant to therapy and successful isolation and removal of them can delay tumor progression by as much as 45%.With these findings, we can continue using this cell line for testing various immunotherapeutic targeting modalities in immunocompetent animal models for evaluation of hGBM therapies.

P9

Neurocognitive status of aviremic HIV+ subjects is associated with proteomic content of plasma /CSF-derived exosomal extracellular vesicles

Rachel Fields, BS[1]. Allen Caobi, BS[1]. Adriana Yndart, BS[1]. Mario Gomez[2]. Francisco Lima[2]. M. Nair, PhD[1]. Andrea D. Raymond, PhD[1].

[1]Herbert Wertheim College of Medicine, Florida International University, Miami, FL

[2]Mass Spectrometry Facility, College of Arts and Sciences, Florida International University, Miami, FL

Keywords: Exosomes, Human Immunodeficiency Virus (HIV), Neurocognitive Status

Introduction and Objectives: Despite successful suppression of HIV viral loads by anti-retroviral therapy (ART) to undetectable levels, many aviremic HIV-infected individuals still develop neurocognitive deficits. The mechanism of HIV-associated neurocognitive deficits (HAND) or asymptomatic neurocognitive impairment (ANI) in aviremic patients is still unclear. Currently there are no therapeutics or monitoring systems that directly address the cause of ANI and HAND, in aviremic HIV+ subjects. We hypothesize that the exosomal extracellular vesicles (xEVs) released in the peripheral blood and/or the cerebrospinal fluid (CSF) of aviremic HIV+ subjects contribute to development of HAND or ANI. Given that HAND and ANI negatively impact the quality of life in aviremic HIV+ subjects methods to monitor, diagnose, and treat HAND/ANI are needed. Here our objective is to perform a cross-sectional study comparing the proteomic content of CSF- or serum-derived xEVs from aviremic HIV+ non-drug users at various neurocognitive stages to determine whether xEV proteomic content correlates with neurocognitive stage.

Methods: Perform cross-sectional study correlating proteomic profile of CSF or plasma-derived xEVs cargo from HIV+ non-drug users at different neurocognitive stages. Matched cryopreserved serum (n=10) and CSF (n=10) from aviremic donors were acquired from the National NeuroAIDS Tissue Consortium (NNTC). xEVs were isolated via standard precipitation and differential ultracentrifugation techniques, lysed and contents analyzed via mass spectometry (PEAKS software), SDS/PAGE western blot analysis, and ELISA.

Results: Overall proteomic content of CSF- and serum-derived xEVs did not differ significantly between normal, HAND and ANI subjects. However, the amount(ratio) of proteins such as transferrin (TRFE), apolipoprotein a1(APOA1), alpha-2 macroglobulin (A2MG), and the HIV Nef protein did significantly increase in CSF- and serum-derived xEVs of aviremic HIV+ subjects with HAND/ANI compared to subjects without deficits.

Conclusions-Implications: In conclusion the proteomic content of CSF- and/or serum-derived xEVs can be associated with a specific neurocognitive status in some aviremic HIV-infected subjects. This suggests that the xEV proteomic profile associated with neurocognitive status can also be developed as a monitoring tool of neurocognitive status in the aviremic HIV-infected subject. Taken together the findings of this study clearly demonstrated that xEV proteomic content varied with neurocognitive status in the aviremic HIV-infected patient and that xEV proteomic profiling has the potential to be a “bench-to-bedside-to-bench” approach in which neurocognitive impairment/fluctuation in aviremic HIV+ patients can be monitored.

P10

Sugar-sweetened beverage consumption effect on cholesterol levels among U.S. adults

Jose Roble, MS. Joshua Sixon, BS. Mohammad Yousef, BS. Juan G. Ruiz, MD, MMedSci. Juan C. Zevallos, MD.

Herbert Wertheim College of Medicine, Florida International University, Miami, FL

Keywords: Sugar-Sweetened Beverages, Cholesterol, Hyperlipidemia, Metabolic Syndrome, Diabetes

Introduction and Objectives: Sugar-sweetened beverages (SSB) are the leading source of added sugar in the American diet, and a major contributor to adult and childhood obesity. The intake of SSB has shown to be independently associated with increased BMI, waist circumference, HbA1c, and insulin resistance. In addition, recently, there has been an increased interest in understanding the association of SSB intake with cardiovascular risk factors, including hypercholesterolemia. The purpose of this study was to determine whether there is an association between the consumption of sugar-sweetened beverages and reported hypercholesterolemia in U.S. adults.

Methods: We conducted a cross-sectional study based on secondary analysis of the 2017 data from the Behavioral Risk Factor Surveillance System (BRFSS) in ten U.S. states. The exposure variable was defined as reporting daily soda and sugary drinks consumption in the last 30 days. The outcome variable was reporting hypercholesterolemia. We initially performed an analysis of the distribution of selected demographics and comorbidities according to the main exposure and outcome variables. We then performed a multivariate analysis utilizing a binary logistic regression approach to adjust for potential confounders.

Results: Our sample included 46,853 adults. The unadjusted logistic regression indicated that consuming between 0-1 SSB daily had a 25% lower odds of having hypercholesterolemia (OR=0.75, 95%CI:0.69-0.81) compared to no SSB consumption, and a 41%

lower odds for those consuming 5+ SSB (OR=0.59, 95%CI:0.42-0.83). However, the adjusted analysis showed no association between the exposure and outcome (OR=1.01, 95%CI:0.92-1.11; and OR=0.84; 95%CI:0.57-1.25, respectively). Secondary findings indicated that being in the 65+ year-old age group increased by 5 times the odds of reporting hypercholesterolemia (OR=5.03, 95%CI:4.23-5.98) compared to those in the 18-34 year-old age group. There was also a 9% (OR=1.09, 95%CI:0.10-1.19) increase in odds of hypercholesterolemia among males compared to females, and a 21% decrease in odds among blacks (OR=0.79, 95%CI:0.68-0.92) compared to whites. Being overweight or obese increased odds of hypercholesterolemia by 60% (OR=1.6 95%CI:1.44-1.78) and 72% (OR=1.72, 95%CI:1.55-1.92), respectively.

Conclusions-Implications: Our findings suggest that there is no statistically significant association between SSB intake and reporting hypercholesterolemia. Incidentally, we found that increased age, male sex, blacks, and overweight/obesity were significantly associated with reporting hypercholesterolemia. Further research should include a prospective study design to clarify the impact of SSB intake and hypercholesterolemia.

P11

Gender differences in hospital mortality based on anatomical location of acute myocardial infarction in the Puerto Rican population

Jennifer Palacio, BS. Carly Rabin, BS. Jacqueline Sroka, BS. Juan C. Zevallos, MD. Juan M. Acuña, MD, MSc, FACOG. Melissa Ward-Peterson, MPH, PhD.

Herbert Wertheim College of Medicine, Florida International University, Miami, FL

Keywords: Myocardial Infarction, In-Hospital Mortality, Hispanic, Gender

Introduction and Objectives: Myocardial infarction is a prominent diagnosis worldwide. Published scientific literature has associated acute myocardial infarction (AMI) at the anterior location with increased in-hospital mortality. Our study targets a rapidly-growing, underrepresented minority of Hispanic men and women for which there is limited information relating to cardiac health. Our objective is to examine the association of anatomical location of AMI and in-hospital mortality between men and women in a Puerto Rican population.

Methods: Patients from the Puerto Rican Cardiovascular Surveillance System hospitalized in 2007, 2009 and 2011 with a newly diagnosed AMI at 21 medical centers in Puerto Rico were included for analysis. Anterior location of AMI based on ECG was compared to all other locations, including posterior, inferior, lateral, septal and indeterminate. We utilized multivariate logistic regression analysis to identify the association between anatomical location of AMI and in-hospital mortality while controlling for age, smoking status, gender, obesity, hyperlipidemia, diabetes, hypertension, congestive heart failure, and type of AMI (STEMI/NSTEMI).

Results: Our study included 2,965 patients (45% women) with the largest proportion (26.4%) of patients between the ages of 65 and 74 years. The adjusted odds ratio in patients with anterior AMI was 30% higher for in-hospital mortality compared to all other locations (OR=1.3, 95% CI 0.8-2.2), while men had 20% lower the odds for in-hospital mortality than women (OR=0.8, 95% CI 0.5-1.1), although both these results were not statistically significant. Conversely, the odds for in-hospital mortality were significantly higher for increased age (OR=3.9, 95% CI 1.5-10.6), congestive heart failure (OR=1.9, 95% CI 1.2-2.9), and STEMI (OR=2.1, 95% CI 1.3-3.4) but significantly lower for hypertension (OR=0.5, 95% CI 0.3-0.7).

Conclusions-Implications: Although our findings failed to demonstrate an independent association between in-hospital mortality and anterior AMI location or gender, further research is warranted with an older, at-risk population.

P12

Lowered fasting blood glucose (FBG) in a prediabetic individual with HIV despite struggle with weight control management

Alicia Sneij-Perez, MS. Javier Tamargo, MS. Leslie Seminario, MS. Fatma Huffman, PhD. Florence George, PhD. Mary Jo Trepka, MD. Sabrina Sales Martinez, PhD. Adriana Campa, PhD. Marianna Baum, PhD.

Florida International University, Miami, FL

Keywords: HIV, Diabetes, Nutrition, Intervention, Waist Circumference

Introduction and Objectives: HIV infection has previously been associated with malnutrition and wasting; however, with the initiation of antiretroviral therapy (ART), a growing number of people living with HIV (PLWH) are becoming centrally obese, with disproportionate weight accumulation around the abdominal area and fat losses in the rest of their body (periphery face, arms and legs), indicative of lipodystrophy. As a result, some PLWH may struggle simultaneously with central fat accumulation and peripheral losses, trying to balance these 2 opposite effects.

Case Presentation: PB is a 62-year-old, African-American male infected with HIV for 12 years, receiving an NRTI regimen. Participating in the Miami Adult Studies in HIV (MASH) Cohort, PB started a 6-month nutrition intervention targeted to lower diabetes risk in prediabetic PLWH. Baseline body mass index (BMI) was 24.1kg/m2 and waist circumference (WC) was 36.5 inches. Despite having the initial intention to lose weight, PB gained ~12.4lbs just a month after initiation. When questioned about the weight gain, PB revealed that he had started taking an appetite stimulant (Megace) to address the wasting on his periphery, claiming that he looked "sickly". PB stopped taking Megace after he gained >20lbs (12.3% WtΔ) in 4 months. BMI at this time was 26.3 kg/m2 and WC was 45.5 inches, reflecting a substantially increased risk for metabolic complications. With WC increasing 9 inches and hip circumference increasing only 2 inches, it is evident that a considerable amount of the weight accumulation occurred around the waist. As can be seen, he among others in his situation, are struggling with conflicting goals by simultaneously trying to reduce central obesity and prevent peripheral losses and wasting, something that may be unique to PLWH.

Conclusions-Implications: Despite the participant's difficulties in weight management, his fasting blood glucose (FBG) improved after the 6-month nutrition intervention, with a -14 mg/dL improvement, lowering associated risk for diabetes and cardiometabolic complications. This improvement in FBG levels suggests that despite the difficulty of effective weight management in these patients, proper glucose values may still be achieved with nutrition counseling and education, thus lowering risk for diabetes and associated complications.

P13

Effectiveness of a 6-month nutrition intervention in lowering diabetes risk in prediabetic people living with HIV (PLWH) in MASH cohort

Alicia Sneij-Perez, MS. Adriana Campa, PhD. Leslie Seminario, MS. Fatma Huffman, PhD. Mary Jo Trepka, MD. Florence George, PhD. Sabrina Sales-Martinez, PhD. Marianna Baum, PhD.

Florida International University, Miami, FL

Keywords: HIV, Diabetes, Nutrition, Intervention, Fasting Blood Glucose

Introduction and Objectives: People living with HIV (PLWH) have a higher risk of developing diabetes than the general non-HIV infected population, primarily due to HIV infection as well as the chronic use of antiretroviral therapy (ART). The objective of this study is to assess the effectiveness of a 6-month nutrition intervention to improve glycemic parameters and inflammation in prediabetic PLWH on stable ART with undetectable HIV viral load.

Methods: A 6-month randomized, controlled nutrition intervention was conducted in prediabetic PLWH. The study participants for the intervention were recruited from the Miami Adult Studies for HIV (MASH) cohort at the FIU-Borinquen Research Clinic. Upon their consent, the participants were randomized into the intervention group or the control group. Participants randomized in the intervention group met once a month for approximately 1 hour where they received medical nutrition therapy, nutrition counseling and nutrition education; participants randomized into the control group received educational material at baseline. Blood was drawn at baseline and at 6-month to measure fasting blood glucose (FBG) and high sensitivity C-reactive protein (hs-CRP).

Results: A total of 38 participants were recruited and randomized into either the intervention group (n=20) or the control group (n=18). We found that the FBG for the 6-month follow-up for the intervention group was significantly lower than the baseline FBG values of the same study group (paired t-test; p=0.031). No significant difference was found in the control group between the baseline and 6-month fasting blood glucose values (p=0.068). Moreover, no significant difference was found in pre/post C-reactive protein (CRP) levels in the intervention or control group (paired t-test; p=0.404 and p=0.117 respectively). There was a significant difference in CRP levels at baseline (p=0.028) between the study groups but no difference at the 6-month follow up (Mann Whitney U test: p=0.430).

Conclusions-Implications: The results from this intervention support the notion that a nutrition intervention is effective in prediabetic PLWH to lower diabetes risk by significantly lowering fasting blood glucose and may be implemented into larger scale interventions; however, no significant changes was seen in hs-CRP values between the 2 groups.

P14

Racial disparity in survival for women with ovarian cancer

Justin J. Cheng, BS. Bu Jung Kim, BA. Catherine Kim, BS. Pura Rodriguez de la Vega, MPH. Marcia H. Varella, MD, PhD, MHS. Carolyn Runowicz, MD. Juan G. Ruiz, MD, MMedSci.

Herbert Wertheim College of Medicine, Florida International University, Miami, FL

Keywords: Race, Ethnicity, Disparity, Survival, Ovarian Cancer

Introduction and Objectives: Ovarian cancer is the fifth-leading cause of cancer-related mortality in United States women. Previous studies have documented disparities in survival between non-Hispanic black (NHB) and non-Hispanic white (NHW) women. This study aimed to assess if insurance status and extent of disease were effect modifiers of the survival difference between NHW and NHB women diagnosed with ovarian cancer from 2007 to 2015.

