Fusion

A student-led research publication of the George Washington University School of Medicine and Health Sciences | Spring 2023, Volume XVI

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The William Beaumont Research Awards are given to three students for outstanding research accomplishments from work submitted for publication in Fusion, the student-run research magazine at GW School of Medicine and Health Sciences.

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Fusion

is a publication of the GW SMHS William H. Beaumont Medical Research Honor Society.

This research journal is published by students in collaboration with the Office of the Dean and the Office of Communications

ON THE COVER: The 2023 edition of Fusion examines and utilizes innovation in medicine – from artificial intelligence to diagnose atherosclerosis, to laser trabeculoplasty to treat glaucoma, to machine learning to detect malignant tumors. This innovation is showcased in this year's cover art, designed by Fusion editor Nanami Miyazaki, MSI.

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MEDICAL EDUCATION

Looking to the Future: Post-Pandemic Medical Innovation


Scarlett Bergam, MSI


Jeffrey Wang, MSI


Nanami Miyazaki, MSI


Adam Odolil, MSI


Uzma Rentia, MSI

The Fusion Editorial Board is thrilled to introduce this year's edition of Fusion, the George Washington School of Medicine and Health Sciences (GW SMHS) medical student research journal. Our publication provides a written platform for students to showcase their original research in the fields of basic science, clinical and translational research, and clinical public health within and outside of the GW SMHS. We are excited to include work from all areas of science and health care, including collaborations between medical students, residents, and attendings at our institution.

After the GW SMHS has resumed in-person scholarship following the global pandemic, we are proud to showcase 68 abstracts, one of the largest collections of scholarly work in Fusion's history. The 2023 edition of Fusion examines and utilizes innovation in medicine — from artificial intelligence to diagnose atherosclerosis, to laser trabeculoplasty to treat glaucoma, to machine learning to detect malignant tumors. This innovation is showcased in this year's cover art, designed by Fusion editor Nanami Miyazaki, MSI.

We are grateful for all of the exceptional submissions by GW medical students and hope that this publication can provide an open venue for discussion, advancement, and engagement in the scientific community. The top three abstracts from Fusion were awarded the annual William Beaumont Research Award, and their authors delivered oral presentations at Medical Student Research Day.

This past year has been an exciting one for GW SMHS student researchers. At the 2022 HIV Summit, MSIs were honored to hear Dr. Anthony Fauci's last address as a public servant, in person. In addition, GW elected its first female president, Dr. Ellen Granberg, a sociology scholar and innovative leader. As 2023 progresses, we eagerly await another year of scholarship and innovation from the medical student body.

We gratefully acknowledge the following faculty members who made this edition of Fusion possible: David Leitenberg, MD, PhD, associate professor of microbiology, immunology, and tropical medicine at GW SMHS; medical director of flow cytometry and immunology at Children's National Hospital; and director of medical student research at GW SMHS and Thomas Kohout, director of publications at GW SMHS. We would also like to extend our gratitude to last year's Fusion editors, Jake Adelman, MSII and Mary Pasquale, MSII, for their mentorship.

We sincerely hope you enjoy the 2023 edition of Fusion.

FUSION CO-DIRECTORS
Scarlett Bergam, MSI
Jeffrey Wang, MSI

FUSION EDITORS
Nanami Miyazaki, MSI
Adam Odolil, MSI
Uzma Rentia, MSI

Faculty Advisor Letter for Fusion

David Leitenberg MD, PhD,
associate professor of microbiology, immunology, and tropical medicine at SMHS, and medical director of flow cytometry and immunology at Children's National Hospital

I'm very pleased to start another faculty advisor letter without a long paragraph describing our response to the COVID-19 pandemic. Finally, it looks like we are back to something close to normal!

Medical student research activity at GW continues to thrive. As Director of Medical Student Research and a long time observer of medical students it seems clear that over the last several years there has been a significant increase in students pursuing research activities while in medical school. This is reflected in the record number of submissions to this years' Fusion student research magazine, sustained increases in participation in Medical Student Research Day, and the high percentage of students participating in extracurricular scholarly concentration programs. These trends are also reflected in national data. In a review of graduation questionnaire data from 2015 until 2022, the percent of students nationally who reported pursuing mentored research increased from 69% to 84%. Similarly, the percent of students reporting authorship of a peer reviewed manuscript or presentation at a national meeting increased from 48% to 63%. The experience of our own students is similar with reports of research participation and publication continuing to be slightly above national means.

Explanations for the increasing interest and participation in research among students vary and are almost certainly multifactorial. Changes in the curriculum structure, especially in the pre-clinical phase, over the last several years in most medical schools have increased opportunities for independent study and provided more flexibility for students to become involved with research. Of course, we hope that students are participating in research because of sincere interest and the intellectual stimulation they receive by pursuing in activities outside of the required curriculum. However, another major factor in driving increased research participation is the increasingly selective residency match process. Residency program directors report that in addition to performance in clinical rotations and USMLE Step 2 scores, research accomplishment can be a significant factor in whether students are offered interviews and in match ranking. This corresponds with nationwide trends in adopting a Pass/Fail grading scheme in the preclinical curriculum as well as with the USMLE Step 1 exam moving to a Pass/Fail standard. These changes have resulted in students perceiving increased pressure to distinguish themselves by other measures, including research.

Regardless of the reasons that students participate in research, I believe that the effort itself is valuable. Research can promote the development of valuable problem-solving skills, critical thinking and encourage intellectual curiosity. Although most students do not go on to pursue a career in academic medicine, research experience can be beneficial for any future medical career.

As seen in this issue of Fusion, medical student research interests at the George Washington University are very diverse. The studies described in this issue demonstrate significant breadth of research interest spanning basic science research, clinical studies in a wide variety of disciplines, as well as public health and medical education research. These accomplishments would not be possible without the active engagement of faculty mentors. The significant effort and value of faculty in mentoring and training our students cannot be overstated. On behalf of our students, I thank you all for your efforts!

GW MEDICAL STUDENT RESEARCH

2022 SPECK AWARD GOES TO ERIC CHALIF, MD '23


Eric Chalif, MD '23

The 2022 recipient of the recipient of the annual Doris DeFord Speck, BA '41, and George Speck, MD '41, Endowed Prize for outstanding accomplishments in medical student research was Eric Chalif, MD '23. Chalif boasts an impressive record of research accomplishments during his time at the George Washington University School of Medicine and Health Sciences, including several comprehensive database analyses of factors that affect brain tumor outcomes, as well as more basic studies related to developing immunotherapeutic approaches for the treatment of glioblastoma. He produced seven peer-reviewed manuscripts, two invited reviews, and has several other manuscripts under review, all predominantly related to neurosurgery and neuro-oncology. In addition, Chalif received competitive fellowships from both the Neurosurgery Research and Education Foundation and the Carolyn Kuckein student fellowship from the Alpha Omega Alpha honor society, and he was a previous recipient of an outstanding abstract award at Medical Student Research Day.

MEDICAL STUDENT RESEARCH DAY


William Beaumont Research Awards are presented to three students for outstanding research accomplishments from work submitted for publication in Fusion. The 2022 Beaumont Award winners were (from left) Wayde Dazelle, Alisa Malyvako, and Jacob Bjork.

Medical student research day is an annual event that provides an opportunity for all medical students to showcase their work through submission of abstracts, poster presentations and selected oral presentations. Awards are presented for outstanding abstracts and posters. All medical students are invited to present posters regardless of the area of focus. For the last 3 years over 160 students/year have presented posters at Medical Student Research Day.

METEOR PROGRAM

The Mentored Experience to Expand Opportunities in Research (METEOR) program is a competitive fellowship for underrepresented-in-medicine students. For more information, visit the *website smhs.gwu.edu/academics/md-program/admissions/METEOR.*

RESEARCH FELLOWSHIP OPPORTUNITIES

A number of competitive scholarship programs are available to assist in funding exceptional projects in health care and medicine, including diversity targeted fellowships, including the Jean L. Fourcroy, MD, Research Award; Health Services Scholarships; the Lazarus Family Scholarship Program; and the WT Gill Fellowship, among others.

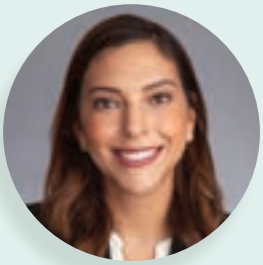
In 2021, 22 students were awarded a Gill Summer Research Fellowship and 54 students were earned Health Services Scholarships, both of which are internally funded programs providing stipend support for medical student summer research.