Methods: A secondary data analysis of the National Cancer Institute's Surveillance, Epidemiology, and End Result (SEER) program from 2007-2015 was performed. Participants were selected based on postmenopausal status (age over 51 years), NHB and NHW race/ethnicity, epithelial histology, and regional/distant disease at diagnosis. The exposure was race/ethnicity (NHB and NHW). Outcome was time from diagnosis to cause-specific death up to five years. Potential effect modifiers were insurance status (uninsured/Medicaid or insured/insured not specified) and extent of disease (regional or distant). A multivariate Cox proportional hazards model was fitted, which included two first-order interaction terms: race by extent of disease and race by insurance status. For each statistically significant interaction, stratified Cox regression models were fitted for the identified effect modifier.

Results: A total of 6,880 women were included. Interaction test for insurance status was non-significant but was significant for extent of disease (regional vs. distant). Stratified multivariate Cox regression model showed that NHB experienced worse prognosis compared to NHW with regional disease (adjusted HR = 1.63; 95%CI 1.07-2.48), but this difference was not evident for distant disease (adjusted HR =1.05; 95%CI 0.93-1.18).

Conclusions-Implications: We found evidence for greater cause-specific mortality among NHB women but only in patients with regional disease. The reasons for such a difference need further research but could be related to disparities in access to quality cancer treatment or biological factors affecting response to treatment.

P15

Racial disparities in cancer related mortality in patients with urinary bladder malignancy in the US

Juliana Morales, BS*. Aaron Malles, BS*. Marrell Kimble, BS*. Pura Rodriguez de la Vega, MPH. Grettel Castro, MPH. Alan Nieder, MD. Noël C. Barengo, MD, MPH, PhD.

Herbert Wertheim College of Medicine, Florida International University, Miami, FL

Keywords: Urinary Bladder Neoplasms, Disease-Free Survival, Mortality, Transitional Cell, Survival Rate

Introduction and Objectives: It is estimated that in 2018 there will be 81,190 new cases of bladder cancer with an estimated number of new deaths projected to be 17,240, making it the fifth most common cause of cancer in the U.S. Current evidence shows a racial disparity in survival, though studies assessing whether the association differs according to insurance status are scant. The objective of our study was to determine if the association between race and bladder cancer 5-year survival differs according to health insurance.

Methods: A retrospective cohort study was conducted using the 2015 SEER database. The inclusion criteria for study participants was >18 years, who presented with primary malignancy of the urinary bladder (n=39,587). The independent variable was the patient's reported racial status (White, Black and Asian Pacific Islanders (API)), the main outcome was 5-year cancer-specific survival. The covariates included in the analysis were age, gender, marital status, stage, grade, recurrence, and surgery. Unadjusted and adjusted Cox regression analysis were used to calculate the hazard ratios (HR) and 95% confidence intervals (CI).

Results: The adjusted hazard ratios for 5-year overall survival stratified by insurance status indicated that Blacks with any Medicaid were 1.44 times more likely to die of bladder cancer (95% CI 1.28-1.62) compared with Whites. The corresponding hazard of death in uninsured Blacks was 1.30 (95% CI 1.00-1.69). However, there was no statistically significant association between race and survival between insured Black and insured White patients (HR 1.10; 95% CI 0.54-2.24). API had a similar 5-year survival compared with Whites among the insured and any Medicaid categories. However, the uninsured API group had increased survival (HR 0.71 95% CI 0.51-1.00) compared with uninjured White patients.

Conclusions-Implications: While race is accepted as a poor prognostic factor in the mortality from bladder cancer, insurance status can help to explain some of the survival differences across races. We suggest empowering clinicians to identify high-risk patients and connect them with additional services to improve access to quality care. Future research should be conducted to explore the variation in access/quality of care for patients of varying insurance status to minimize disparities in mortality between races for patients with bladder cancer.

P16

The association between race/ethnicity and cancer stage at diagnosis of bone malignancies

Alyssa N. Eily, BS. Moawiah S. Mustafa, BS. Luai S. Mustafa, BS. Pura Rodriguez de la Vega, MPH. Grettel Castro, MPH. Marcia H. Varella, MD, PhD, MHS. Noël C. Barengo, MD, MPH, PhD.

Herbert Wertheim College of Medicine, Florida International University, Miami, FL

Keywords: Bone Malignancy, Cancer Stage, Disparity, Race, Ethnicity

Introduction and Objectives: Evidence has shown disparities and delays in diagnosis of both breast and colorectal cancers in both Black and Hispanic populations when compared to White population. Limited data exists analyzing disparities in diagnosis in regards to primary bone neoplasms (PBN). The objective of our study was to determine if there is an association between race/ethnicity and advanced stage of diagnosis of PBN.

Methods: This population-based retrospective cohort study included patient demographic and health information extracted from the NCI Surveillance, Epidemiology, and End Results Program (SEER). Our patient population includes patients less than 85 years of age with a diagnosis of PBN (osteosarcoma, Ewing sarcoma, chondrosarcoma, and giant cell tumor) from 1973-2014. The main exposure variable was race/ethnicities categorized as Non-Hispanic White (NH-W), Non-Hispanic Black (NH-B), Non-Hispanic Asian Pacific Islander (NH-API) and Hispanic. The main outcome variable was advanced stage at diagnosis. Age, sex, tumor grade, type of bone cancer, decade and geographic location were added as co-variates to the statistical models. Unadjusted and adjusted logistic regression analysis were conducted. Odds ratios (OR) and their corresponding 95% confidence intervals were calculated.

Results: Race/ethnicity was not statistically significantly associated with late stage disease. Adjusted OR for NH-B was 0.94 (95% CI 0.78-1.38), for NH-API 1.07 (95% CI 0.86-1.33) and for Hispanic 1.03 (95% CI 0.85-1.25). Ewing sarcoma was associated with 28% increased odds of presenting with metastases using the adjusted analysis when compared to osteosarcoma (OR=1.28 (95% CI 1.10-1.49). Additionally, men had a 1.35-fold increase in odds of presenting with late stage disease compared to women (OR 1.35; 95% CI 1.22-1.51).

Conclusions-Implications: The lack of association between race and advanced stage of disease could be attributed to cheap, readily available initial screening of bone malignancies and a decreased pain threshold of bone tissue. High availability and low cost for initial management of bone malignancies though plain radiographs might attenuate a potential relationship among race/ethnicity and advanced stage of diagnosis. The rich sensory innervation of bone may prompt early symptomatology and initiate an early work up. Future studies may include socioeconomic status and insurance coverage as covariates in the analysis.

P17

Insurance status as a modifier of the association between race and stage of prostate cancer diagnosis in Florida during 1995 and 2013

Tiffany Beguiristain. Julieta Morano. Evelyn C. Ramirez. Noël C. Barengo, MD, MPH, PhD. Grettel Castro, MPH. Pura Rodriguez de la Vega, MPH. Alan M. Nieder, MD.

Herbert Wertheim College of Medicine, Florida International University, Miami, FL

Keywords: Prostate, Cancer, Insurance, Race, Medicare

Introduction and Objectives: Cancer stage at diagnosis is a critical prognostic factor regarding a patient's health outcomes. Historically, it has been identified that black males are at increased risk of presenting with late stage prostate cancer when compared with whites. This study aimed to investigate whether insurance status was a modifier of the association between race and stage of prostate cancer at the time of diagnosis in Florida between 1995 and 2013.

Methods: This secondary data analysis of a cross-sectional survey used information from the Florida Cancer Data System. Study participants included black and white males diagnosed with prostate cancer in Florida between 1995 and 2013. Those with missing data regarding race, stage of cancer at diagnosis, and/or insurance status were excluded. The main outcome variable was stage of prostate cancer at diagnosis. The main independent variable was race (black vs white). The possible effect modifier variable was insurance status (injured, uninjured, Medicaid and Medicare). Unadjusted and adjusted logistic regression models were used to explore the association between race, insurance status and stage at diagnosis. Odds ratios (OR) and 95% confidence intervals (95% CI) were calculated.

Results: This study included 224,819 participants. Black males were more likely to be diagnosed with late stage prostate cancer (OR) 1.31; 95% CI 1.27-1.35). Being uninsured (OR 2.28; 95% CI 2.13-2.45) or having Medicaid (OR 1.84; 95% CI 1.70-1.98) was associated with a diagnosis of late stage cancer. (The interaction term black*Medicare was statistically significant. Stratified analysis for health insurance revealed that blacks had an increased risk for late stage cancer if uninjured (OR 1.29; 95% CI 1.07-1.55) and if having Medicare (OR 1.39; 95% CI 1.31-1.48).

Conclusions-Implications: Insurance status may modify the effect of race on late stage prostate cancer in black patients. Racial disparities and the effects insurance status has on stage of prostate cancer at diagnosis were elucidated. These findings along with the observed regional differences call for public health initiatives and intervention programs that target vulnerable communities with the greatest disparities, allowing for proper expansion of care and adequate acquisition of services.

P18

The association between health insurance status and stage of primary cutaneous melanoma at presentation

Deannys Batista. Manuel E. Borobia. Ricardo A. Collazo. Grettel Castro, MPH. Pura Rodriguez de la Vega, MPH. Juan M. Acuña, MD, MSc, FACOG. Juan C. Zevallos, MD.

Herbert Wertheim College of Medicine, Florida International University, Miami, FL

Keywords: Insurance Status, Melanoma, Socioeconomic Status, Stage of Presentation

Introduction and Objectives: Annually, melanoma only accounts for 5% of all skin cancer diagnoses; however, it has a 63% and above mortality rate if diagnosed in later stages. Recently published literature suggests a correlation between low socioeconomic status (SES) and increased incidence of melanoma diagnoses at advanced stages. A similar association has been found between Medicaid users and melanoma diagnosis at advanced stages. The objective of our study is to determine the association between health insurance status, as a proxy for SES, and stage of melanoma at diagnosis.

Methods: This is a retrospective cohort study that utilized the Surveillance, Epidemiology, and End Results (SEER) data from years 2007 to 2018. We included patients 18- 64 years old with first diagnosis of cutaneous melanoma, excluding patients with prior diagnosis of skin cancer, unknown insurance status, or unknown or un-staged cancer. The association of selected characteristics by exposure and outcome was analyzed using Chi-squared and Student's t-test. Binary logistic regression was conducted to obtain unadjusted and adjusted odds ratios and 95% confidence intervals to assess the effect of health insurance status (Uninsured v. Insured) on cutaneous melanoma stage at presentation (Early v. Late).

Results: Our sample included 31,338 patient records. After adjusting for age, sex, race, ethnicity, marital status, and geographic location, the odds of being diagnosed with a later stage of melanoma is 2.8 times greater in uninsured patients compared to insured patients (OR = 2.82, CI 95% 2.51-3.17, p<0.001). The odds of presenting with later stage melanoma was 1.5 times greater in Spanish-Hispanic-Latino patients (OR = 1.50, 95% CI 1.22-1.82, p<0.001) than in non- Spanish-Hispanic-Latino patients; 1.3 times greater in Single/Unpartnered patients (OR = 1.33, 95% CI 1.22-1.45, p<0.001) than in married/Partnered patients; and 1.2 times greater in patients living in non-metropolitan areas (OR = 1.23, 95% CI 1.10-1.38, p<0.001) than those living in Metropolitan areas.

Conclusions-Implications: Our findings suggest that uninsured patients had significantly higher odds of presenting with later stages of cutaneous melanoma. Other risk factors for later stage presentation include being Spanish-Hispanic-Latino, being Single/Unpartnered, and living in non-metropolitan areas. Future research is needed to elucidate if lower SES is associated with later melanoma stage diagnosis at presentation in other minority groups, single/unmarried patients living in rural areas.

P19

The association between household income and childhood depression in American children aged 5-18 years old

Carole Marie Fraley, BS. Christian Oliveros, BS. Tiffany Race, BA. Juan M. Lozano, MD, MSc. Melissa Ward-Peterson, MPH, PhD.

Herbert Wertheim College of Medicine, Florida International University, Miami, FL

Keywords: Depression, Household Income Level, Poverty Level, Childhood, Prevalence

Introduction and Objectives: Childhood depression is an under-recognized illness that can have long-term detrimental effects. Risk factors should be studied in order to identify children who could benefit from early interventions. Our research question is testing the association between a family's income level and childhood depression.

Methods: This is a cross-sectional study using data collected in the 2011 National Survey of Children's Health, a telephone survey conducted to households in the United States. We stratified household income into eight categories in relation to poverty level and tested the association between the presence of childhood depression, and other possible confounders. Childhood depression was determined using the question "has a doctor or other healthcare provider ever told you that [their child] had depression?" To adjust for the potential confounders, we used multivariate regression analysis.

Results: 62,950 of the 95,677 responses were included. The number of responses was limited by our exclusion criteria, which was not having data on either depression or income level. We found that there is an inverse association between household income and the prevalence of childhood depression. There was a notable drop off between the 151-185% and 186-200% poverty level. Below 185%, the prevalence of depression is greater than 5.2%, but above 186% the prevalence is less than 4.5%. After observing other variables that were cited as potential confounders in the literature review, the variables mother's mental health, child services, child problems, and age showed statistically significant increased odds of depression. After adjusting for these potential confounders, there remained a significantly increased odds of depression across several income levels (</=100%, 101-133%, 134-150%, 151-185%, 201-300%, and 301-400%). The adjusted odds ratios for childhood depression were as follows: <100% of poverty level OR=2.8 (95% CI 1.8-4.4), 101-133% OR=2.3 (95% CI 1.4-3.7), 151-185% OR =2.1 (95% CI 1.2-3.5), 201-300% OR=1.7 (95% CI 1.1-2.7), and 301-400% OR=2.1 (95% CI 1.4-3.1). All other income levels showed OR>1 but had non-significant p values.

Conclusions-Implications: This study highlights that, after adjusting for potential confounders, several household income levels are associated with increased odds of childhood depression.

P20

Health characteristics associated with Affordable Care Act Marketplace enrollment in 2017

David M. Mendoza, BS. Ashley Miller, BS. Sonny Arre, BA. Pura Rodriguez de la Vega, MPH. Frederick W. Anderson, MD. Natalie Castellanos, JD. Marcia H. Varella, MD, PhD, MHS.

Herbert Wertheim College of Medicine, Florida International University, Miami, FL

Keywords: Patient Protection and Affordable Care Act, Health Insurance Exchanges, Insurance Coverage, Health Reform, Health Economics

Introduction and Objectives: The affordability and sustainability of the health insurance marketplaces established by the Patient Protection and Affordable Care Act (ACA) are of concern, possibly due to a lack of diversity of Marketplace enrollees as a risk-pool. This study aims to assess whether selected health characteristics of Marketplace enrollees differ from those of individuals with employer-sponsored insurance (ESI).

Methods: Exploratory, secondary analysis of data from the 2017 National Health Interview Survey (NHIS). Adults (18-64 years old) with family incomes that qualify for Marketplace tax subsidies (100-399% of Federal Poverty Level) were included. Those with Marketplace enrollment were compared to adults with ESI based on demographic characteristics, health-related behaviors, presence of chronic medical conditions (including hypertension and diabetes), and health care utilization patterns. Independent associations were assessed through multivariate logistic regression and reported as odds ratios and corresponding 95% confidence intervals.

Results: We studied 4,090 eligible respondents. About 9.2% had Marketplace insurance. The odds of having Marketplace insurance over ESI were higher for participants: 46-64 years old [compared to those 27-45 years old, adjusted odds ratio (aOR)=2.1, 95% confidence interval (CI)=1.5-2.9]; with incomes lower than 300% of FPL (aOR=3.8, 95%CI=2.6-5.5 for the income group 100-199% of FPL); who were not working in the week prior to the survey (aOR=2.2, 95%CI=1.7-2.9); and who were current moderate/heavy alcohol users (aOR=1.5, 95%CI=1.0-2.1 compared to those who drink alcohol &<4/week). Compared to Whites, Blacks had lower odds of having Marketplace insurance (aOR=0.5, 95%CI=0.3-0.8). We found no independent association between BMI, smoking, functional status, any chronic medical condition, or health care utilization pattern, and having Marketplace insurance over ESI.

Conclusions-Implications: Marketplace enrollees were not surprisingly, more socioeconomically vulnerable (lower income and "not working") than those with ESI. Yet, even after adjusting for socioeconomic factors, they were also older, which could represent a greater risk to insure. Further studies are indicated to affirm the presence of an age imbalance among Marketplace enrollees and its potential implications on Marketplace sustainability. Additionally, a decreased likelihood among black adults to enroll in Marketplace insurance over ESI may underscore a need to better understand.

P21

Memory CD4 T cell recall responses against influenza A virus are retained during pregnancy

Valeria Flores Malavet, BS. Ashley A. Gilchrist, BS. Fahmida Alam, BS. Tara M. Strutt, PhD.

University of Central Florida, Orlando, FL

Keywords: Immunological Memory, CD4 T Cells, Influenza A Virus, Pregnancy

Introduction and Objectives: Despite widespread annual vaccination, Influenza A virus (IAV) remains a global health concern. Serious illness can occur in susceptible individuals including children, the elderly and pregnant women. The physiological changes associated with pregnancy are well known to cause alterations in the immune system, resulting in a bias towards the generation of humoral or antibody responses at the cost of cell mediated immunity. The latter is essential for anti-viral immune responses. While much is known about alterations to the generation of primary immune responses, how memory or secondary immune responses, such as those induced by vaccination, are impacted during pregnancy is unexplored. We examine here, the responsive capacity of memory CD4 T cells specific for influenza A virus in gravid and non-gravid hosts during recall infection.

Methods: Timed-pregnant female Balb/c mice and non-gravid controls were adoptive transfer recipients of in vitro generated IAV-specific memory CD4 T cells that were challenged with sublethal doses of A/PuertoRico/8/1934 (PR8) virus. Briefly, naïve HNT CD4 T cell receptor transgenic cells, which are specific for a peptide of the hemagglutinin of PR8, were isolated and polarized in vitro to generate the Th1 CD4+ effectors that were subsequently rested to generate the donor in vitro memory cells (rested effectors). On day 7 post infection, the number of donor memory cells, surface expression of CD127 (IL-7 receptor), and production of the cell-mediated response associated cytokines IFN-g, TNF, and IL-2 in the spleen, draining lymph nodes, and lung was determined in recipient hosts by flow cytometry. The fetal outcomes in similarly treated animals and unmanipulated controls were also monitored.

Results: The recovery of donor memory CD4 T cells in all organs was found to be similar between gravid and non-gravid female mice on d7 of sublethal IAV infection. Likewise, the functional capacity of memory CD4 T cells in terms of multi-cytokine IFN-g, TNF, and IL-2 production, which is associated with protective cell mediated immunity, was unaltered by the pregnancy environ. However, surface expression of CD127 that is essential for memory CD4 T cell survival was found to be significantly increased on donor memory CD4 T cells responding in gravid females versus non-gravid controls.

Conclusions-Implications: Our preliminary observations suggest that in contrast to the known impacts on the generation of primary immune responses, the altered physiological environment of pregnancy has a minimal impact on the responsiveness of in vitro generated Th1 memory CD4 T cells. Future work will explore the implications of altered CD127 expression on the ability of memory CD4 T cells to survive as well as the impact of functional memory responses on fetal outcomes.

P22

Cryopreserved influenza A virus (IAV)-specific memory CD4 T cells are capable of mediating protection against lethal doses of virus

Fahmida Alam, BS. Ashley Gilchrist, BS. Tara M. Strutt, PhD.

University of Central Florida, Orlando, FL

Keywords: Influenza A Virus, Adoptive T Cell Therapy, Memory CD4 T Cells

Introduction and Objectives: Pregnant women are at a higher risk of Influenza-related illness compared to the general adult population. However, in the last 10 flu seasons, at best, only 50% pregnant women got vaccinated, leaving half the pregnant population, their prenates, and neonates unprotected from seasonal Influenza A Virus (IAV). The only FDA-recommended flu antiviral drug for pregnant women possesses fatal risks to pregnancy and prenatal development. In this study, we address whether adoptive therapy with cryopreserved virus-specific memory cells has potential as a therapeutic to protect against serious IAV infection.

Methods: Naïve cells were isolated from spleen and peripheral lymph nodes of HNT-CD4+ transgenic mice that express a TcR specific for the A/Puerto Rico/8/1934 (PR8) strain of IAV. TH1 effector were generated in vitro using standard protocols. Day 4 effectors were rested for 3 days in the absence of antigen to generate in vitro memory cells (rested effectors) that were then cryopreserved and stored in -80°C. The thawed memory cells used in adoptive transfer experiments were untreated or cultured for 24 hours with growth factor cytokines, IL-7 or IL-7 and IL-2 prior to use. Recovered memory cells were adoptively transferred to congenic BALB/c hosts that were subsequently challenged with lethal doses of PR8 virus and morbidity and mortality monitored. At day 19 post infection, the numbers of and multi-cytokine producing potential of the transferred donor CD4+ T cells in spleens, draining lymph nodes (dLN), and lungs were enumerated by flow cytometry.

Results: Cryopreserved and thawed in vitro-generated CD4+ memory T cells, both untreated and cultured for 24 hrs with cytokines IL-7 or IL-7 and IL-2, mediate protection against lethal doses of IAV. Enhanced recovery as early as day-5 post infection is seen with thawed cells cultured overnight with IL-7 as well as the combination of IL-7 and IL-2. At day 19 post-infection, donor memory CD4 T cells derived from thawed cells cultured overnight with cytokines were found to produce significantly more IFN-g, IL-2, and TNF in the lungs and draining lymph nodes (dLN) of infected mice.

Conclusions-Implications: Cryopreserved IAV-specific memory cells are efficient at mediating protection against lethal doses of virus. Overnight culture with the growth factors IL-7 and IL-2 post thaw enhances the protective and multi-cytokine producing potential of the cryopreserved IAV-specific memory CD4+ T cells. These observations suggest that adoptive therapy with cryopreserved IAV-specific memory cells has potential as a therapeutic to protect against serious virus infection.

P23

Therapeutic plasma exchange in immune thrombocytopenia (ITP) related hospitalizations: Real world practices for a category III apheresis indication

Sarah Makhani, BA[1]. Joseph Schwartz, MD, MPH[2]. Aaron Tobian, MD, PhD[3]. Saurav Chopra[4]. Ljiljana Vasovic, MD[4]. Robert Andrew Desimone, MD[4]. Patricia Shi, MD[5]. Shipra Kaicker, MD[4]. Cassandra Josephson, MD[4]. James Bussel, MD[4]. Ruchika Goel, MD, MPH[4].

[1]*Herbert Wertheim College of Medicine, Florida International University, Miami, FL*

[2]*Columbia University Medical Center*

[3]*Johns Hopkins Medicine*

[4]*Weill Cornell Medicine*

[5]*New York Blood Center*

Keywords: Therapeutic Plasma Exchange, Immune Throbocytopenic Purpura, Apheresis, Hematology, Plasmapheresis

Introduction and Objectives: Therapeutic plasma exchange (TPE), is used in various hematological disorders. Per the American Society for Apheresis (ASFA) guidelines, TPE is a Category III indication in the management of ITP. Category III means the optimum role of apheresis therapy is not established and decision making should be individualized. This study evaluates nationwide TPE use in hospitalized adults with a primary admission diagnosis of ITP.

Methods: Hospitalizations with ITP as the primary admitting diagnosis were analyzed from the 2010-2014 National Inpatient Sample (NIS). NIS is the largest all-payer inpatient database for United States hospitalizations. Univariate and multivariable logistic regressions were used to determine predicting factors of TPE and clinical outcomes in ITP patients undergoing TPE.

Results: From 2010-2014, analyzing hospitalizations with ITP listed as 'one of all diagnoses' during hospital course, there were total of 282,285 admissions of which 1,452 admissions (0.6%) reported TPE. Of the 60,940 primary ITP admissions, 1.04% admissions (n=635) reported TPE during the hospital course. Most subjects getting TPE were the highest disease severity class: Major (30.4%) and Extreme severity (49.5%). There were approximately 50% co-morbidities among ITP admissions undergoing TPE: acute kidney failure (27.3%), hemolytic anemia (11.1%), acute respiratory failure (10.6%), systematic lupus erythematosus (4.8%), human immunodeficiency virus (2.4%), and hepatitis C (2.4%). Among all ITP admissions, 12.3% reported at least one bleeding complication (gastrointestinal, 6.2%, genitourinary, 5.3%, and intracerebral hemorrhage, 1.05%). Among ITP hospitalizations with TPE, 20.9% cases reported at least one bleeding complication ($p<0.05$). After multivariable analysis, underlying severity of illness remained the most significant predictor of undergoing TPE ($p<0.001$). Admissions categorized as major (adjOR=3.53, 95%CI=2.01-6.19, $p<0.001$) and extreme severity of illness (adjOR=33.07, 95%CI=19.22-56.90, $p<0.001$) had substantially higher odds of undergoing TPE than less severe hospitalizations. Admissions with TPE also had significantly longer mean length of stay ($p<0.001$). All-cause mortality was 1.4% among all ITP hospitalizations and 7.8% in ITP hospitalizations with TPE. However, patients with TPE showed neither an improvement nor a worsening in the adjusted odds of all-cause mortality (p-value=0.142) bleeding status (p-value=0.755).

Conclusions-Implications: TPE was reported in about 1% of hospitalizations with ITP as the primary diagnosis in this nationally representative sample between 2010-2014. TPE was performed in patients with highest severity of underlying illness, more significant bleeding, and a high (50%) rate of comorbidities. No clear associations with improvement or worsening of mortality or bleeding outcomes was seen in ITP hospitalizations reporting but neither was there any evidence of increased bleeding or morbidity with the procedure

P24

Effect of short and long sleep duration in predicting obesity among various racial groups of a large multi ethnic organization

Muhammad Aziz, MD, MPH. Tanuja Rajan, MD. Dorty Morency, MD. Mythili Penugonda, MD. Nicole Ross, DO. Muhammad Latif, MD. Maribeth Rouseff. Henry Guzman, RN. Theodore Feldman, MD. Ehimen Aneni, MD, MPH. Emir Veledar, MD. Khurram Nasir, MD, MPH.

Baptist Health South Florida

Keywords: Sleep Duration, Obesity, Racial Disparities

Introduction and Objectives: Background Literature shows strong association of abnormal sleep duration with obesity and increased CVD morbidity and mortality, but less is known how abnormal sleep duration is related to obesity among racial groups. The purpose of this study is to predict relationship of self-reported sleep duration with obesity across different racial groups.

Methods: Annual Health Risk Assessment is done yearly at Baptist Health South Florida for employees. According to CDC. gov, we categorized self-reported sleep duration (hrs) as short (<7), reference (≥7 - ≤ 9) and long sleep (>9), while obesity (BMI kg/m2) was categorized as class 1 (BMI=30-34.9), class 2 (BMI= 35- <40) and class 3 (BMI ≥40).

Results: Population consisted n=9701; 74% female; mean age 42.6 ±12 yrs. Racial groups were 57% Hispanics, 16% Black,17% White, 5% Asian and 5% Non-Hispanic-other. In fully adjusted model, when compared to Hispanic group sleeping 7-9 hours (reference), odd of class 1 obesity was higher among black sleeping <7 hrs; however, the odds of class 2 and class 3 obesity were significantly higher among Hispanic, Black, White and Non-Hispanic-other sleeping <7 hrs. Asian group was the only group that showed decreased odds of obesity across any sleep duration (figure 1).

Conclusions-Implications: Study shows that sleep durations have varied effects on obesity among different races. Short or long sleep duration for one group may not be a better predictor of obesity in another racial group. Further studies are needed to revise the current sleep duration categories among various races.

P25

Weapon carrying and mental health concerns among victims of cyber-bullying

Dickran Nalbandian, MS. Christina Rios. Daniela Sosa. Daniel Castellanos, MD. Juan M. Lozano, MD, MSc.