For a list of SMHS student research funding opportunities, timelines, and application tips visit the website *smhs.gwu.edu/research/research-workforce/medical-student-research/medical-student-funding-opportunities*.

FREEMAN AWARD AND GLEW PRIZE WINNERS

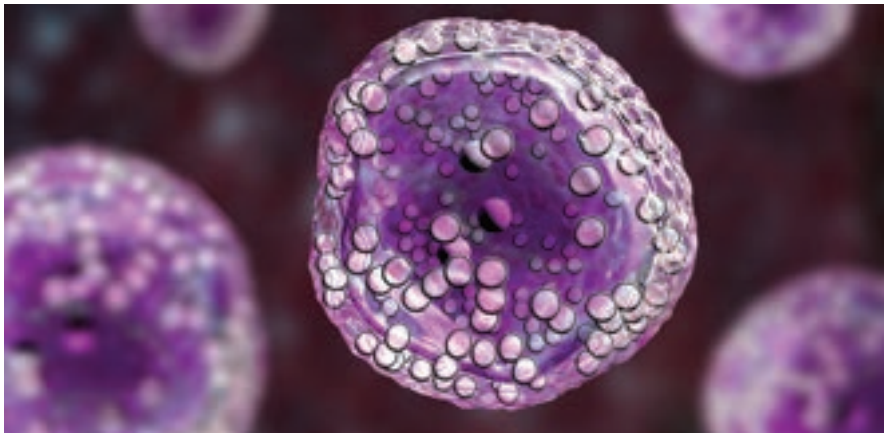
The Freeman Award is given to the graduating senior who submits the best scientific paper based on original research. For 2022, this award was given to Allison Distler, MD '21, for her manuscript titled "Plasma cell dependence on histone/protein deacetylase 11 reveals a therapeutic target in multiple myeloma" published in the Journal of Clinical Investigation Insight.

Paul Boyd, MSII, received the 2022 Donald H. Glew Prize for his abstract and poster, titled "The Impact of Magnetoencephalography-Directed Stereo-Encephalographic Depth Electrode Implantation on Seizure Control Outcome: A Single Institution's Experience." The Glew Prize is presented to the medical student with the best abstract and poster presentation at Medical Student Research Day.



Allison Distler, MD '21

Paul Boyd, MSII



NATIONAL INSTITUTES OF HEALTH SUMMER INTERNSHIP PROGRAM

Angela Sarkisian, MSII

Angela Sarkisian, MSII, was awarded a fellowship as part of the National Institutes of Health Summer Internship Program. The is a summer research immersion program that fosters career development for students interested in becoming physician scientists. Sarkisian's project was within the Pediatric Oncology Branch at the National Cancer Institute, under the mentorship of Nirali Shah, MD, MHSc, head of the Hematologic Malignancies Section, where she studied clinical outcomes of patients with B-cell type acute lymphoblastic leukemia following treatment with chimeric antigen receptor immunotherapy (CAR-T therapy).

Summer Research Opportunities with W.T. Gill Summer Fellowship and Health Services Scholarship

Esin Namoglu (right) and Katie Webber (left) were funded by the W.T. Gill Summer Fellowship and Health Services Scholarship respectively to pursue projects related to assessing changes in the immune response following adoptive T-cell immunotherapy. This work was performed within the Cell Enhancement and Technologies for Immunotherapy program, with faculty mentorship provided by Michael Keller, MD, and Catherine Bollard, MD, MBBCh.

First-year GW medical students are invited to apply for the Gill Fellowship for select research internships at GW SMHS, Children's National Hospital, and the Washington DC Veterans Affairs Medical Center. The Health Services Scholarship provides funding for summer experiential opportunities in a dozen specialty areas including community health, disaster medicine, environmental health, global health, health policy, and integrative medicine.

To learn more, please contact the Office of Student Professional Enrichment smhs.gwu.edu/ospe.

Molecular Stratification of the Pancreatic Cancer Microenvironment

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Pancreatic cancer (PC) is the third leading cause of cancer-related death in both men and women in the U.S. with a five-year survival rate of 11%.1 Despite the excitement surrounding immunotherapy and targeted therapies, PC remains resistant to these treatments. Investigating the PC tumor microenvironment (TME) is critical to understand how PC evades modern therapies. Using digital pathology analysis, we quantitatively characterized the TME of human specimens, particularly in the aggressive squamous-like subtype of PC. Using clinical, genetic, and immune data from bioinformatics databases, we also examined how specific genetic alterations and immune features drive the landscape of the PC TME and inform prognostication of a patient's disease. With these computational tools, we confirmed squamous-like histology on a human PC specimen and identified genetic and immune features that are potentially prognostic of poorer survival.

METHODS

To first visualize the human PC TME, we performed immunohistochemistry (IHC) on de-identified human pancreatic specimens from the George Washington University (GW) Hospital.

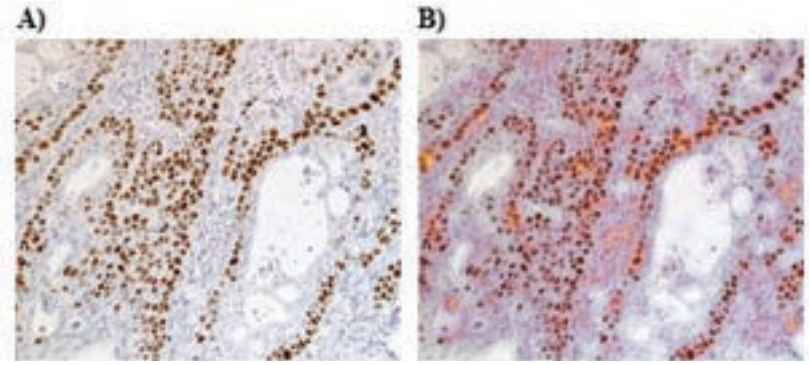

FIGURE 1 A: Representative IHC image of human squamous-like pancreatic cancer with cells in DAB staining positive for p63. **B:** Same image as **A** overlaid with density map generated in QuPath.

Digital pathology analyses were conducted with QuPath. Our IHC analyses were then complemented with an examination of the human PC genome. Clinical, genetic, and immune data from the pancreatic adenocarcinoma (PAAD) patient cohort from The Cancer Genome Atlas (TCGA) were extracted via cBioPortal and iAtlas. Statistical analyses were conducted in RStudio using the R survival package.

RESULTS

The aggressive squamous-like subtype of PC is associated with a genetic alteration in TP63, a key tumor suppressor gene in the TP53 gene family.[2] We conducted histologic and genetic analyses to characterize TP63 in human PC. We performed IHC using p63 antibodies labeled with 3,3'-Diaminobenzidine (DAB) (Figure 1A). Then, we used QuPath to map the density of p63+ cells (Figure 1B). We counted 846 of 1825, or 46.36%, p63+ cells in this image, thus confirming squamous-like histology. Next, we used the R survival package on the TCGA cohort data to quantify clinical outcomes based on squamous-like histology. Survival analysis revealed a lower median overall survival in p63+ patients (15.32 vs 20.19 months, p = 0.0301). Cox regression of log2 copy number values of the TCGA cohort yielded a hazard ratio (HR) of 11.4659 for p63+ patients (p = 0.0000567). These statistics confirm that TP63 alterations confer a survival hazard. Finally, we constructed a master dataset that combines data from the TCGA PAAD cohort to identify additional important prognostic associations. Cox regressions were exhaustively performed

The aggressive squamous-like subtype of PC is associated with a genetic alteration in TP63, a key tumor suppressor gene in the TP53 gene family.[2]

on immune variables from the iAtlas database; notable findings included worse prognosis predicted with M2 macrophages (HR = 8273.054, p = 0.002679), Th2 cells (HR = 1.001, p = 0.0002), and hypoxia score (HR = 1.034, p = 0.001) (Table 1). Thus, patients with PC with an increased presence of these immune features may have worse clinical outcomes.

CONCLUSION

Further studies are needed to characterize the human PC TME and develop additional ways to prognosticate clinical outcomes, which may have the potential to inform therapeutic directions for patients with PC.

TABLE: Table reporting hazard ratios from Cox regression analyses of key immune features.