Herbert Wertheim College of Medicine, Florida International University, Miami, FL

Keywords: Weapon-Carrying, Cyberbullying, Mental Health

Introduction and Objectives: School violence has recently gained national attention. In several cross sectional studies, weapon carrying was associated with multiple interrelated factors which include demographic, psychosocial, behavioral, and school-related characteristics of high-school age adolescents. This study examined the association between electronic bullying and carrying weapons to school in high school students in the United States.

Methods: The data for this cross-sectional study was extracted from the Center for Disease Control's (CDC's) 2017 Youth Risk Behavior Surveillance System (YRBS) database. The questionnaire was administered to statistically representative samples of high school students in grades 9-12 across the United States. The association between experiencing cyberbullying and carrying a weapon in school was evaluated through multivariate (logistic) regression analysis while controlling for several confounders (age, gender, race, sexual orientation, BMI, mental health issues, academic performance, experiencing traditional physical bullying, and drug and alcohol abuse).

Results: Among 11,637 students included, 14.2% and 14.6% reported being victims of cyberbullying and carrying a weapon to school in the past 30 days, respectively. No significant association was found in carrying weapons for victims of cyberbullying when compared to students not cyberbullied (adjusted OR 0.9, 95% CI 0.7-1.2, p=0.47). This study confirmed the association between carrying weapons in school and male gender (aOR 5.3, 95% CI 4.3-6.5, $p<0.0001$), victim of traditional physical bullying (aOR 1.4, 95% CI 1.1-1.7, p=0.002), poor academic performance (aOR 1.3, 95% CI 1.1-1.6, p=0.002), previous suicidal attempt (aOR 1.6, 95% CI 1.2-2.2, p=0.003), alcohol lifetime use (aOR 2.5, 95% CI 1.9-3.2, $p<0.0001$), and illicit drug use (aOR 2.0, 95% CI 1.7-2.4, $p<0.0001$).

Conclusions-Implications: Cyberbullying was not significantly associated with increased risk of weapon carrying into campus in high school students. Weapon carrying was significantly associated with multiple interrelated factors including male gender, traditional bullying, poor academic performance, and behavioral health issues. Decreasing rates of weapon carrying would be a viable strategy in order to decrease severity of violence in schools. Implications of this study for prevention indicate a need for comprehensive multidisciplinary services in high schools that include mental health counseling aimed at behavior change, as well as programs directed at decreasing adolescent substance abuse.

P26

3D conformal radiotherapy versus intensity-modulated radiotherapy for patients with frontal lobe cancer

Shahodat Voreis, BA. Michelle Trieu, BS. Grettel Castro, MPH. Juan M. Lozano, MD, MSc.

Herbert Wertheim College of Medicine, Florida International University, Miami, FL

Keywords: 3D Conformal Radiotherapy, Intensity Modulated Radiotherapy, Frontal Lobe Tumor

Introduction and Objectives: Frontal is the largest lobe of the brain and is vital to executive and motor functions. Tumors in this area require targeted treatment. Both intensity-modulated radiation therapy (IMRT) and 3D-conformal radiation therapy (3D-CRT) are external beam radiotherapies. IMRT is a more advanced version of 3D-CRT. This study assessed whether surgery and IMRT conferred better survival rates than surgery and 3D-CRT to patients with frontal lobe cancers.

Methods: This is a retrospective cohort study using 2014 Florida Cancer Data System (FCDS), which contains aggregated data from all cancer patients in Florida from 1981 to 2014. All patients who had frontal lobe cancer and surgery with either IMRT or 3D-CRT were included in the analysis. The Kaplan-Meier method was used to compare survival curves and the Wilcoxon test to compare median time of survival. A Cox proportional hazards model was used to generate hazard ratios adjusted for age at diagnosis, extent of surgical excision and tumor staging.

Results: The analysis included 505 and 60 patients who received IMRT and 3D-CRT respectively. More patients in IMRT group had local tumor excision (39.4% versus 25.4%) and were older at time of diagnosis than patients in 3D-CRT group (54.8 versus 50.6 years old). On the contrary, more patients in 3D-CRT group had total lobectomy than the IMRT group (40.7% versus 25.6%). Sex, stage of cancer, insurance status, adjuvant chemotherapy or grade of cancer showed no statistically significant difference between radiation therapies. Median survival time was higher in patients who underwent 3D-CRT (25 months) compared to patients who underwent IMRT (18 months) (p=0.043). Cox regression adjusted for age at diagnosis, extent of surgical excision and tumor stage showed no statistically significant difference in survival between the two radiation treatments (HR=0.95, CI 0.65-1.4; p=0.8). Further, age at diagnosis, extent of tumor excision and adjuvant chemotherapy were associated with statistically significant differences in survival.

Conclusions-Implications: There is no difference in mortality of patients with frontal lobe cancer treated with surgery and either 3D-CRT or IMRT. A randomized controlled study is necessary to determine whether this conclusion holds true for different types of tumors despite the anatomical location.

P27

Demographic variation in the frequency of glioma in Florida

Dharam Persaud-Sharma, MSBE, PhD. Joseph Burns, BSc. Jeran Trangle, MSc. Grettel Castro, MPH. Noël C. Barengo, MD, MPH, PhD. Sabyasachi Moulik, PhD. Juan M. Lozano, MD, MSc.

Herbert Wertheim College of Medicine, Florida International University, Miami, FL

Keywords: Glioma, Brain Cancer, Race, Florida, Demographics

Introduction and Objectives: Glial brain cancers affect nearly 20,000 individuals in the United States (U.S.) annually. Currently, SEER database data exploring the relationship between race and gliomas is available and have shown that cerebral gliomas have a higher frequency in Caucasian men. However, such analyses did not include demographic data specific to the state of Florida. This study assessed the association between race and glial vs. non-glial Central Nervous System (CNS) cancers in Florida, U.S.

Methods: This case-control study utilized the Florida Cancer Data Registry (FCDS) in which race was considered the exposure and development of glioma as the measured outcome. The sample was comprised of patients in Florida diagnosed with brain tumors from 1981 to 2013. Relative racial frequencies were compared between patients with glial brain tumors and those with other CNS tumors in Florida. Data was analyzed using logistic regression analysis in order to determine any associations between race and frequency of diagnosis adjusting for several confounders (age, sex, smoking status, year of diagnosis, and insurance status).

Results: Between 1981 and 2013 a total of 14,092 patients meeting the inclusion and exclusion criteria were diagnosed in Florida with a primary brain tumor. Being of non-white race was associated with a 60% decreased odds of glioma diagnosis compared to the reference white population (adjusted OR 0.4, 95% CI 0.34-0.47). Secondary findings include associations between increasing age and male sex with increased odds of glioma diagnosis. Decreased adjusted odds of glioma diagnosis were found with former smoking status (reference non-smokers), diagnosis between 2001 and 2010 (reference 1981-1990), and Medicaid or Medicare insurance (reference private insurance). Hispanic ethnicity, current smoking status, no insurance/self-pay, and geographical location (urban vs. rural) all had no association with glioma diagnosis.

Conclusions-Implications: These finding are consistent with and help reinforce previous studies utilizing national databases (SEER) which also showed increasing odds of glioma diagnosis in older white males. Various potential explanations for these findings include genetic predisposition, lifestyle and behavioral factors, and socioeconomic status, including access to healthcare. Future research aims at identifying potential genetic etiologies.

P28

Stroke outcomes in Florida pediatric and adult sickle cell patients: A retrospective, secondary analysis of the Florida hospital discharge database for stroke, 2008-2012

Francisco Irizarry, BS. Nicholas Schmoke, DPT. Jason Llaneras, BS. Juan G. Ruiz, MD, MMedSci. Melissa Ward-Peterson, MPH, PhD.

Herbert Wertheim College of Medicine, Florida International University, Miami, FL

Keywords: Sickle Cell, Stroke, Risk Factors

Introduction and Objectives: Due to the high incidence of stroke in patients with sickle cell disease coupled with the severe, costly, and long-lasting effects, it is crucial to investigate this population. To date, there is minimal published data on stroke outcomes in pediatric and adult patients with sickle cell disease. The purpose of this study is to provide a modern look at the association between age and stroke outcome in a population of sickle cell disease patients.

Methods: A retrospective secondary analysis of the Florida Hospital Discharge Database for Stroke was conducted which included all patients (N=333,367) admitted to Florida hospitals with a primary diagnosis of stroke between January 1, 2008 and December 31, 2012. The exposure variable was age at admission which was dichotomized into two comparison groups: pediatric and adult. The dependent variable was stroke outcome. Variables of interest were mechanism of stroke, comorbidities and patient demographics.

Results: 210 hospitalizations for stroke in patients with sickle cell disease were identified. While the overall prevalence of adverse outcome was 50%, the odds was significantly higher in the adult subgroup (OR=3.20, 95% CI=[1.57,6.76]) compared to the pediatric subgroup. Additionally, the rate of adverse outcomes was significantly higher in patients with a hemorrhagic stroke compared to an ischemic stroke (OR=2.70,95% CI=[1.46-4.99]).

Conclusions-Implications: In a statewide patient population sample, the odds of having an adverse outcome in adult patients with sickle cell disease was significantly higher when compared to a pediatric subgroup. Clinicians should take into consideration a patient's age to guide assessment, management and prognosis of stroke in the sickle cell disease population.

P29

MMP-13 as a therapeutic target in paclitaxel-induced neuropathy

A. Cirrincione, BS[1]. A. Pellegrini, BS[2]. J. Dominy[2]. B. Buonocore[1]. S. Rieger, PhD[1].

[1]*University of Miami, Miami, FL*

[2]*MDI Biological Laboratory*

Keywords: Peripheral Neuropathy, Neurodegenerative Disease, Toxicology, Neuropharmacology, Regenerative Medicine

Introduction and Objectives: Paclitaxel is a chemotherapeutic agent administered as a first-line treatment to breast, ovarian, and lung cancer patients. Sixty to 70% of patients experience paclitaxel-induced peripheral neuropathy (PIPN), which is characterized by pain, temperature sensitivity, tingling, and numbness in the hands and feet due to sensory axon degeneration. Why patients develop this side effect remains unclear. One theory is that pathogenesis stems from mitochondrial dysfunction and damage, which has been observed to precede pain and sensory axon degeneration. However, a mechanism linking mitochondrial damage as a source of PIPN has not yet been established.

Methods/Results: We developed a zebrafish in vivo model of paclitaxel neurotoxicity and identified that hydrogen peroxide (H2O2) formation in the epidermis of the skin plays a critical role in paclitaxel-induced sensory axon degeneration. We show that H2O2 formation upregulates MMP-13 expression specifically in keratinocytes, whereas MMP-13 inhibition prevents axon degeneration. To determine the source of H2O2 we performed transient transgenesis to target the H2O2 sensor HyPer to the mitochondria in epidermal keratinocytes and sensory axons. This revealed increased mitochondrial H2O2 upon paclitaxel treatment, consistent with previous literature, suggesting mitochondrial damage could play a role. To further confirm this, we analyzed mitochondria structure with confocal imaging and transmission electron microscopy, which indicates that paclitaxel causes distinct mitochondrial defects in keratinocytes and in sensory axons. Keratinocyte-specific mitochondria show acute toxicity evident by shrinkage and subsequent long-term effects by which these organelles swell. Sensory axons also display acutely damaged mitochondria that obtain vacuoles, which are interestingly not present in keratinocyte mitochondria. However, these vacuoles remain similar even in non-degenerating axons after prolonged treatment. This suggests that vacuole formation might not be directly linked to axon degeneration. We are currently also employing time-lapse imaging to study mitochondrial dynamics in both cell types in response to paclitaxel treatment.

Conclusions-Implications: These findings demonstrate that mitochondria in sensory axons and epidermal keratinocytes are distinctly affected by paclitaxel treatment, but that acute keratinocyte stress is playing a critical role in axon degeneration.

P30

Exosomal amyloid beta (Aβ) DNA sequence as a potential Alzheimer's disease marker

Akshaykumar Galande, MS. Kiminobu Sugaya, Ph.D.

University of Central Florida, Orlando, FL

Keywords: Alzheimer's Disease, Exosomes, Amyloid Beta (Aβ), Diagnostic Biomarker, Human Neural Stem Cells (hNSC)

Introduction and Objectives: Alzheimer's Disease (AD) is a neurodegenerative disease affecting more than 44 million people worldwide. Although recent advancements have shed lights on mechanisms and pathways responsible for its origin, development, and pathogenesis, we are still unsuccessful in finding an effective cure. Brain-imaging methods are used for the detection of AD, but it does not allow early detection of the disease and is ineffective in monitoring disease progression. Furthermore, amyloid plaques, a major hallmark of AD, resulting from the aggregation of amyloid beta (Aβ), is a consequence of abnormal processing of the Amyloid precursor protein (APP) gene. As exosomes, microvesicles of size 30-100nm, secreted by almost all type of cells are thought to play a crucial role in cellular communication and Aβ clearance, we aim to investigate the APP DNA sequence associated with exosomes to look for differential Aβ sequence.

Methods: Normal and AD ips-derived human neural stem cells (hNSC) were maintained in a human neural stem cell culture media. Exosomes were collected from 80-90% confluent cell culture media and precipitated using a modified PEG-NaCl method. Further, PCR was carried out to amplify Aβ sequence using specific Aβ primer sequences followed by electrophoretic analysis.

Results: We've found the presence of Aβ sequence associated with exosomes in ips-derived human neural stem cells (hNSC) used as a control, but not with AD-hNSC. Our future goal is to analyze the Aβ sequence associated with exosomes that can be identified as a prognostic/diagnostic biomarker of AD.

Conclusions-Implications: As exosomes can cross the blood-brain barrier (BBB) and is abundantly in body fluids such as blood, urine, and serum, this study could provide a minimally-invasive biomarker to detect disease well before its clinical appearance.

P31

Postoperative complications as related to body mass index in total robotic hysterectomy: A retrospective study

Rommel Chiriboga. Angel Porras, BS. Grettel Castro, MPH. Noël C. Barengo, MD, MPH, PhD. Juan M. Acuña, MD, MSc, FACOG. Emery Salom, MD.

Herbert Wertheim College of Medicine, Florida International University, Miami, FL

Keywords: Hysterectomy, BMI, Complications, Total Abdominal Hysterectomy

Introduction and Objectives: With the increasing use of total robotic hysterectomy (TRH), comes the challenge of minimizing negative postoperative outcomes associated with this procedure. Considering the negative impact on patient well-being, knowing if there is an association between BMI and the risk of developing postoperative complications could help in preparing physicians to act earlier with this subset of patients. The objective of the study was to test for the association between BMI post-operative complications in women that underwent THR.

Methods: A retrospective cohort study using the Gynecological Research Group database using patients who had undergone TRH between 2002-2016 in Miami Dade and Broward Counties, Florida was conducted. Patients with missing information on key variables

and patients with underweight were excluded from the study. The independent variable was BMI categorized as normal weight (18.5 - 24.9 kg/m2), overweight (25 - 29.9 kg/m2), obese (30 - 39.9 kg/m2) and morbidly obese (greater than 40 kg/m2)). The dependent variable was the development of a postoperative complication within thirty days. Unadjusted and adjusted Cox proportional hazard regression models were performed. Hazard ratios (HR) and 95% confidence intervals (CI) were calculated.

Results: Of all included patients (n=1121), 27% (n=305) belonged to the normal BMI group, 33% (n=368) to the overweight group, 32% (n=358) to the obese group and 8% (n=90) to the morbidly obese group. No association between BMI and post-operative complications were found. The adjusted HR for overweight patients was 1.2 (95% CI 0.9-2.4), 1.15 (95% CI 0.7-2.0) for the obese group and 1.08 (95% CI 0.5-2.3) for the morbidly obese group. A diagnosis of cancer increased the hazard of post-operative complications by a factor of 1.50 (95% CI 1.01-2.25). Patients with asthma had a 150% increased hazard of complications (HR 2.5 (95% CI 1.4-4.2)).

Conclusions-Implications: The results suggest that special perioperative attention may not be needed, based on BMI. Further research with larger sample sizes to reduce the chance of type II error, studies analyzing other covariates such as race, previous abdominal surgeries, and abdominal circumference, and studies with asthma as the primary independent variable, should be performed.

P32

A rare case of an unruptured 13-week spontaneous heterotopic pregnancy

Rahil H. Shah, BS[1]. Carlos E. Linares, BS[1]. Pooja Gurnani, BS[1]. Charles II Agustus, MD[2].

[1]Herbert Wertheim College of Medicine, Florida International University, Miami, FL

[2]Baptist Health System

Keywords: Heterotopic Pregnancy, Second Trimester Pregnancy, Ectopic Pregnancy

Introduction and Objectives: Heterotopic pregnancy (HP) is the coexistence of intrauterine and extrauterine (ectopic) gestations. In assisted reproduction techniques (ART) the incidence of HP is 1 in 3,900 pregnancies. On the other hand, spontaneous pregnancies will rarely produce HP, with an incidence of 1 in 30,000. Of those, only about 10% of HP are diagnosed after 11 weeks. Objective: We present the case of a rare heterotopic pregnancy that was discovered at 13 weeks gestation and successfully treated with sapingecto-oophrectomy for the extrauterine pregnancy and a successful 39 week delivery for the viable intrauterine pregnancy.

Case Presentation: A 37 year old African American woman G6P6006 (including twins) of 13 weeks since LMP presents to the Emergency Department at Homestead Hospital at 12:30 AM with complaints of a progressive right lower quadrant abdominal pain that radiates to her right leg since the past four days. She denies any vaginal bleeding or trauma. The patient denies any alcohol, tobacco or recreational drug use of any history of STIs, PID, dysmenorrhea or fibroids. Of her five pregnancies, three were spontaneous vaginal deliveries and two were cesarean sections. On physical exam, she was afebrile with normal vitals. Her abdomen was diffusely tender with marked pain on the right lower quadrant without rebound tenderness. On pelvic exam, her external genitalia was normal with no bleeding. On sterile bimanual exam, no cervical motion tenderness was elicited and no evidence of mucopurulent discharge. CBC, CMP, urinalysis, RPR and transabdominal/transvaginal ultrasound, were ordered. Ultrasound revealed a viable intrauterine fetus with a crown to rump size of 72 mm, consistent with a gestational age of 13 weeks 2 days. Fetal heart rate was 169 beats/minute. However, the ultrasound also revealed a non-viable ectopic fetus in the right adnexa consistent with a gestation age of 7 weeks 4 days. No free fluid in the intraperitoneum was seen. The surgeon performed an emergent right unilateral salpingo-oophorectomy to remove the ectopic pregnancy while sparing the intrauterine pregnancy. Anesthesia induction and maintenance was carefully selected to include lidocaine, propofol, fentanyl, rocuronium, cefazolin, ephedrine, glycopyrrolate, neostigmine and desflurane. Post-operative course was uneventful with regular follow up. At 39 weeks, the intrauterine pregnancy was successfully delivered via c-section.

Conclusions-Implications: Spontaneous heterotopic pregnancy is a very rare condition that poses serious risks for patients if not diagnosed early. This case was particularly remarkable because the patient presented much later than usual, at 13 weeks, even though the ectopic fetus stopped growing at 7 weeks. Multiple precautions must be taken before, during and after the surgery to avoid complications for the mother and fetus. Patient was successfully treated with unilateral salpingo-oophorectomy, and delivered a healthy baby via C-section at 39 weeks gestation.

P33

Detection of somatic cancer associated mutations in tampons of women with germline BRCA1 mutations: A pilot study

Lauren E. Dittman, BA[1]. Jessica Seigel, BS[1]. Leah Cohen, BA[1]. Ebony R. Coats, MSc[1]. Joseph A. Rantus, BS[2]. Yong Shi, PhD[2]. Qi Wei, PhD[2]. Carolyn D. Runowicz, MD[1]. Juan M. Lozano, MD, MSc[1]. Sheldon Cherry, MD[1]. Jeff Boyd, PhD[2].

[1]Herbert Wertheim College of Medicine, Florida International University, Miami, FL

[2]Miami Cancer Institute

Keywords: Ovarian Cancer, BRCA, P53, Screening, Tampon

Introduction and Objectives: Serous epithelial ovarian cancer is frequently diagnosed at advanced stages, partially due to a lack of adequate screening methods. Women with germline BRCA1 mutations have a dramatically increased lifetime risk for the development of ovarian cancer. Therefore the development of noninvasive screening modalities is of interest. To investigate this, we sought to determine whether cancer associated somatic mutations in the TP53 gene could be identified in cellular DNA isolated from tampons in a clinically-well population of germline BRCA1 mutation carriers, and if present, to compare their mutational frequency to a control population.

Methods: A cross-sectional study was designed in which carriers and non-carriers of the BRCA1 mutation were recruited from the community. Participants were recruited in person at a Facing Our Risk of Cancer Empowered (FORCE) conference or through email. Participants qualified for the study if they were over the age of thirty, had intact fallopian tubes, ovaries, and uterus, were comfortable using a tampon and had no history of significant radiation or chemotherapy. They placed a vaginal tampon for 6-8 hours at home and returned the samples to the laboratory through overnight mail. The tampon samples were de-identified, cells were isolated, and DNA was extracted. The DNA was interrogated for the presence of TP53 mutations in 12 exons using the MisSeq/NextSeq sequencer. Archer Analysis 6.0 pipeline was used for data analysis using three ovarian cancer cell lines with known mutations as positive controls and sensitivity controls.

Results: Sixty-six participants were enrolled. Thirty-two BRCA1+ and thirty-four control participants were included for analysis, with an average age of 37.7 and 37.0, respectively. TP53 mutations were not identified in any of the sixty-six samples.

Conclusions-Implications: There were no TP53 mutations detected in either population of clinically-well women. Despite the limitations of our study, the use of tampons for sample collection was an effective and well accepted strategy for DNA collection in our population. Therefore future studies should continue to investigate vaginal tampons as a possible tool for the screening of gynecologic malignancies.

P34

Vaginal microbial profile and socio-demographic characteristics of young African American women with asymptomatic bacterial vaginosis in the United States

Makella Coudray[1]. Daniel Ruiz-Perez, MSc[1,2]. Brett Colbert, BSc. Kalai Mathee, PhD, MPH[1]. Giri Narasimhan, PhD[1]. Purnima Madhivanan, MBBS, MPH, PhD[1].

[1]Florida International University, Miami, FL

[2]University of Miami, Miami, FL

Keywords: Bacterial Vaginosis, Microbiome, Pregnancy

Introduction and Objectives: Approximately 50% of cases of bacterial vaginosis (BV) are asymptomatic and as such remain untreated. Untreated BV can progress and lead to damage of the vaginal epithelium. This compromises the integrity of the vaginal mucosa, increasing the risk of HIV infection. HIV positive women co-infected with BV experience increased viral shedding.

Methods: The vaginal swabs of 10 African American (AA) women were analyzed. These swabs were obtained from a previously conducted prospective, randomized, open label trial of home screening and treatment of young women with asymptomatic BV who were also at high risk for sexually transmitted diseases. Whole genome sequencing (WGS) was conducted on the vaginal swabs and descriptive analyses of sociodemographic characteristics conducted using SPSS 23.

Results: The mean age of the sample was 21 years (range 18-25 years). The highest level of education attained in the sample was a master's or advanced degree while the lowest was high school attendance (no diploma). 80% of the population had never been treated for BV in their lifetime and 60% have had prior pregnancies. In the past year 60% of the women have had 2 or more different sexual partners and 40% of women had new sexual partners. The microbial taxa of the sample included species from the genus Annaerococcus (tetradius, prevotii, and lactolyticus), genus Actinomyces (turicensis and urogenitalis), order Lactobacillales (Facklamia genus and Peptostreptococcus stomatis) and Prevotella amnii and Atopobium vaginae. Novel co-occurrence patterns were observed through network analysis, the most significant of which includes the species from the genus Annaerococcus and Actinomyces. Maximum variance was observed among Gardnerella vaginalis, however, this was not significant.

Conclusions-Implications: The use of whole genome sequencing to analyze the vaginal microbiome can aid in identifying potential biomarkers that may be associated with increased risk for HIV and increased viral shedding.

P35

The effect of race on survival in pulmonary squamous cell carcinoma in adults

Janine Suarez. Phillip M. Palomino, MPH. Noël C. Barengo, MD, MPH, PhD. Juan M. Lozano, MD, MSc.

Herbert Wertheim College of Medicine, Florida International University, Miami, FL

Keywords: Lung Cancer, Race, Squamous Cell Carcinoma

Introduction and Objectives: Lung Cancer is the leading cause of cancer death in men and women. Non-small cell lung cancer (NSCLC) accounts for 90% of lung cancers and squamous cell cancer comprises 25% of lung cancers. The objective of this study is to evaluate the association between race and survival in adults with pulmonary squamous cell carcinoma.

Methods: This is a secondary analysis based on the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program on cancer statistics. The sample were adults older than 18 diagnosed with pulmonary squamous cell carcinoma from 2007 onward. Survival over time was compared between Non-Hispanic Caucasians (NHC), Non-Hispanic Blacks (NHB), Non-Hispanic Asians (NHA) and Hispanics (H) while adjusting for confounders. Kaplan-Meier curves were estimated for each study group and the log-rank test was used to compare survival distributions. Cox proportional hazard models were used to determine the independent effect race played in survival by estimating adjusted hazard ratios (HR) with 95% confidence intervals (95% CI).

Results: Our total sample was 18,112 adults. The adjusted multivariate analysis showed that race other than NHC did not significantly affect survival outcome (NHB: HR 0.94, 95% CI 0.88-1.0; NHA: HR 1.0, 95% CI 0.93-1.09; H: HR 1.07, 95% CI 0.96-1.18; all p-values > 0.01,). Other variables that independently affected survival were gender (male: HR 1.12, 95% CI 1.08-1.8, p<0.001), age at diagnosis (age 60-79 y: HR 1.16, 95% CI 1.09-1.23, p<0.001; age >80 y: HR 1.46, 95% CI 1.36-1.57, p<0.001), stage at

diagnosis (Regional/Direct: HR 1.82, 95% CI 1.71-1.95, p<0.001; Regional/Direct/Lymph: 3.69, 95% CI 3.46-3.94, p<0.001), marital status (single: HR 1.13, 95% CI 1.06-1.20, p<0.001; separated/divorced: HR 1.16, 95% CI 1.09-1.23, p<0.001;widowed: HR 1.15, 95% CI 1.09-1.22, p<0.001), insurance status (uninsured: HR 1.21, 95% CI 1.05-1.39, p=0.008) and surgery status (surgery: HR 0.34, 95% CI 0.32-0.36, p<0.001).

Conclusions-Implications: Our study did not find a significant association between race and survival in adult pulmonary squamous cell carcinoma patients from 2007-2015. We did find significant secondary outcomes that future studies could explore. By understanding the factors that play a role in pulmonary squamous cell carcinoma, we hope to improve survival outcomes.

P36

Pancreatic intraepithelial neoplasia (PanIN) as a morphologic marker of pancreatobiliary type of ampullary carcinoma

Kritika Krishnamurthy[1]. Vathany Sriganeshan[1,2].

[1]A.M. Rywlin, MD Department of Pathology, Mount Sinai Medical Center, Miami Beach, FL

[2]Florida International University, Department of Pathology, Miami, FL

Keywords: PanIN, Ampullary Adenocarcinoma, Intestinal Subtype, Pancreatobilliary Subtype

Introduction and Objectives: In 1994, Kimura reported two main histological subtypes of ampullary adenocarcinoma, the intestinal and the pancreatobiliary (PB). This classification was later found to be important in predicting the prognosis as well as determining the therapeutic strategy. Isolated histological analysis is hindered by inherent subjectivity and considerable interobserver variability. Additionally, undifferentiated or poorly differentiated tumors cannot be classified based purely on tumor morphology. PanIN is a well recognised precursor to pancreatic adenocarcinoma. Three studies have shown concurrent PanIN in patients with ampullary carcinoma, but their association with the two subtypes has not yet been reported. Reports of similar molecular alterations in pancreatic adenocarcinoma and PB type of ampullary adnocarcinoma hint at a common carcinogenic pathway. The purpose of this study was to evaluate the association of PanIN with the two major ampullary adenocarcinoma subtypes.

Methods: Fourteen cases of segmental resection for ampullary adenocarcinoma were retreived from the archives. The cases were classified into two groups based on the presence of concomitant PanIN. All the cases were stained for CK7, CK 20 and CDX 2 and were classified as intestinal or PB types based on the staining pattern.