Immune Feature	Hazard Ratio	p-value
M2 Macrophages	8273.054	0.02679
Th2 cells	1.001	0.0002
Hypoxia	1.034	0.001

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Endovascular Rat Glioma Model for IA Therapeutics

Bennett R. Levy, MSIII

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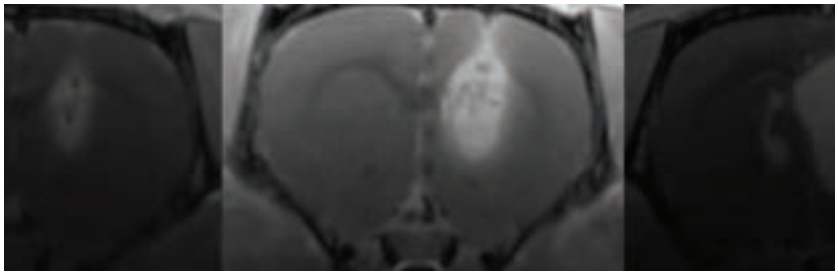

FIGURE 1: C6 Glioma MRI brain T1 with contrast Imaging. MRI T1 sequences with contrast obtained on (A) day 3, (B) 7, and (C) 14.

Many of the current clinical trials aim to assess the effectiveness of intra-arterial (IA) delivery of chemotherapy in patients with glioblastoma multiforme (GBM) that are non-responsive and refractory to standard first line therapies of the Stupp protocol.[1] Due to the poor prognosis of patients with GBM as well as their limited life expectancy of 14–16 months, assessment of chemotherapeutic agents and novel delivery methods in newly diagnosed GBM patients has been a challenge.[2] We aimed to create an endovascular translational animal model to test IA therapies as a first-line treatment for GBM, and we present the first, to our knowledge, endovascular rodent glioma model with technique to perform BBBB.

Wistar rats were sedated with isoflurane, and C6 glioma cells were implanted in the left frontal lobe through a small burr hole created 2 mm anterior and 4 mm lateral to the left from the bregma using a motorized drill and 2 mm drill bit. 100,000 C6 glioma cells were introduced through the burr hole to a depth of 5 mm. C6 Glioma-Implanted Rats (C6GRs) were monitored for overall survival. C6GRs underwent MRI brain imaging (9.4 Tesla Bruker Preclinical MRI) at days 6/7, 13/14, and 17 to 19 days to monitor tumor growth. An example on MRI T1 sequences with contrast are shown in Figure 1 A-C. Tumor volumes were calculated utilizing 3D slicer. Additional rats underwent left femoral artery catheterization (Figure 2A) with a Balt Magic 1.2F catheter (Balt inc., Irvine, California, USA) and Asahi Chikai 0.008 micro guidewire (Asahi Intecc USA, Inc., Santa Ana, California, USA) which was navigated to the left internal carotid artery under fluoroscopy (Figure 2B). 25% mannitol was administered to test BBBB confirmed by 2% Evan blue dye staining. Additional rats underwent up-titrated dose injections of bevascizumab, carboplatin, and irinotecan to test for dosing safety.

With this model, the researchers aim to measure actual tumoral changes to IA chemotherapies such as bevascizumab in the C6 rat glioma model and then further investigate such therapeutics with human GBMs implanted in a rat model.

Ten rats were successfully implanted with C6 gliomas. Overall survival was 19.75 ± 2.21 days. Five rats were utilized for development of our femoral catheterization protocol as well BBBB testing. Rats tolerated our targeted 10 mg/kg of bevascizumab, 2.4 mg/kg of carboplatin, and 15 mg/kg of irinotecan IA ICA injections. The rats exhibited no neurological deficits and had stable weights after being monitored for at least 16–19 days post-injection.

This pilot study presents the first endovascular IA rat glioma model that allows selective catheterization of the intracranial vasculature and delivery of chemotherapeutics for tumor treatment with BBBB. This rat glioma model and endovascular IA route of treatment can be a new way to test novel GBM treatments and assess their efficacy via serial imaging and measurement of overall survival. By inserting a catheter through the femoral artery, there are opportunities to test multiple treatments with one animal at a time and assess for tumoral shrinkage and response. In addition to the two femoral arteries, the tail artery can be utilized to gain access as well.[3] With this model,

the researchers aim to measure actual tumoral changes to IA chemotherapies such as bevascizumab in the C6 rat glioma model and then further investigate such therapeutics with human GBMs implanted in a rat model.

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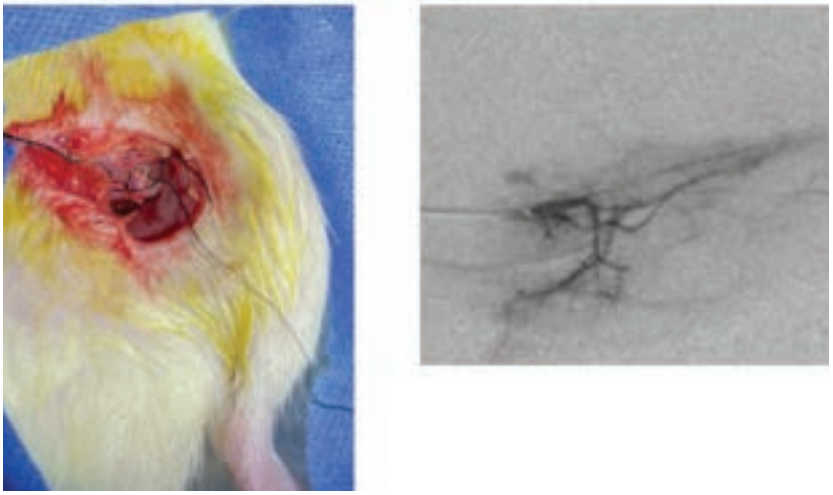

FIGURE 2: IA Chemotherapy Injection. (A) The main femoral artery isolated by careful microdissection under a microscope. (B) Digitally subtracted angiographic image demonstrating contrast filling of the L ICA and intracranial circulation including the anterior and middle cerebral arteries and respective capillary phase.

Socioeconomic Influence on Surgical Management and Outcomes in Patients with Craniosynostosis: A Systematic Review

Melanie Bakovic, MSII

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Disparities in insurance and socioeconomic status (SES) may impact surgical management and subsequent postoperative outcomes for patients with craniosynostosis. This systematic review summarizes and assesses evidence on possible differences in surgical care including procedure type and age at surgery, and differences in surgical outcomes such as complications, length of hospital stay, and child development based on SES.

METHODS

The databases Scopus, PubMed, and CINAHL were searched between May and July 2022. Following participants, intervention, comparison, outcome (PICO) criteria, studies included focused on: patients diagnosed with craniosynostosis; corrective surgery for craniosynostosis; comparison of insurance, income or zip code; and surgical management of postoperative outcomes.

RESULTS

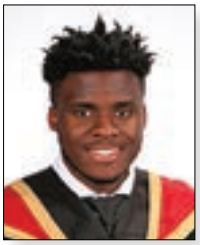
The initial search yielded 336 articles. After three stages of screening, 15 studies were included. Assessed outcomes included: type of procedure (six articles), age at time of surgery (three articles), post operative complications (three articles), referral delay (two articles), length of stay (two articles), child development (one article) and hospital costs (one article). Of the studies with significant results, insurance type was the main SES variable of comparison. While some findings were mixed, these studies indicated that patients with public medical insurance were more likely to have open rather than endoscopic procedures, cranial vault remodeling rather than strip craniectomy, older age at time of surgery, more complications, greater referral delays, longer length of stay, and higher medical charges.

CONCLUSIONS

This systematic review demonstrated that SES may be associated with several differences in the management of patients with craniosynostosis, though insufficient data precluded any definitive, quantifiable results. Further investigation into the impact of SES on the management of patients with craniosynostosis is warranted.

Making the Diagnosis: Utilization of Quality Improvement Methodology to Improve Diagnosis of Obesity and Diet-Related Chronic Disease in an Urban Academic Community Health Center

Richard Fagbemigun, MSIII



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ADVISOR: Kofi Essel, MD, MPH[1,2]

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2. Children's National Hospital

Obesity is a chronic multifactorial disease affecting 20% of children and adolescents.1 National guidelines recommend a diagnosis of obesity starting at age 2, with body mass index (BMI) greater than the 95th percentile, as well as screening for specific comorbidities based on risk factors.2 However, proper use of diagnosis codes are not always utilized appropriately, and many clinicians lack the knowledge of the recommended labs to order.

OBJECTIVE

The aim of this study was to conduct a quality improvement (QI) initiative to drive practice change in the diagnosis of obesity and its comorbidities through appropriate clinical screening, documentation, and coding.