Results: All the 10 cases with PanIN stained negative for CDX2 and were classified as PB type (p=0.01). Of the cases without PanIN, 3 were classified as intestinal subtype based on CDX2 positivity and 1 was classified as PB type. Concomitant PanIn was present in 91% of PB type of ampullary adenocarcinoma. The grade of PanIN did not influence the grade or stage of the adenocarcinoma (p>0.05). CK 7 was positive in 13 cases and CK 20 was positive in 12 cases (p>0.05).

Conclusions-Implications: The histologic subtying of ampullary adenocarcioma appears to have significant prognostic and therapeutic implications. But due to the considerable variablity in isolated morphology based subtyping, higher frequency of poorly differentiated cancers and low incidence of the disease, the histomorphologic classification of ampullary adenocarcinomas remains one of the grey zones in surgical pathology. In this scenario, the co-occurence of PanIN in a high percentage of the PB subtype and its complete absence in the intestinal subtype may serve as a strong differentiator between the two subtypes. This is supported by the establishment of PanIN as a definite precursor of pancreatic adenocarcinoma and the identical molecular lanscape of pancreatic adenocarcinoma and PB type ampullary adenocarcinoma.

P37

Predictive outcomes of ultrasound guided biceps tendon sheath corticosteroid injection

Fong H. Nham, BS[1]. Adam Singer, MD[2]. Carlos M. Barrera, BS[3]. Ty K. Subhawong, MD[3]. Mark Barton, MD[3]. Michael Baraga, MD[3]. Lee Kaplan, MD[3]. Jose Perez, MD[3]. Jean Jose, DO[4].

[1]Herbert Wertheim College of Medicine, Florida International University, Miami, FL

[2]Emory University Department of Radiology, Atlanta, GA

[3]Jackson Memorial Hospital, UHealth Sports Medicine Institute, Department of Orthopedic Surgery, University of Miami Miller School of Medicine, Miami, FL

[4]Jackson Memorial Hospital, Department of Radiology, University of Miami Miller School of Medicine, Miami, FL

Keywords: Ultrasound, Corticosteroid, Injection, Tendinopathy, Biceps

Introduction and Objectives: Identify factors predictive of therapeutic success following ultrasound guided sheath injection. Introduction: Various structures are involved in the complex shoulder joint anatomy including the muscles of the rotator cuff, glenoid labrum, long head of the biceps brachii (LHB) tendon, various ligaments, osseous structures, cartilage and bursae. Each of these are potential sources of pain and there are often several concomitantly injured structures that may contribute to symptoms. Although studies have demonstrated the efficacy of both NSAIDs and intra-articular corticosteroid injection, there are recorded studies aimed at determining factors that predict the long term efficacy of non-surgical management, especially related to direct corticosteroid injection into the LHB sheath. This is the first documented study specifically aimed at determining factors predicting the likelihood of treatment success or failure with direct long head of the biceps tendon sheath corticosteroid injection in patient's presenting with clinical evidence of biceps related pain.

Methods: 162 cases divided into three groups based on clinical responses: complete, partial or no relief. These patients were referred for injection on the basis of clinical signs and symptoms suggestive of biceps tendinitis as determined by three orthopaedic surgeons. Differences in age and sex among subjects from the four response groups were compared using ANOVA and Fisher's exact test. Ordered logistic regression for treatment response was carried out using those variables which were significantly different between subject groups in univariate analyses. Differences were considered significant at $p < 0.05$. The statistical analysis was performed using Stata 11.1.

Results: Of the 115 injections with follow-up, 19.1% reported no clinical response while 53.0% had a complete response and those with fibromyalgia or chronic spine pain were strongly associated with a poor outcome (OR = 5.7, $p < 0.001$).

Conclusions-Implications: The data in our study supports LHB tendon sheath injection as a reasonable alternative in the non-surgical treatment of LHB tendon pathology, even in patients with known rotator cuff or labral pathology, as well as arthritic changes. Simultaneous SA/SD bursa injection should be considered in patients who undergo USGI if there is clinical and/or sonographic suspicion of concomitant bursitis or clinical evidence of subacromial impingement. We propose a treatment algorithm beginning with USGI of the LHB tendon sheath injection in all patients without "pain syndrome" presenting with acute LHB tendinopathy before proceeding to surgery. Not only did most patients have good relief or partial relief outcomes, but USGI is less invasive, has fewer associated risks and results in less overall cost compared to surgery. Ultrasound guided intrasheath injection is an effective method of non-surgical management for biceps tendinopathy.

P38

An unusual case of lung mass. Neoplasm? Pulmonary sequestration!

Odille Patricia, MD[1]. Bentley Syler, MD[1,2]. Monica Recini, MD[1,2].

[1]A.M. Rywlin, MD Department of Pathology, Mount Sinai Medical Center, Miami Beach, FL

[2]Herbert Wertheim College of Medicine, Florida International University, Miami, FL

Keywords: Neoplasm, Lung, Sequestration, Mass, Vessel

Introduction and Objectives: Pulmonary sequestration is characterized by lung tissue supplied by an anomalous artery usually from the systemic circulation without connection with the tracheobronchial tree. They are classified as ILS (contain within the visceral pleura) and ELS (separate from surround parenchyma by its own pleural investment). Symptoms vary and are usually nonspecific including cough, fever, recurrent infection and hemoptysis especially in ILS. Imaging studies sometime can be misleading as they may manifest as masses or cystic/cavitary lesions. We presented a case of intralobar sequestration in a 69 y/o asymptomatic women with an incidental consolidation/mass in the right lower lobe with the presumed diagnosis of a neoplastic process.

Case Presentation: A 69-year-old woman present with a history of an incidental right lower lobe consolidation found during a cardiac CT-Scan. Follow-up CT showed development of a new nodular component (1.8 cm), which caused suspicion for a neoplastic process. Biopsy performed showed no evidence of tumor or granulomas. The PET-scans on follow-up showed enlargement and increased uptake of the right lower-lobe lung "mass". The patient underwent a robotic video-assisted thoracoscopy during which an abnormal vessel coming directly off the aorta and supplying the right lower lobe was identified. The finding was consistent with a pulmonary sequestration.

Conclusions-Implications: Pulmonary sequestration is a very rare anomaly characterized by the occurrence of lung tissue that does not communicate with the tracheobronchial tree, and has a systemic, instead of a pulmonary, arterial supply. It is subdivided into two variants, intra-lobar sequestration (ILS) and extra-lobar sequestration (ELS), depending on its relationship to the visceral pleura. This entity can mimic a neoplasm. Therefore it is important to accurately differentiate from other lung lesions that will require more aggressive treatment.

P39

Massive lipomatosis of the small intestine causing intussusception

Michael Pagacz. John Alexis, MB, ChB.

Florida International University, Miami, FL

Keywords: Lipomatosis, Intussusception, Lipoma

Introduction and Objectives: Intestinal lipomatosis is a disease of unknown etiology which may remain asymptomatic or present with complications such as intussusception. It is exceedingly rare, and the presentation as intussusception is rarer still. We report a case of a symptomatic man with intestinal lipomatosis of the small bowel.

Case Presentation: The patient is a 40 year old man with a history GERD and a family history of colon cancer. He presented with severe abdominal pain and episodes of diarrhea. He had lost 22 lbs over two months, had abdominal pain pre- and post-prandially, and fecal urgency. An abdominal CT and colonoscopy showed a severely lipomatous, bulbous and protuberant ileo-cecal valve, with intussusception of the ileum into the cecum. Exploratory laparotomy revealed marked enlargement of the ileum due to massive fat deposition, and adhesions between the ascending colon and the right lateral lower abdominal wall.

Conclusions-Implications: This is an unusual case of lipomatosis of the small intestine presenting as an intussusception of a submucosal mass into the ileocecal valve. The etiology of lipomatosis is unknown. Theories include embryonic displacement of adipose tissue, post-chemotherapeutic fat deposition, chronic irritation such as chronic inflammatory bowel disease, low-grade infection and hamartomatous syndromes. Only 14 documented cases of diffuse intestinal lipomatosis exist and only 2 documented cases of intussusception caused by diffuse lipomatosis. Most patients in reported cases of intestinal lipomatosis were asymptomatic, however some presented with sub-acute intermittent obstruction, colonic perforation, and intussusception, the rarest of complications. Early diagnosis of adult intussusception is difficult because most

cases present with non-specific signs and symptoms and may present in an acute, sub-acute or chronic manner. The classic triad of intermittent abdominal pain, currant jelly stools, and a palpable tender mass seen in children is rarely present in adults. However, in adults, nausea, vomiting, gastrointestinal bleeding, changes in bowel habits and abdominal distension are more common.

P40

Distribution and density of FOXP-3-positive cells in thymus with and without follicular hyperplasia: A clinicopathological correlation with autoimmunity

Christopher A. Febres-Aldana[1]. Kritika Krishnamurthy[1]. Sofia Garces[1]. Juan Carlos Alvarez[1]. Pukhraz Basra[1]. Anthony Febres-Aldana[2]. Vathany Sriganeshan[1,3].

[1]A.M. Rywlin, MD Department of Pathology, Mount Sinai Medical Center, Miami Beach, FL

[2]Department of Internal Medicine, Mount Sinai Medical Center, Miami Beach, FL

[3]Florida International University, Department of Pathology, Miami, FL

Keywords: T Regulatory Cells, FOXP3, Autoimmunity, Thymus

Introduction and Objectives: The thymus is the anatomical organ for T-cell maturation and differentiation. Regulatory T cells (Tregs) play an important role in immune tolerance. Generation of self-reactive cells has been associated with a low production of Tregs. The distribution of thymic FOXP3+ Tregs in autoimmune (AI) diseases is poorly characterized.

Methods: Thymus specimens collected in the last 10 years from surgical specimens and autopsies, excluding thymomas, were reviewed and classified as follicular hyperplasia versus others (i.e. thymic hyperplasia, involution or normal). History of AI disease was obtained retrospectively. Hematoxylin-eosin slides and FOXP3 immunohistochemical stains were evaluated in 9 cases with a history of AI disease and compared to 9 thymus controls without a history of AI disease. Three independent blind observers counted FOXP3+ cells in 4 random fields centered in the thymic medulla. Average cellular densities were calculated on captured images with ImageJ 1.51t (National Institutes of Health, USA).

Results: FOXP3+ cells were located within medullary lymphocytic aggregates, occasionally inside Hassall's corpuscles and rarely in the cortex. The mean average density of FOXP3+ cells was significantly higher in thymi with than without follicular hyperplasia, independent of the history of AI disease (2072.3±786.9 cells /mm2 vs. 958.76±402.1 cells/mm2, P=0.002). The density of FOXP3+ cells in thymus from patients with AI diseases did not differ from patients without a history of AI disease.

Conclusions-Implications: The production of FOXP3+ cells is present in the medulla of thymus with and without hyperplastic changes. Thymi with reactive follicular hyperplasia showed a higher density of FOXP3+ cells. While no differences in the density of FOXP3+ cells were noted in the thymi of patients with versus without a history of AI disease, the density of FOXP3+ cells present in this organ may be a potential modifier of clinical phenotype of AI disorder.

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Trapped in the NET- A report of two autopsy cases of NETosis

Kritika Krishnamurthy, MD[1]. Kailee Imperatore, MD[1]. Christopher A. Febres-Aldana, MD[1]. Vathany Sriganeshan, MD[1,2]. Robert J. Poppiti, MD[1,2].

[1]A.M. Rywlin, MD Department of Pathology, Mount Sinai Medical Center, Miami Beach, FL

[2]Herbert Wertheim College of Medicine, Florida International University, Miami, FL

Keywords: Neutrophil Extracellular Traps, Autopsy, Carcinomatosis, Sepsis

Introduction and Objectives: Recent studies reveal that neutrophil extracellular traps (NETs) play a significant role in pathologic thrombosis through platelet entrapment and consequent activation of the coagulation cascade. NETosis is a type of cell death, distinct from necrosis and apoptosis. NETs are composed of DNA, granular antimicrobial proteins, neutrophil elastases and enmeshed neutrophils. Bacteria, fungi, activated platelets and numerous inflammatory stimuli can induce dramatic changes in the morphology of the neutrophils inducing NETosis. The chromatin and proteases released by the neutrophils during NET formation regulate procoagulant and prothrombotic factors and participate in intravascular clot formation. The granulocyte colony-stimulating factor produced by many tumors is another chemical stimulus that has been found to trigger NET formation.

Case Presentation: Herein we present two autopsy cases. The first case is a 76 year old man, with metastatic squamous cell carcinoma of the lung, admitted for acutely worsening respiratory failure and atrial fibrillation. Computed tomography of the chest revealed worsening metastatic disease with complete consolidation of the right lung. The patient developed asystole and expired 5 days post admission. The second case is a 73 year old man who suffered a cardiopulmonary arrest and was brought to the emergency room after resuscitation. He was in severe metabolic acidosis at the time of presentation and had a hemoglobin of 2 g/dl. He was started on pressors and mechanical ventilation, but expired 2 days post admission. Autopsy on the first case revealed the right lung to be almost entirely replaced by extensively necrotic poorly differentiated squamous cell carcinoma along with metastatic disease in contralateral lung and pancreas. A 30 cm cylindrical thrombus was identified extending from the left ventricle to the thoracic aorta and a 5 cm thrombus was identified in the right ventricle. Microscopic examination of the thrombi revealed numerous neutrophils enmeshed in abundant fibrin representing a NET. Autopsy in the second case revealed a 5 cm mural thrombus with numerous neutrophils in the descending aorta consistent with NET, bilateral bronchopneumonia and infarcted bowel.

Conclusions-Implications: These two autopsies highlight the pathogenic role of NET in causing thrombosis. Neutrophil extracellular traps may be the cause of pathological thrombosis in varied conditions and could be therapeutically targeted for the prevention of thrombosis.

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Correlates of non-supine infant sleep position in the US: Results from the PRAMS 2012-2015

Amara Fazal, BA. Jasmyne Patel, BS. Anusha Reddy, BS. Grettel Castro, MPH. Marcia H. Varella, MD, PhD, MHS.