METHODS

Two academic primary care clinics in Washington, D.C., completed a 12-month QI initiative after a clinician needs survey demonstrated the potential for more institutional support to address barriers identified in addressing the diagnosis of obesity and diet-related chronic diseases. A 12-month baseline (02/2020 - 02/2021) of the current clinic documentation practices was identified by reviewing charts of patients between 2- and 18-years-of-age and with a BMI greater than the 95th percentile. Four variables were tracked, including documentation of BMI percentiles utilizing Z-codes, documentation of diagnosis codes associated with weight status utilizing E-codes, ordering of appropriate screening labs based on current guidelines, and documentation of diagnoses associated with abnormal lab results. The QI initiative (03/2021-03/2022) incorporated the integration of evidence-based clinical algorithms, monthly educational training, and coaching sessions on appropriate ways to document diagnoses and order

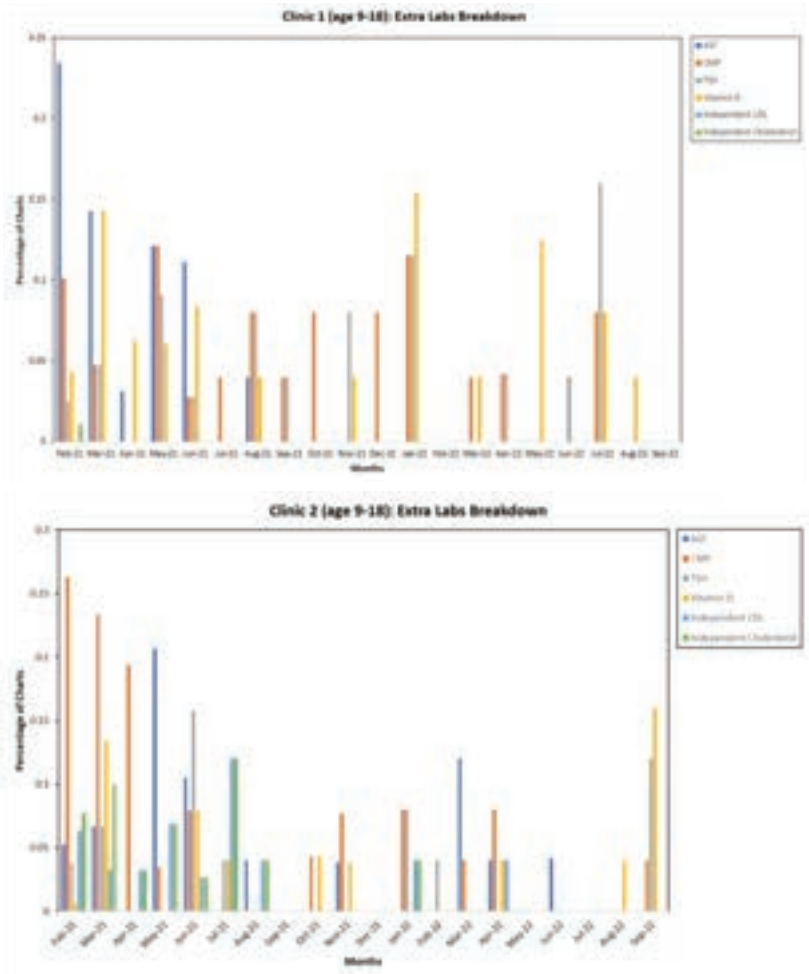

FIGURE 1: Breakdown of extraneous labs ordered at Clinic 1 and Clinic 2.

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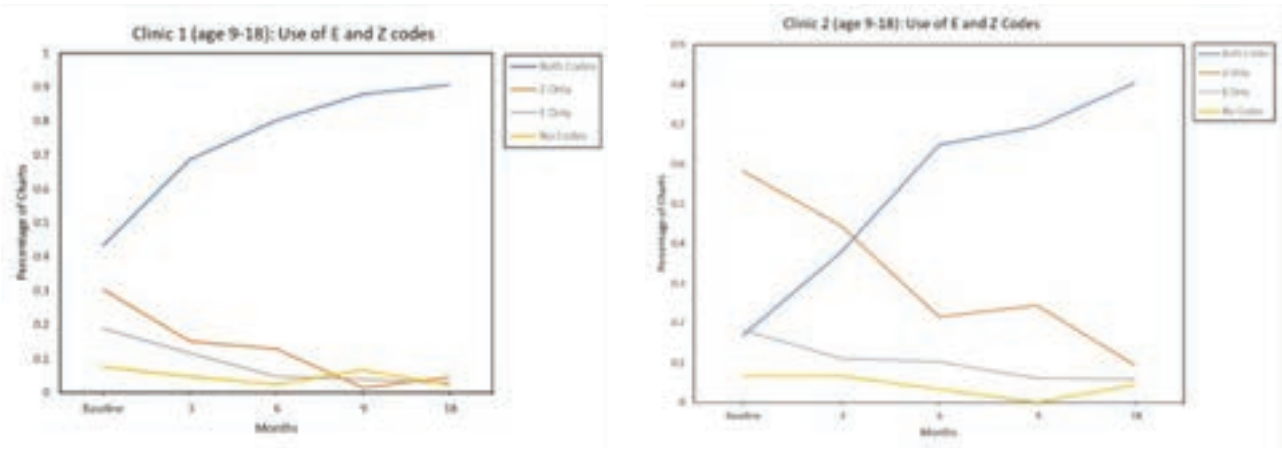

FIGURE 2: Use of E (Obesity Diagnosis) and Z(BMI descriptor) codes at Clinic 1 and Clinic 2.

Continued from p. 13

labs. Chart reviews were performed throughout the QI initiative and six months afterward to observe how documentation of diagnostic criteria changed during and after interventions.

RESULTS

Baseline data showed significant clinician differences in screening. During the intervention, an observable downward trend in extraneous labs was noted in both clinics, with an increase in extraneous labs during the post-intervention period (Fig 1). After multiple training sessions, the use of both E & Z obesity codes significantly increased at both clinics, going from a baseline of less than 20% to a sustained >75% of charts through the post-intervention period (Fig 2).

CONCLUSIONS

Data from both clinics suggest that with a QI program consisting of training and education, pediatricians can improve their clinical decision-making when it comes to diagnosing, billing, and documenting obesity and diet-related chronic diseases.

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Provider Understanding and Experiences of Mental Health and Substance Use Services in the UK's Sexual Assault Referral Centres: A Qualitative Analysis

Veri Seo, MSIV

ADVISOR: Kylee Trevillion, PhD[1]

1. Section of Women's Mental Health, Health Service and Population Department, Institute of Psychiatry, Psychology & Neuroscience, King's College London

There is a strong association between sexual assault (SA) and mental health and substance use (MH/SU) disorders.[1] In the UK, Sexual Assault Referral Centres (SARC) were established as "one-stop" clinics to provide survivors with medico-forensic examinations, psychological support, risk assessments, and victim advocacy, with referrals to additional services as needed. As many as 40% of SARC attendees are known to have significant MH/SU needs, and recent SARC guidelines have named psychological care as a key priority to improve within the service.[2,3] However, SARCs vary widely in the MH/SU treatments they offer in-house and in referral practices to behavioral health specialists, resulting in gaps in the care pathway.[4]

AIM

To qualitatively explore health, behavioral health, and social service providers' understanding of MH/SU care in SARCs, and to elucidate perceived barriers and facilitators to coordinating MH/SU care for SARC attendees in England.

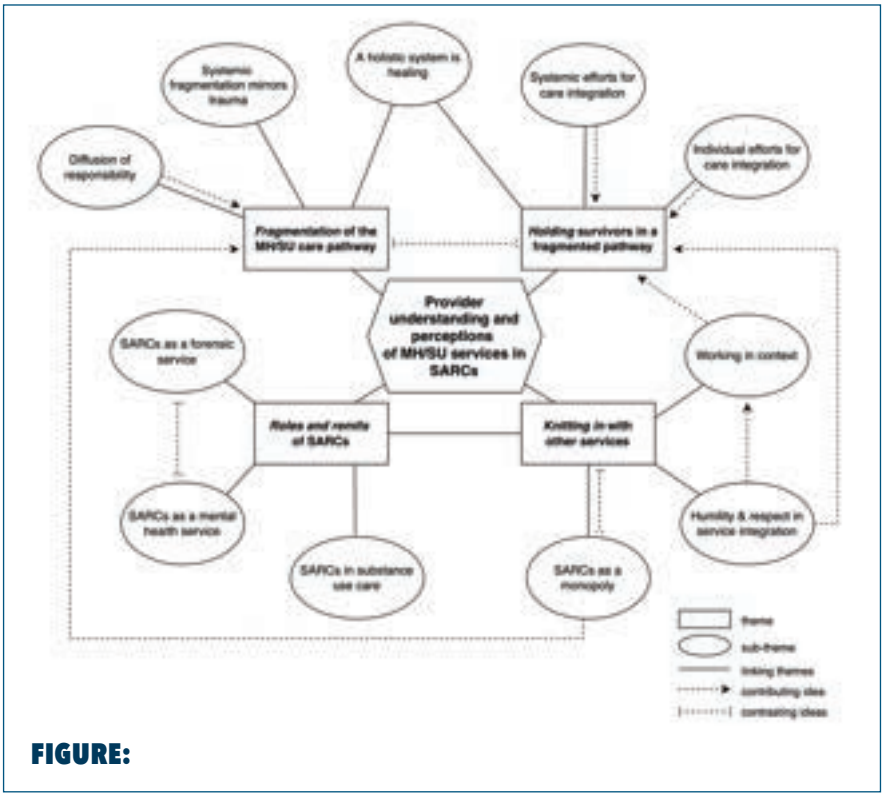

FIGURE:

METHODS

Secondary qualitative analysis of individual interviews/focus groups conducted with twenty-eight providers working in SARCs and partner organizations across England. Participants were purposively sampled to represent a range of geographic regions, types of organizations (e.g., SARC vs. voluntary sector organization), and provider roles (e.g., forensic examiner, clinic/organization manager, psychologist/counselor). Reflexive thematic analysis with a constructivist theoretical framework was used to generate themes and sub-themes, which were arranged into a thematic map (Figure 1).[5]

RESULTS

Participants held a shared perception that MH/SU care was highly disjointed for SARC attendees, which may exacerbate the trauma and destabilization experienced by SA survivors (Fragmentation). They described multiple systems- and provider-level strategies to overcome these gaps, including providing follow-up counseling/therapy within SARCs and commissioning referral pathways between SARCs and behavioral health specialists in the community (Holding). Participants varied widely in their knowledge of the MH/SU treatments offered in their local SARC, as well as their perspectives on SARCs' intended role within behavioral health care (Roles and Remits). These views differed by participants' professional identity and existing service structures in their

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area; however, there was a notable disconnect between SARCs and substance use care across all regions, even in those with robust SARC-based or community-based mental health services. Finally, participants discussed how SARCs must better integrate into the existing milieu of health, behavioral health, and social services – particularly with non-statutory voluntary sector organizations specializing in sexual/domestic violence (Knitting In).

DISCUSSION

It remains a challenge to create a coherent MH/SU care pathway for SA survivors, even for those attending "one-stop" SARCs. While SARCs have employed different strategies to better address attendees' behavioral health needs, providers in other violence organizations. Systems-level, not just provider-level, efforts are needed to help ensure that interagency partnerships are in place from the outset and maintained; such collaborations, in turn, will create a truly holistic system of care for survivors. Future areas of research include exploring the perspectives of SARC attendees in navigating the MH/SU care within and post-SARC, and those of local organizations — including those in the mental health, substance use, or sexual violence sectors — may have a limited understanding of SARCs' role in MH/SU care. This highlights the potentially missed opportunities for SARCs to collaborate with important sources of psychosocial care for the most vulnerable within their communities. Specifically, there needs to be greater collaboration between SARCs and substance use specialists, as well as with voluntary sector sexual/domestic policymakers overseeing behavioral health care provision within SARCs.

While SARCs have employed different strategies to better address attendees' behavioral health needs, providers in other organizations – including those in the mental health, substance use, or sexual violence sectors – may have a limited understanding of SARCs' role in MH/SU care.

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Opportunities and Challenges to Emergency Department-Based HIV Testing Services and Self-Testing Programs: A Qualitative Study of Health Care Providers and Patients in Kenya

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Young people in Sub-Saharan Africa, especially males, have been insufficiently engaged through HIV Testing Services (HTS). In Kenya, younger persons are often treated in emergency departments (EDs) for injuries, where HTS and HIV self-testing (HIVST) can be leveraged. Data from stakeholders on ED-HTS and HIVST is needed to understand opportunities and barriers for HIV testing and inform program implementation.

METHODS

Between December 2021 and March 2022, 32 in-depth interviews (IDIs) were conducted with 16 male and 16 female patients who had been treated in the Kenyatta National Hospital (KNH) ED, half of whom had been HIV-tested. Six focus group discussions (FGDs) were conducted with 50 ED nurses, doctors, HIV testing counselors, and administrators. All transcripts were double-coded and thematically analyzed using Dedoose software and parallel inductive and deductive coding to capture both a priori and emergent themes.

RESULTS

Patients and providers agreed that ED-HTS are facilitated by friendly staff, patient education, high perceived HIV risk, and confidentiality. However, ED-HTS is limited by burdens on staff, resources, time, and space, as well as the severity of patient injuries limiting the ability to consent to or prioritize HIV testing. These limitations provide opportunities for ED-HIVST: particularly the ability to test at a comfortable time and place, especially when provided alongside sufficient HIV and testing education, contact with health care providers, and psychosocial support. Barriers to ED-HIVST included patients' concerns about HIVST accuracy and mental health impacts of a positive test, as well as providers' concerns for loss to follow-up and inability to complete confirmatory testing.

Patients and providers agreed that ED-HTS are facilitated by friendly staff, patient education, high perceived HIV risk, and confidentiality.

CONCLUSION

ED stakeholders are receptive to HTS and HIVST, and patients desire the opportunity to use HIVST. Potential challenges — such as psychological effects of testing positive, worries about access to follow-up care, and confusion about how to self-administer testing, may be addressed through programming designed to promote education, access, and follow-up.

What Telehealth Services are Appropriate to Reimburse for a Medicaid Population to Ensure Equitable Access to Quality Care?

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When the United States Department of Health and Human Services instituted a State of Public Health Emergency (PHE) during the COVID-19 pandemic, many new telehealth flexibilities were fast-tracked to care for sick populations that were isolated at home. These flexibilities allowed for State Medicaid programs to issue reimbursement for new telehealth specialty services, new sites of care, and new mediums such as Skype to communicate with patients.[1] Effectively, a new system of care was created that allowed many financially vulnerable patients in the Medicaid space to access care more easily, as evidenced by an uptick in telehealth utilization rates during the COVID-19 pandemic.[2] Research-to-date has mostly focused on telehealth reimbursement for more narrow use cases such as rural primary care, with limited consideration for how telehealth can be appropriately mainstreamed and sustained.[3]

OBJECTIVE

This study sought to do the following: (1) evaluate the continuation of telehealth reimbursement flexibilities more broadly beyond the COVID-19 pandemic, (2) analyze the clinical effectiveness of the new telehealth services, and (3) offer code-by-code reimbursement guidance to State Medicaid leaders.

METHODS

We surveyed 10 State Medicaid Medical Directors who are responsible for the scientific and clinical appropriateness of Medicaid policies in their respective states. Participants were asked to complete an online survey with a list of CPT/HCPCS codes, grouped by service type, and asked if they believed they should be reimbursed by Medicaid on a permanent basis beyond the PHE. Additional questions covered more detailed recommendations, such as: reimbursing video-with-audio vs audio-only, guardrails for certain specialty services, and motivations behind responses.

RESULTS

State Medicaid Medical Directors felt that the majority of services should be reimbursed via some modality of telehealth after the PHE, although some were more comfortable with video combined with audio compared to audio-only. More than half of supportive respondents also felt that there should be continued guardrails for reimbursement. There were exceptions on both ends of the spectrum, where services such as pulmonary diagnostics were not recommended to be reimbursed in any form and services such as psychotherapy for mental health which had the most support for audio-only. The full list of code-by-code guidance is attached in the appendix. Motivations for continuing reimbursement flexibility were largely attributed to improving access to care, improving outcomes, and improving equity amongst the Medicaid patient population.

CONCLUSIONS

There is strong clinical endorsement to continue the telehealth flexibility enabled by the PHE, primarily for video-combined-with-audio telehealth with caution for audio-only telehealth. This endorsement is scoped to services approved by HHS during the pandemic. Disapproval was shown for clinical situations where visualization or hands-on-intervention was necessary for diagnosis or treatment. These results are primarily from a perspective of clinical appropriateness and health equity on a state-by-state level and should be complemented with other factors such as fiscal and technical implementation.