Herbert Wertheim College of Medicine, Florida International University, Miami, FL

Keywords: SIDS, Infant Sleep Position, Risk Factors

Introduction and Objectives: Sudden Infant Death Syndrome (SIDS) is the leading cause of death of infants between one month and one year of age. A key recommendation for preventing SIDS is placing infants in the supine position for sleep, yet up to 33.8% of parents still place their infants in non-supine sleep positions. The objective of this study is to explore whether selected infant and maternal factors are associated with the use of non-supine infant sleep position.

Methods: We analyzed data from 11,853 mother-infant pairs who participated in the 2012-2015 Pregnancy Risk Assessment and Monitoring System (PRAMS) in the states of Minnesota, New Jersey, Pennsylvania, West Virginia, and Wisconsin, for which more comprehensive data on infant sleep habits was collected. Multivariate logistic regression models were used to explore factors independently associated with adherence to the infant supine sleep position. Maternal age, race, education, smoking and alcohol use during pregnancy, and history of specific stressors, as well as infant's sex, gestational age at birth, and history of postnatal ICU stay were explored. Analysis accounted for the complex survey design using Stata software.

Results: Of the 11,310 participants with information on infant sleeping practices, about 20% placed their infants in the non-supine sleep position. More than 90% of the mothers received counseling on sleep position. Some characteristics were independently associated with use of non-supine infant sleep positioning. Black race as compared to white race [adjusted odds ratio (AOR)=2.17; 95% confidence interval (CI)=1.69-2.78, p<0.001], younger maternal age (AOR=1.23; 95% CI=1.02-1.47, p=0.028), lower maternal education level (AOR=1.51; 95% CI=0.75-1.05, p=0.004), and mothers who reported relational stressors (AOR=1.51; 95% CI=0.75-1.05, p=0.004) were independently associated with lower adherence to the recommended supine infant sleep position. Lastly, compared to non-drinker mothers, mothers who reduced or stopped drinking alcohol during pregnancy were 29% less likely to use the non-supine sleep position (AOR=0.71; 95% CI=0.59-0.85, p<0.001).

Conclusions-Implications: Our study has built on previous studies as well as identified novel risk factors associated with SIDS, such as young mothers, black mothers, women with lower levels of education, and women with relational stressors. Preventative efforts could be focused on development of interventions targeted towards at risk populations.

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Treatment modality and social functioning in children with attention deficit hyperactivity disorder

Eric Marten. Matthew Cannavo. Patrick Valente. Pura Rodriguez de la Vega, MPH. Juan G. Ruiz, MD, MMedSci. Juan M. Lozano, MD, MSc.

Herbert Wertheim College of Medicine, Florida International University, Miami, FL

Keywords: Attention Deficit Hyperactivity Disorder (ADHD), Treatment Modality, Social Functioning, Pharmacotherapy, Cognitive Behavioral Therapy (CBT)

Introduction and Objectives: Attention deficit/hyperactivity disorder (ADHD) is the most common neurobehavioral pediatric disorder, affecting 3-7% of school age children. ADHD in the developmental period of age 7 to 17 years is associated with poor sociometric outcomes and decreased quality and number of dyadic friendships. This study aims to determine whether pharmacotherapy, cognitive behavioral therapy (CBT), or a combination of both, is associated with improved social function in children with ADHD when compared to control subjects receiving neither pharmacotherapy nor CBT.

Methods: This is a secondary analysis using information from the 2009-2010 National Survey of Children with Special Healthcare Needs (NSCSHN). Children whose parent reported clinical diagnosis of ADHD and currently have ADHD were selected. The independent variable is treatment modality - pharmacotherapy only, CBT, combination, and none. The dependent variable is social functioning, defined as making/maintaining friendship, aggression/acting-out, participation in activities, and participation in play. The associations between treatment modality and social functioning and covariates were explored through a bivariate analysis. Adjusted odds ratios with 95% confidence intervals while controlling for confounders were obtained using logistic regression.

Results: 7,775 children were included in this study, with 54.2% receiving medication only, 31.9% receiving combination therapy, 6.9% receiving only behavioral therapy, and 7% receiving no therapy. Only gender and parental education level were not associated with treatment modality at baseline. After unadjusted analyses there was no difference in social functioning between children with medication-only as compared with no therapy (OR 0.8, 95% CI 0.6-1.1, p=0.157), whereas the CBT alone (OR 2.0, 95% CI 1.3-3.0, p=0.002) and combination therapy (OR 2.2, 95% CI 1.6-3.1, p<0.000) had significantly inadequate social functioning. However, after adjusting for confounding variables the association between inadequacy of social function and medication (aOR 0.7, 95% CI 0.5-1.1, p=0.134), CBT (aOR 1.4, 95% CI 0.8-2.3, p=0.201), and combination therapy (aOR 1.2, 95% CI 0.8-1.8, p=0.342) disappeared.

Conclusions-Implications: No significant differences in social functioning were found between patients in the four treatment modalities. Identification and treatment of inadequate social functioning can have far-reaching implications in future relationships. Additional studies investigated treatment modalities in the severity of ADHD are suggested.

P44

Level of parental education and physical activity in the pediatric epileptic population

Andrew Payomo*. Kelly Nguyen*. Helen Rynor*. Grettel Castro, MPH. Juan G. Ruiz, MD, MMedSci. Marcia H. Varella, MD, PhD, MHS.

Herbert Wertheim College of Medicine, Florida International University, Miami, FL

Keywords: Epilepsy, Exercise, Parents, Education, Children

Introduction and Objectives: Epilepsy in the pediatric population has a noticeable impact on the quality of life of the afflicted. Physical activity positively benefits epileptic children; however, epileptic children are less likely to participate in physical activity than non-epileptic children, potentially, further decreasing the quality of life of these children. Objective: To assess whether the level of parental education is associated with participation in physical activity of epileptic children living in the US.

Methods: We performed secondary analysis of data collected by the National Survey of Children's Health, year 2016. Children aged 6-17 years with a previous diagnosis of epilepsy were studied. The independent variable was the highest level of parental education (categorized as "up to high school" and "above high school"). The dependent variable was adequate physical activity, defined present if the child participated in exercise, played sport, or performed any physical activity for 60 minutes for at least 4 days a week. Any level of activity done less than 4 days a week was considered not adequate. Independent associations were assessed using multivariate logistic regression models. P-values ≤0.05 were considered statistically significant (two sided test).

Results: We studied 310 epileptic children. Of those, only 43% exercised adequately. About 20% of the parents had an educational level up to high school. The level of parental education was not associated with adequate physical activity in the pediatric epileptic population [the unadjusted odds ratio for parents with up to high school education level to exercise adequately was (OR)=0.8, 95% Confidence Interval (CI)=0.3-2.0; and the corresponding adjusted OR=1.4, 95% CI=0.5-3.6, accounting for severity of epilepsy, parental physical activity levels and mental health status, and child's race, sex, and age).

Conclusions-Implications: More than half of children with epilepsy perform inadequate amounts of exercise. Physicians at medical institutions could educate parents of children with epilepsy about the benefits of and barriers to exercise for their children to increase child participation in physical activity. In this sample of epileptic children, we found no evidence for association between the level of parental education and adequacy of physical activity.

P45

Risk factors associated with decreased condom use in adolescents

Gina Furicchia, BS. Jennifer Navarro, BS. Christophe de Lespinasse, BS. Juan M. Lozano, MD, MSc. Juan M. Acuña, MD, MSc, FACOG.

Herbert Wertheim College of Medicine, Florida International University, Miami, FL

Keywords: Adolescents, Condom-Use, Risk Factors

Introduction and Objectives: The CDC reported an increase in STD prevalence and, coincidentally, a concurrent decrease in condom use during sexual intercourse in adolescents. By understanding the determinants that are associated with reduced condom use in high school students, a more directed approach to community funding and interventions can be pursued.

Methods: We used the 2017 YRBSS database, a national survey administered since 1990 to assess health behaviors amongst high school students in the United States. Our cross-sectional sample included students in grades 9-12 and excluded subjects who have never been sexually active. The dependent variable was condom use during sexual intercourse and our independent variables were age, race, gender, sexual identity, academic performance, physical activity, cigarette use, age at first intercourse, number of lifetime sexual partners, HIV testing, victimization by bullying or dating violence, concurrent OCP use, and depression. Bivariate and multivariate analysis with logistic regression were conducted to calculate adjusted odds ratios (aOR) and 95% confidence intervals (95% CI) for the associations between potential predictors and condom use.

Results: Our analytical sample included 2,575 students. Analysis identified a significant decrease in condom usage with the following factors: females (aOR 0.8, 95% CI 0.6-1.0), gay/lesbian sexual identity (aOR 0.2, 95% CI 0.1-0.3), failing grades (aOR 0.5, 95% CI 0.3-0.9), <14 years old at first intercourse (aOR 0.4, 95% CI 0.3-0.7), use of OCPs (aOR 0.2, 95% CI 0.2-0.2), and drug use (aOR 0.6, 95% CI 0.5-0.8). There was a significant increase in the association between condom use and >3 days/week physical activity (aOR 2.5, 95% CI 1.6-3.9). There was no significant association between dating violence, bullying, or depression with condom use.

Conclusions-Implications: Our study identified several behaviors that were independently associated with a reduced use of condoms in US adolescents; however, it was exploratory in nature. Thus, future research into each individual association that we identified is needed. A limitation of our study is reporting bias, since behaviors were self-reported.

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An observational study: Environmental and other risk factors for pediatric depression

Kristina D. Chung, BS, MD. Pavinarmatha Ketheeswaran, MSc, MPH, MD. Natasha N. Llanes, BS, MD. Juan C. Zevallos, MD. Juan M. Acuña, MD, MSc, FACOG.

Florida International University, Miami, FL

Keywords: Depression, Neighborhood, Environment, Pediatric

Introduction and Objectives: Poor environmental characteristics have been associated with poor mental health, but research directed at pediatric mental illness in disadvantaged social conditions remains an area of further exploration. With suicide climbing as the second leading cause of death among children, it is imperative that we better understand the causes of pediatric depression. The goal of this study is to understand the association between environmental conditions on depression in pediatric populations. Specifically we aim to assess the association between unfavorable environmental physical characteristics and depression in pediatric populations in the US.

Methods: We used a nationally representative sample (N= 82,197) from the National Survey of Children's Health from 2011/2012 focused on children ages of 2-17 years to assess the association between neighborhood amenities and depression. We completed descriptive analysis of sociodemographic characteristics and neighborhood characteristics, as well as unadjusted and adjusted multivariate logistic regression analysis.

Results: Decreased amenities had higher odds of childhood depression in the unadjusted analysis; after controlling for confounders there was no longer statistical significance. Secondary factors that were statistically significant for higher odds of childhood depression in our adjusted analysis included: children 8-17 years ($p< 0.05$); child's overall health reported as less than excellent had a greater odds of depression (fair, AOR = 12.3, 95% CI 6.7-22.5; and poor health, AOR = 12.3, 95% CI 4.9-30.9); household income at 0-100% FPL (AOR= 2, 95% CI 1.3-3.0) and at 301-400% of FPL (AOR = 1.5, 95% CI 1.1-2.2); and lastly, one parent with poor mental health had a greater odds of childhood depression than two parents with poor mental health (AOR=3.7, 95% CI 2.6-5.3; AOR = 2.4, 95% CI 1.4-4.1 respectively). Protective factors include black race (AOR = 0.5, 95% CI 0.3-0.9); maternal education at or below high school (AOR = 0.7, 95% CI 0.5-1; AOR = 0.5, 95% CI 0.3-0.9 respectively); and second generation households (AOR = 0.3, 95% CI 0.2-0.5).

Conclusions-Implications: These findings indicate the need for further exploration of the role of environmental factors in pediatric depression. Better understanding of associations and potential risk factors for pediatric depression may offer insight in guiding counselling interventions, inform future policy, and may initiate prevention programs aimed at neighborhood and housing improvement.

P47

Association between poverty and the prevalence of ADHD in children aged 4-17

Dana Perez. Nicholas Romano, MPH. Ana Luiza Graneiro. Pura Rodriguez de la Vega, MPH. Daniel Castellanos, MD. Noël C. Barengo, MD, MPH, PhD.

Herbert Wertheim College of Medicine, Florida International University, Miami, FL

Keywords: Mental Health, Socioeconomic Status, Children, ADHD, Poverty

Introduction and Objectives: Attention-deficit/ hyperactivity disorder (ADHD) is one of the most common neurodevelopmental disorders of childhood and with symptoms and/or impairment often continuing into adulthood. This study will examine trends in parent-reported ADHD by household annual income during 2016, which is valuable given the increasing prevalence of ADHD in the United States The objective is to assess the association between the poverty level experienced in the household and the prevalence in 2016 of reported ADHD diagnoses among children in the United States aged 4-17.

Methods: This cross-sectional study uses data from the National Survey of Children's Health, which collects data from parents regarding the health and functional status of their children across the US via a random telephone survey. The independent variable was poverty status of the household, collected as annual household income according to federal poverty level: <100%, 100-199%, 200-399%, and >+400%. The outcome variable was ever having a reported diagnosis of ADHD. The covariates included among others, were age, sex, race, ethnicity, health insurance type. Unadjusted and adjusted logistic regression models were used to study the association between a household's poverty level and reported ADHD diagnosis. Odds ratios (OR) and 95% confidence intervals (CI) were calculated.

Results: The total number of participants in this study was 40,422. The adjusted results demonstrated a 35% decrease in odds of ADHD among participants in the lowest poverty level of <100% compared to the highest poverty level of >400% (OR 0.65; 95% CI 0.46-0.92). The adjusted odds ratios for the other poverty levels (100-199% and 200-399%) and ADHD were not statistically significant (OR 0.91; 95% CI 0.68-1.22 and OR 0.83; 95% CI 0.68-1.02, respectively) when compared with the highest poverty level.

Conclusions-Implications: Although most studies showed an increased likelihood of ADHD among lower socioeconomic demographics, we observed a decreased likelihood among children living in a household with an annual income of <100% below the federal poverty level. Future studies may consider methodology to better elucidate underlying mechanisms and the directionality of the named associations.