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Breaking the Cycle of Acute Coronary Syndromes in the Young and the Emerging Role of Artificial Intelligence

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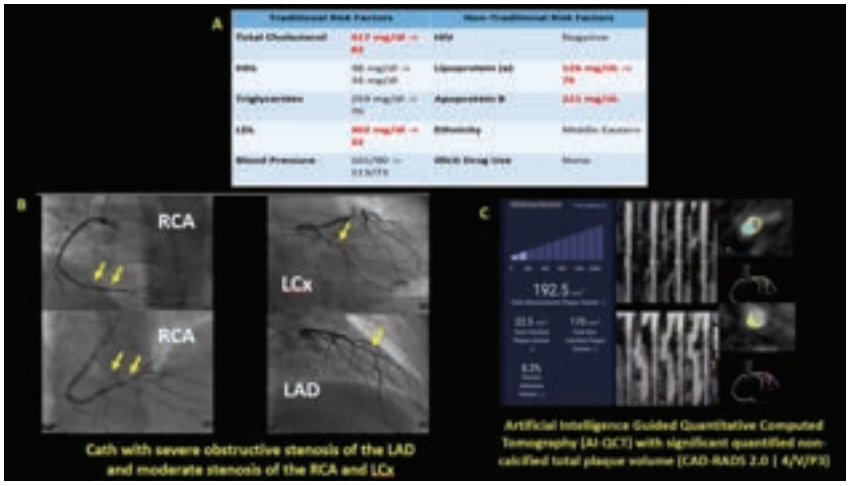

FIGURE:

Acute coronary syndromes (ACS) in young adults are rising. New treatments and artificial intelligence (AI) may enhance long-term prevention.

CASE

A 28-year-old healthy, but obese, male smoker presented with possible cardiac chest pain (CP). By the 2021 ACC CP guideline, he was low risk with normal ECG with the exception of a mildly elevated troponin-I (0.121 ng/mL).

DECISION MAKING

Coronary computed tomography angiogram (CCTA) showed multi-vessel CAD including obstructive (≥70%) stenosis of the mid-left anterior descending and moderate obstructive (50–69%) stenosis of the distal right and proximal left circumflex coronary arteries (Figure). CAD was confirmed on invasive angiography with revascularization of the LAD. Labs (Figure) showed heterozygous familial hyperlipidemia and elevated lipoprotein (a). As he was very high risk and with significant burden of atherosclerosis, by 2022 ACC non-statin therapy expert consensus, the patient was placed on high dose statin with evolocumab and lifestyle changes with significant improvement (Figure). Novel AI guided quantitative computed tomography (AI-QCT, Cleerly, New York) enabled precise quantification of non-calcified plaque (Figure).

CONCLUSION

Breaking the cycle of ACS in young adults requires improved early identification, risk assessment and lifestyle intervention. Novel methods of CAD evaluation (e.g., AI-guided) may enhance efforts for long-term prevention via non-invasive means for treatment response and plaque regression through future trials.

Assessment of Atherosclerotic Plaque Burden: Comparison of AI-QCT Versus SIS, CAC, Visual, and CAD-RADS Stenosis Categories

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Quantitative assessment of plaque burden may enable risk prognostication beyond the paradigm of % stenosis in current guidelines, but is uncommonly utilized in clinical practice. Atherosclerosis Imaging-Quantitative Computed Tomography (AI-QCT) through artificial intelligence may enable rapid, accurate assessment, but has not been compared to standard clinical methods of plaque assessment.

METHODS

Consecutive patients from the CLARIFY (CT Evaluation by Artificial Intelligence for Atherosclerosis, Stenosis and Vascular Morphology) study of patients undergoing cardiac computed tomography angiography (CCTA) for chest pain were evaluated. Studies were analyzed by a blinded core laboratory through FDA cleared software that performs AI-QCT through artificial intelligence including % stenosis, plaque volume and composition (Figure 1). AI-QCT plaque volume was staged (0-10 mm3, 11-250 mm3, >250-750mm3 and >750mm3) by prognostic thresholds. This staging was compared to clinical methods of plaque evaluation that include segment involvement score (0, 1-4, 5-7, ≥8), visual plaque estimate (None, Mild, Moderate, Severe), CAD-RADS % stenosis category (0, 1-2, 3, 4-5) and coronary artery calcium score (0, 1-100, 101-300, >300) as identified by a consensus of visual assessment by consensus of an Independent Practitioner (IP) and Advanced Practitioner (AP) blinded to the AI-QCT core lab reads using categorical methods of interobserver agreement and the kappa statistic.

TABLE: Contingency Table of SIS vs AI-QCT Plaque Volume. In comparing AI-QCT whole heart plaque quantification to SIS, there was high agreement (93%; k= 0.87 [95% CI: 0.79-0.96]). The AI-QCT was more sensitive to mild plaque burden (P1).

N = 102		AI-QCT Plaque Volume Category			
		0-10 mm³	11-250 mm³	250-750 mm³	>750 mm³
Segment Involvement Score (SIS)	0	29	8	0	0
	1-4	0	52	0	0
	5-7	0	0	12	0
	>=8	0	0	0	4

SIS vs AI-QCT
Overall Agreement = 93%
K = 0.87 (0.79-0.96)

RESULTS

There were n=102 patients (Mean age: 59±11 years; 44% female). AI-QCT median plaque volume was 95 mm3 ± 238 mm3. AI-QCT plaque burden stage had high agreement 93% (k=0.874 95% CI: 0.79-0.959) with segment involvement score categories (Table 1). However, the agreement between AI-QCT and categories of visual assessment (64%; k=0.51 [0.395-0.631]), coronary artery calcium score (66%; k=0.49 [0.363-0.614]) and CAD-RADS (59%; k=0.448 [0.32-0.576]) was modest.

CONCLUSION

In this assessment of plaque burden, AI-QCT and SIS demonstrated high agreement, while agreement was modest between AI-QCT and other methods. With ongoing validation, AI-QCT may enable a rapid, reproducible, quantitative approach to CAD

burden categorical assessment beyond time consuming visual approaches.

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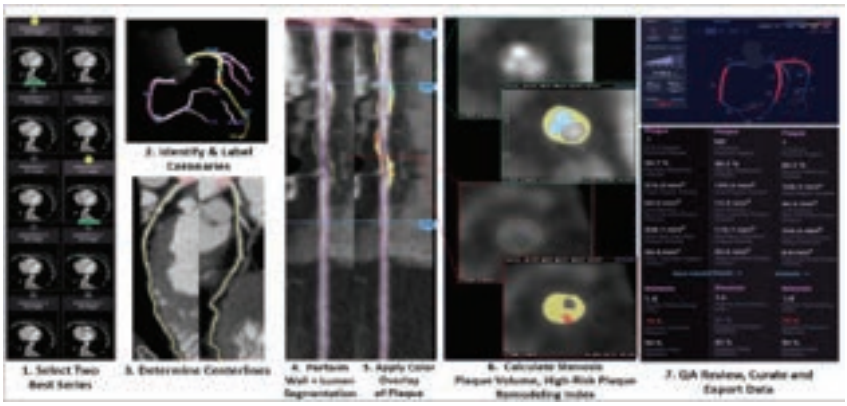

FIGURE: Artificial Intelligence-Quantitative Computed Tomography (AI-QCT. As shown above, the AI-QCT first selects the two best series, then identifies and labels the coronaries, and determines the centerlines. Then, there is automated segmentation of the coronary artery wall and lumen, after which it applies a color overlay to the plaque. Next, there is calculation of % stenosis plaque volume and high-risk plaque remodeling index. After a quality assurance review, the data is exported and curated in a graphic interface.

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Abnormal PTFV1 Size is Associated with Development of Atrial Fibrillation in an Obstructive Sleep Apnea Cohort

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This study aimed to investigate the interaction between obstructive sleep apnea (OSA) and development of atrial fibrillation (AF) by analyzing P-wave terminal force in V1 (PTFV1), an ECG parameter related to left atrial (LA) abnormalities. One retrospective analysis of a sleep clinic cohort identified an association between OSA severity and ECG-defined LA abnormalities.[1] ECG-defined LA abnormalities, indicative of some structural or electrical remodeling, is suggestive of a predisposition to AF. PTFV1, P-wave duration, and PWAV1 are useful ECG markers that can be used independently to stratify the risk of incident ischemic stroke but require more thorough investigation.[2] We hypothesize that in patients with OSA, the odds of having an ECG with an abnormal PTFV1 value (as defined by > -4000 μV*ms) are higher in those who developed AF, compared with controls.

METHODS

A retrospective review was conducted in patients who underwent a polysomnography (PSG). Inclusion criteria for data collection were completion of PSG, diagnosis of OSA, and record of ECG. Manual measurements which were done using the EP Calipers software (EP Studios, Inc.) to standardize our approach (Figure 1).