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The relationship between social support and psychological distress in Latina mothers living in Miami-Dade County

Jake Levine, BS. Anton De Witte, BS. Pedro Ferrer, BS. Grettel Castro, MPH. Marcia H. Varella, MD, PhD, MHS. Patria Rojas, PhD. Juan M. Acuña, MD, MSc, FACOG. Diana M. Sheehan, PhD.

Herbert Wertheim College of Medicine, Florida International University, Miami, FL

Keywords: Social Support, Psychological Stress, Acculturation, Latina, Mental Health

Introduction and Objectives: Previous studies have demonstrated a link between social support and mental health. However, few studies have explored this relationship among adult Latina women. This study analyzed the relationship between social support and psychological distress in Latina women living in Miami-Dade County. In addition, acculturation was examined as a potential modifying factor.

Methods: The study included baseline data of 155 Latina mothers in Miami-Dade County collected as part of a longitudinal study of Latina mother and daughter dyads in the year 2005. Social support was measured using the Interpersonal Support Evaluation List (ISEL)--score ranging from 0 to 80, and categorized into tertiles: low (<62), medium (62-72), high (>73). Psychological distress was assessed based on participants self-report of occurrence of depression, anxiety, or suicidal ideation. Acculturation was measured by an English proficiency composite score (ranging from 3-12), interview language, and length of residence in the U.S.

Results: Results of multivariate logistic regression models showed that compared to women with a high level of social support, women with low social support had higher odds of reporting psychological distress (Odds Ratio = 7.8 (95% Confidence Interval = 2.74-22.14). Level of acculturation, however, did not modify the association between social support and psychological distress (P = 0.74).

Conclusions-Implications: The study had two primary findings. First, social support was strongly associated with psychological distress among Latina women. Second, acculturation did not moderate the relationship between social support and mental health. This lack of interaction may be due to the small sample size. Although the study's findings are preliminary, the results have clinical implications for the development of future social support scales and for Latina women's well-being, especially in the context of mental health prevention.

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Generation net: Exploring internet usage and its association with academic performance, mental health, and sleep habits amongst college students

Shaina Johnson, MPH. Amanda Ichite, MPH. Wissam Al Khoury, MD, MBA. Derrick Forney, MPH. William W. Darrow, PhD.

Florida International University, Miami, FL

Keywords: College Students, Internet Use, Social Media, Insomnia, Mental health

Introduction and Objectives: Pathological internet use, also known as problematic internet use (PIU) is excessive internet use that interferes with one's daily life. PIU has been linked to insomnia, mental health issues, and negative academic performance. This pilot study aimed to measure the degree to which such an association existed among a student population at a large Hispanic-serving research university in South Florida. The purpose of this research was to investigate the phenomena of increased internet usage and its impacts on college students' sleep habits, mental health, and overall academic performance.

Methods: A cross-sectional study design employing venue-based sampling was used to recruit students from seven high traffic locations on campus. To be eligible students had to be at least 18 years of age and currently enrolled in at least one three-credit hour course. Students completed a self-administered questionnaire assessing PIU, insomnia severity, psychological distress, student health center services use, academic performance, and top reasons for internet use. Cross tabulations and bivariate correlations were run to find significant associations among variables and a multiple linear regression was run to identify explanatory variables of PIU.

Results: Data were collected from 405 students from November 7th-19th, 2018. More than half of respondents (58%) had indicators of PIU. Of those, 30% scored positive for depression, 33% for moderate and severe psychological distress, and 29% for moderate and severe insomnia. Bivariate correlations were significant between PIU and all of those variables ($p<0.01$). PIU was highly associated with insomnia severity and selecting "dating" and "reading news" as top reasons for internet use. Most students (79%) knew about wellness and health services on campus but 51% never utilized them.

Conclusions-Implications: College students are at risk for PIU. PIU is associated with negative sleep and mental health outcomes. Though students are aware of services on campus that may provide support, they do not take advantage of them. College administrators should investigate ways to publicize services and prompt students to decrease their internet use. Colleges can offer counseling in a tech-free environment through internet "fasting camps" and "internet detox" programs and organize support groups to help decrease dependence on online social connections.

P50

Describing the relationship between sexual orientation and sexual contacts among US adolescents

Stefani Butts, BA[1,2]. Kemely Guzman, BSc[1]. Anil Cheddie, MD[1].

[1]*Robert Stempel College of Public Health and Social Work, Florida International University, Miami, FL*

[2]*University of Miami Miller School of Medicine, Division of Infectious Diseases, Miami, FL*

Keywords: Sexual Health, Adolescents, LGBTQIA, Sexual Minorities

Introduction and Objectives: Of late, sexual activity during adolescence is increasingly considered a normative behavior. Nearly half (47%) of all high school students in the United States have ever had sex and more than one-third (34%) are sexually active currently. However, higher rates of negative sexual health outcomes among sexual minority youth raise questions about sexual identity and current sexual practices. Namely, whether or not this group has a higher prevalence of sexual activity and risky sexual practices than the majority. We utilized data from the Youth Risk Behavior Surveillance Survey (YRBSS) to describe the association between sexual orientation and sexual activity among US high-school students in grades 9-12.

Methods: US adolescents, (n = 14,765) in grades 9 through 12 throughout the United States were recruited to participate in the YRBSS. Specific questions from the YRBSS were selected to determine sexual identity, sexual activity, and preventive sexual practices of participants. Associations between independent and outcome variables were assessed by chi-square tests of associations. In order to obtain a measure of effect size and pseudo R2, a series of four binomial logistic regressions were conducted, using odds ratios as effect sizes.

Results: Sexual minorities were significantly more likely than non-minorities to have ever had sex, sexual minorities were also more likely to be sexually active currently. However, sexual minorities were more likely than non-minorities to report using a condom at last sexual intercourse. Persons who identified as bisexual were an exception, as this sub-group was less likely to report using a condom at last sexual intercourse than both minorities and non-minorities. The prevalence of abstinence declined by grade group across the data, but more so among those who identified as heterosexual. Interestingly, boys were significantly more likely than girls to identify as gay or lesbian and less likely to identify as bisexual. Finally, sexual minorities were more likely than non-minorities to have ever had an HIV test.

Conclusions-Implications: There seems to be marked behavioral differences between sexual minority and non-minority youth in the US. These differences may have various implications for sexual health and prevention initiatives designed for sexual minorities and non-minorities. Our findings suggest that, although they may engage in sexual activity at an earlier age and more frequently, sexual minorities may be better informed and/or have a heightened awareness of sexual risk than their non-minority counterparts. This bolsters support for more targeted prevention strategies aimed at this group as their prevention education needs may differ from those of non-minorities. We encourage investigators to consider future research aimed at understanding the implications of behavioral differences between sexual minority and non-minority youth, particularly in the realm of health disparities.

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Two cases of post colonoscopy appendicitis: Case study

Dorty Morency, MD. Marien Yanes, DO. Michael Yurubi, DO. Muhammad Aziz, MD, MPH.

West Kendall Baptist Hospital

Keywords: Colonoscopy, Appendicitis, Colonoscopy Complications, Abdominal Pain

Introduction and Objectives: Colonoscopy is a gold standard method for colorectal cancer screening in asymptomatic individuals and also commonly used for diagnostic purposes to investigate variety of lower gastrointestinal symptoms. According to cdc.gov approximately 15 million Americans underwent screening colonoscopies in 2012. The United States Health System targets to screen about 80% of all adults for colorectal cancer between ages of 50 to 75 by 2024. Some of the complications following colonoscopy examination are well documented and include cardiopulmonary complications related to use of sedatives, bleeding which is usually associated with polypectomy, perforation of bowel, and infection. However, other complications like acute appendicitis following colonoscopy have been less studied and are rarely reported.

Case Presentation: First patient: 53 year old white male presented to ED in the evening with complaint of gradual onset, moderate to severe, right lower quadrant abdominal pain and associated with nausea, non-bloody vomiting, and dizziness. Patient underwent a screening colonoscopy that same morning without any obvious complications and started having abdominal symptoms after he started eating later that day. Abdomen CT showed multiple appendicoliths present within lumen of 1.1 cm dilated appendix and consistent acute appendicitis. Patient underwent a laparoscopic appendectomy under general anesthesia without complications. Second patient: 55 year old Hispanic male with less than one week history of screening colonoscopy, presented to ED with one day history of acute severe abdominal pain, located in periumbilical and right lower quadrant, sharp, moderate to severe in intensity. Pain was associated with chills without fever, and nausea without vomiting. Patient reported having a screening colonoscopy within a week without any complications with normal findings. Abdomen CT showed appendix measures about 12 mm in caliber with a distended lumen and periappendiceal inflammatory changes consistent with acute appendicitis. Patient underwent emergent laparoscopic appendectomy under general anesthesia without complications.

Conclusions-Implications: Colonoscopy is a relatively safe procedure, however it can be associated with rare life threatening complications such as appendicitis presented in these two cases. The pathophysiology of post-colonoscopy appendicitis is not completely understood, however, possible mechanism include barotrauma from over-insufflation, direct injury to appendicular lumen leading to local edema, penetration of stool and debris inside appendiceal lumen and exacerbation of preexisting subclinical disease of appendix. Timely diagnosis of life threatening complications of colonoscopy is crucial and any gastrointestinal symptomatology during post colonoscopy period should be immediately investigated. Patients should be encouraged to seek immediate medical advice if experiencing such symptoms after a colonoscopy procedure.

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Evaluation of race as an effect modifier of the association between diabetes and surgical site infection

Lina Loza. Jacob Bruno-Friedman. Mercy Blanco. Grettel Castro, MPH. Pura Rodriguez de la Vega, MPH. Marcia H. Varella, MD, PhD, MHS. Juan G. Ruiz, MD, MMedSci.

Herbert Wertheim College of Medicine, Florida International University, Miami, FL

Keywords: Hysterectomy, Infection, Diabetes, Race

Introduction and Objectives: Diabetes is a chronic condition that currently affects almost 10% of the adult population in the US. They are at increased risk of surgical site infection (SSI) compared to those without diabetes. Few studies evaluate the role of race in the association between diabetes and SSI. Our objective was to investigate race as an effect modifier of the association between diabetes and SSI in patients undergoing total abdominal hysterectomy (TAH).

Methods: We nested a historical cohort into the 2016 American College of Surgeons National Surgical Quality Improvement Program database (NSQIP). Exploratory analyses included description of baseline characteristics and bivariate analyses to identify potential confounders. To adjust for confounders and test for interaction, multivariable logistic regression models were fitted: a general model including the interaction between race and diabetes, and separate models for each race.

Results: Of the 16,043 included women, 63% were Caucasian and 29% African Americans. Eleven percent were diagnosed with diabetes and the incidence of surgical site infection was 3.8%. After adjusting for age, race, functional status, dyspnea, COPD, hypertension, disseminated cancer, bleeding disorder, and operation time, the odds ratio (OR) of SSI between diabetics and non-diabetics was 1.62 (95%CI:1.29-2.02), and the interaction between race and diabetes was not statistically significant (p=0.540). After stratification, the adjusted ORs of infection between diabetics and non-diabetics were very similar between whites and blacks (1.55; 95%CI:1.18-2.05 and 1.62; 95%CI:1.07-2.45, respectively).

Conclusions-Implications: Our data supports that diabetes increases the risk for SSI after TAH. Obesity, hypertension, dyspnea, and operation time (>2hours) independently increase the odds of developing SSI. Lastly, we didn't find evidence supporting the role of race as an effect modifier of the association between diabetes and SSI in those undergoing TAH.

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Moving away from mannitol infusion for partial nephrectomy: has there been any effect on renal function?

Jeffrey Wei, MS[1]. George Wayne, MD[2]. Kennedy Okhawere[2]. Vivian Wong[1]. Elias Atri[1]. Amr Elbakry[2]. Bheesham Dayal[2]. Akshay Bhandari, MD[2]. Ketan Badani, MD[2].

[1]Herbert Wertheim College of Medicine, Florida International University, Miami, FL

[2]Icahn School of Medicine at Mount Sinai

Keywords: Urology, Partial Nephrectomy, Mannitol, Renal Function, GFR

Introduction and Objectives: Currently, partial nephrectomy is the recommended treatment for localized renal cancer, according to the AUA guidelines. However, one of the major concerns in the setting of partial nephrectomies is the effect of ischemia on the remaining kidney parenchyma. It is understood that ischemia is a significant modifiable factor influencing nephron damage and renal failure due to the effect of organ-induced ischemia and subsequent ischemia reperfusion injury. In response, diuretics such as mannitol have been used in the hopes of mitigating these phenomena. Although mannitol has been used for many years for its purported protective effects, recently multiple studies of mannitol use specifically in the setting of partial nephrectomy have emerged challenging this assertion. This study considers whether mannitol administration has shown any benefit to patients in the contemporary era.

Methods: We retrospectively reviewed a multi-institution database for an association between mannitol administration and subsequent renal function during follow-up. These patients were assessed for de novo chronic kidney disease, stage III (CKD III) and followed with estimated glomerular filtration rate (eGFR). Statistical analysis included Mann-Whitney-U and chi-squared tests for comparing baseline and perioperative variables, and postoperative outcomes. eGFR changes were evaluated with a mixed-effects linear regression model.

Results: Between 2014 and 2017, 915 patients were identified whose operative reports or surgeons' treatment algorithms explicitly described mannitol administration. 667 (73%) of patients did not receive mannitol. They did not differ significantly at baseline in terms of demographics, age, Charlson comorbidity index, nephrometry score, tumor size, grading, or baseline eGFR from those who received mannitol. On follow-up, patients were tracked for a median of 5 months (IQR 0.4-18 months), during which mannitol use was associated with an increase in de novo CKD III (14% v. 9%, $p < 0.001$), and minimally worsened median eGFR on final follow-up (73 v. 76, $p < 0.05$) (table). On multivariate analysis, mannitol was not associated with changes in renal function, which appeared to be most strongly related to ischemia time and length of follow-up. Interestingly, ischemia time and operative time appeared slightly longer with mannitol use.

Conclusions-Implications: Mannitol administration, long believed to prevent ischemic damage during partial nephrectomy, has recently been phased out. Our analysis of partial nephrectomy patients during this shift in practice patterns indicates that mannitol administration likely confers no short- or long-term renal benefit. Mannitol may be used at the surgeon's discretion, but if it prolongs surgery time or ischemia time, it may actually be detrimental to outcome.