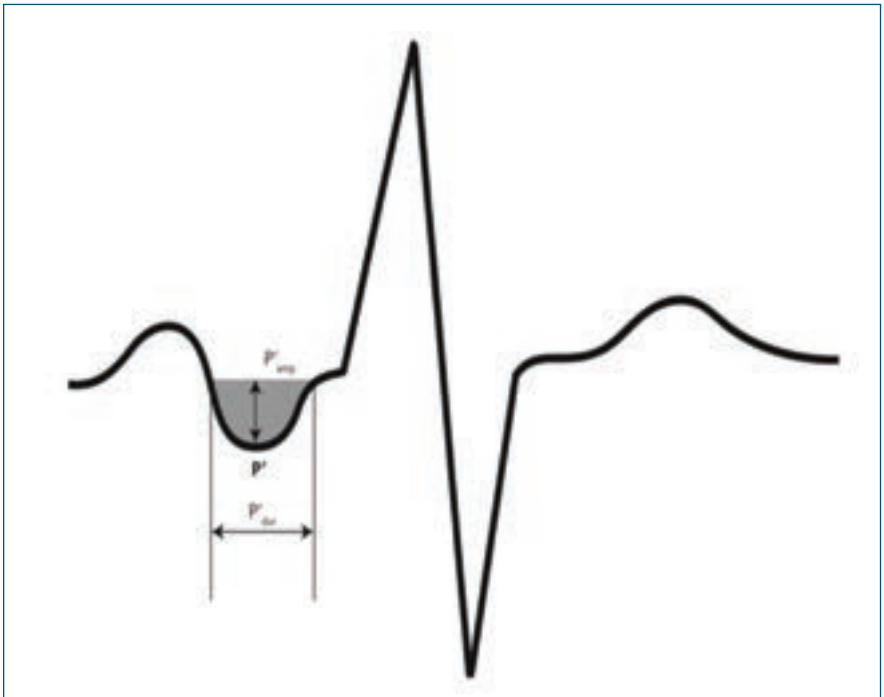

FIGURE: Demonstration of PTFV1 size with shading of negative deflection of biphasic p-wave seen in lead V1.

RESULTS

Sixty-two patients with AF and 377 control patients without AF were included for analysis. Baseline characteristics were similar between the two subgroups (relevant parameters are tabulated in table 1). PTFV1 was significantly higher in the AF subgroup (-4593.01 μV*ms) vs the control subgroup of -1906.2 μV*ms (p <0.001). Of the 62 patients who developed AF, 27 were noted to have an abnormal PTFV1 as defined as a value >[-4,000 μV*ms]. The odds ratio was calculated to be 3.32 (CI 1.89-5.84).

CONCLUSIONS

We found that in a cohort of patients with OSA, the odds of having an ECG with an abnormal PTFV1 value (as defined by > -4000 μV*ms) were higher in those who developed AF, compared with those who did not. This value is comparable to previous odds ratios calculated in the general population, but appears elevated in our cohort, suggesting a heightened risk in individuals with OSA irrespective of OSA severity (as noted by AHI), arousal index, or CPAP usage. Future research should expand on these preliminary results to include a larger sample size and more robust patient demographic data.

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TABLE: Demonstration of clinical characteristics. Data are expressed as the mean + SD or as a number (percentage), with associated p values.

	AF cohort (n=62)	Non-AF cohort (n=377)	p value
Age, years	53.9±10.1	50.4±9.4	0.433
Heart rate, bpm	78.4	74.1	0.512
P wave duration lead II, ms	119.7±19.4	115.5±13.3	0.631
P wave dispersion, ms	71.7±19.9	68.7±13.3	0.458
P wave axis, degrees	53.6±32.5	50.4±22.6	0.392
PR interval, ms	171.0±36.9	164.6±26.1	0.127
PTFV1, μV*ms	-4593±2639.1	-1906.2±1363.5	$1.28x10^{-24}$
QT, ms	391.7±33.8	392.9±33.1	0.785
QTc, ms	422.8±55.2	424.3±35.4	0.789
LVH on ECG	19 (30.7%)	104 (27.5%)	0.417
AHI, events/hr	35.2±23.3	32.0±23.6	0.138
Arousal Index, events/hr	23.9±14.2	22.7±15.0	0.241
Lowest desaturation, %	81%±0.11	81%±0.10	0.84
Mean nocturnal SpO2, %	94%±0.04	95%±0.03	0.093
CPAP usage	36 (58.1%)	227 (60.2%)	0.647
Data are expressed as the mean±SD or as number (percentage)			

Superb Microvascular Imaging vs. Contrast-Enhanced Ultrasound in the Detection of Endoleaks Following Endovascular Aneurysm Repair

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More than 175,000 deaths occur globally each year due to abdominal aortic aneurysms (AAA). Although the advent of endovascular aneurysm repair (EVAR) has improved AAA patient outcomes, approximately 45% of EVAR patients will experience a graft endoleak following their procedure.[1] Endoleaks often remain asymptomatic and pose a high risk of rupture.[1] The current standard of follow-up for patients involves endoleak surveillance using computed tomography angiography (CTA).[2] Regular reliance on CTA for endoleak screening subjects patients to superfluous medical costs, radiation dosages, and nephrotoxic contrast.[2] Safer, more economical imaging modalities with comparable diagnostic accuracy must be considered. Superb microvascular imaging (SMI) and contrast-enhanced ultrasound (CEUS) are promising diagnostic options. This review article will compare SMI to CEUS to determine which method offers higher sensitivity and specificity for endoleak identification.

METHODS

A PubMed database literature review was performed to compare the sensitivity and specificity of SMI to CEUS for identification of endoleaks following EVAR. Results from five studies with a total of 4,199 cases were analyzed based on predetermined inclusion criteria. Of these cases, 209 used SMI, and 3,990 utilized CEUS.[1–5]

RESULTS

Based on the 209 patients assessed with SMI post-EVAR, it offered an average sensitivity and specificity of 88.2% and 98.5%, respectively, in detecting endoleaks.[1,2,3] Alternatively, in the 3,990 patients monitored with CEUS post-EVAR demonstrated an average sensitivity and specificity for endoleaks of 95.7% and 93%, respectively.[4,5] Based on these findings, CEUS offers a significantly higher sensitivity for post-EVAR endoleaks ($p < 0.00001$) while SMI stands as a significantly more specific imaging approach ($p < 0.05$).

CONCLUSION

This study demonstrates that SMI offers a significantly higher specificity for detecting post-EVAR endoleaks, while CEUS is a significantly more sensitive technique.[1-5] Based on these results we conclude that CEUS is recommended over SMI as an alternative to CTA. Due to the limited data that exists regarding SMI detection of endoleaks, further studies must be conducted regarding its efficacy as it could prove to be a useful alternative.

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Early Tracheostomy in Older Trauma Patients Exhibit Comparable Benefits to Those in Younger Patients

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Early tracheostomy is associated with a lower incidence of pneumonia (PNA) and duration of mechanical ventilation (MVD) in hospitalized trauma patients.[1,2] The purpose of this study was to determine if early tracheostomy also benefited older adults compared to a younger cohort.

METHODS

Adult hospitalized trauma patients who received a tracheostomy as registered in Trauma Quality Improvement Program (TQIP) from 2013–19 were analyzed. We excluded patients with tracheostomy prior to admission and patients with AIS of any body region equal to six. Patients were stratified into two cohorts consisting of those aged ≥65 and those aged <65. These cohorts were analyzed separately to compare the outcomes of early (< five days) vs late (> five days) tracheostomy. The primary outcome was MVD. Secondary outcomes were in-hospital mortality, hospital length of stay (HLOS), and PNA. Univariate and multivariate analyses were performed with significance defined as p-value < 0.05.

RESULTS

In patients aged <65, early tracheostomy was performed within a median of 2.3 days (IQR, 0.47-3.8) after intubation and a median of 9.9 days (IQR, 7.5-13) in the late tracheostomy group. The early tracheostomy group's ISS was significantly lower with fewer comorbidities. In patients aged ≥65, early tracheostomy was performed within a median of 2.7 (IQR, 0.67-4.0) days after intubation and a median of 9.8 days (IQR, 7.4-13) in the late tracheostomy group. There were no differences in injury severity or comorbidities when comparing the groups. Early tracheostomy was associated with lower MVD, PNA, and HLOS on univariate and multivariate analyses in both age cohorts, although the degree of benefit was higher in the younger cohort. Mortality did not differ based on time to tracheostomy.

Early tracheostomy was associated with lower MVD, PNA, and HLOS on univariate and multivariate analyses in both age cohorts, although the degree of benefit was higher in the younger cohort.

CONCLUSION

Early tracheostomy benefits hospitalized trauma patients regardless of age. Age should not factor into timing for tracheostomy placement.

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Comparing Midline Versus Central Line Venous Blood Gas Oxygen Saturations: A Novel Pilot Study

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Midlines (ML) are long peripheral intravenous catheters inserted above the antecubital space via the basilic, cephalic, or brachial veins. These catheters provide safe and comfortable mid-term vascular access for critically ill patients. Central venous oxygen saturations (ScvO2) obtained from central venous catheters (CVCs) are often used to approximate cardiac oxygen delivery. However, because CVCs are considerably invasive, there is an incentive to find a less invasive measurement to substitute ScvO2 as a guide for resuscitation. In 2010, simultaneous, paired samples of ScvO2 and femoral venous oxygen saturation (SfvO2) were compared in critically ill patients, but SfvO2 was not found to be a reliable predictor of ScvO2.1 More recently, paired blood samples of peripheral venous oxygen saturation (SpvO2) and ScvO2 were found to be in acceptable to moderate agreement.2,3 However, both studies revealed substantial bias with Bland-Altman analysis, so these values cannot be used interchangeably during resuscitation. Similar results of non-equivalence were found comparing pulmonary artery catheter (PAC) ScvO2 to mixed venous O2.4 One study displayed excellent reliability between different measures of venous oxygen saturation compared to that of a PICC line.[5] However, PICC lines remain more invasive than MLs. Given the proximity of MLs to the axillary vein, we believe there is value in exploring the equivalence of midline oxygen (MO2) saturation and ScvO2. If correlated, MO2 could provide additional physiologic information, while decreasing the need for invasive CVCs.

Our study is a prospective observational study in adult patients with a CVC in the internal jugular or subclavian veins who were planned to have an ML placed or with one already in situ. Venous oxygen saturations were compared between both catheters using a point-of-care blood gas analysis on iSTAT (Abbott ©) machines and analyzed within a 15-minute period.

A total of n= 24 patients were enrolled. The relationship between ScvO2 and MO2 was evaluated by the Wilcoxon Signed Rank Test and Bland-Altman Plot Analysis. Subjects were 67% male and 62.5% Black. The mean age was 57.9 years with an average SOFA score of 8.3 and APACHE II of 19.1. Patients were most commonly admitted for acute respiratory failure (45.8%) and septic shock (25%). The overall mean ScvO2 and MO2 were 66.2% ± 10.6% and 60% ± 16.6%, respectively (p = 0.003), with a mean bias of 6.25% ± 9.59%. A Bland-Altman analysis demonstrated that more than 50% of ScvO2 and MO2 had a discordance of at least 5%; a clinically relevant difference. In a subgroup analysis, samples comparing right-sided MLs to CVCs (n=13) revealed a mean ScvO2 of 66.2% ± 10.3% and mean MO2 of 62.1% ± 16.15% (p=0.17).

MO2 as a potential correlate of ScvO2 is an intriguing concept and its clinical utility remains to be seen. Our preliminary findings showed an approximate aggregate 6.2% difference in mean MO2 vs ScvO2, however, there was significant divergence in >50% of subjects. A right-sided ML is an interesting variable, as the anatomic location may affect the relationship to the ScvO2 in addition to concurrent vasopressor use and various shock states. Further investigation is actively ongoing.

MO2 as a potential correlate of ScvO2 is an intriguing concept and its clinical utility remains to be seen.

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Assessment of Racial Differences of Atopic Dermatitis Characteristics in a Diverse Outpatient Cohort in the United States

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Atopic dermatitis (AD) can present differently across racial groups. To promote equality and consistency, dermatologists and other providers should properly recognize the heterogeneous manifestations of AD across racial groups. Yet, little is known about differences in the features of AD by race. This study assesses racial differences of the key features of AD.

METHODS

The health care claims database from a large metropolitan tertiary care medical center was queried for patients with physician-diagnosed AD using International Classification of Disease, Tenth Revision, Clinical Modification codes L20.x. Medical records were reviewed for demographics, comorbidities, and documentation of Hanifin-Rajka criteria. Frequency of each criterion was evaluated by race (White, Black, Asian, Multiracial-Other).

TABLE: Presence of key features of atopic dermatitis by race.

Hanifin-Rajka criteria	White (n=374)	Black (n=284)	Asian (n=89)	Multiracial/ Other (n=19)	P-value
Major criteria					
Pruritus	324 (97.0%)	254 (97.0%)	74 (97.4%)	17 (89.5%)	0.33
Early Age of Onset	130 (41.8%)	88 (39.3%)	41 (56.9%)	6 (40.0%)	0.07
Flexural Dermatitis	232 (75.3%)	150 (67.3%)	56 (73.7%)	15 (83.3%)	0.14
Chronic Dermatitis	178 (65.0%)	123 (69.9%)	52 (77.6%)	12 (75.0%)	0.20
Personal History of Atopic Disease	184 (57.3%)	197 (81.4%)	46 (59.7%)	10 (58.8%)	<0.0001
Family History of Atopic Disease	119 (42.2%)	108 (63.2%)	22 (31.4%)	5 (33.3%)	<0.0001
Minor Criteria					
Xerosis	150 (73.9%)	154 (84.2%)	31 (68.9%)	13 (86.7%)	0.03
Ichthyosis	25 (16.5%)	27 (23.9%)	7 (24.1%)	2 (18.2%)	0.46
Nipple Eczema	14 (7.7%)	10 (10.6%)	4 (10.5%)	2 (14.3)	0.74
Hand/Foot Dermatitis	164 (56.4%)	132 (56.4%)	36 (49.3%)	8 (53.3%)	0.72
Immediate Skin Reactivity	62 (56.9%)	21 (51.2%)	13 (46.4%)	2 (33.3%)	0.55
Subcapsular Cataracts	2 (1.9%)	3 (4.0%)	1 (4.4%)	1 (14.3%)	0.33
Cutaneous Infections	113 (44.5%)	80 (44.2%)	29 (50.1%)	5 (55.6%)	0.74
Elevated IgE	24 (27.5%)	26 (46.4%)	7 (36.8%)	3 (75.0%)	0.04
Pruritus when Sweating	95 (78.5%)	31 (64.6%)	21 (72.4%)	6 (54.6%)	0.14
Anterior Neck Fold Involvement	48 (25.3%)	41 (24.6%)	20 (42.6%)	1 (12.5%)	0.06
Intolerance to Wool/ Lipid Solvents	53 (57.6%)	21 (52.5%)	14 (56.0%)	1 (20.0%)	0.42
Perifollicular Accentuation	31 (36.9%)	40 (60.6%)	10 (40.0%)	2 (28.6%)	0.02
Food Hypersensitivity	52 (35.1%)	40 (50.0%)	12 (33.3%)	5 (71.4%)	0.04
Environmental/ Emotional Influence	205 (90.3%)	108 (94.7%)	49 (94.2%)	13 (100.0%)	0.31
White Dermatographism	17 (20.2%)	7 (16.8%)	1 (5.6%)	1 (16.8%)	0.52

RESULTS

Overall, 766 patients with AD were included in the study; 374 (48.8%) were White, 284 (37.1%) Black, 89 (11.6%) Asian, and 19 (2.5%) multiracial/other, 558 (68.2%) were female, 50 (6.1%) were age <18 years, 456 (55.7%) age 18-49 years, and 313 (38.2%) age ≥50 years.

Compared to White patients, Black patients had significantly higher

proportions of personal (81.4% vs. 57.3%) and family (63.3% vs. 42.2%) history of atopic disease, perifollicular accentuation (60.6% vs. 36.9%), and xerosis on physical exam (84.2% vs. 73.9%)(P≤0.03 for all). Multiracial/other patients had elevated proportions of history of dry skin (81.3%), xerosis on physical exam (86.7%), and elevated Immunoglobulin E levels (75.0%). Black and multiracial/other patients had food hypersensitivity compared to White patients (50.0% and 71.4% vs. 35.1%, P=0.04). There were marginally significant differences in the proportion of early age of AD onset (56.9% vs. 41.8%, P=0.07) and anterior neck fold involvement (42.6% vs. 25.3%, P=0.06) in Asian compared to White patients. There were no significant racial differences in the likelihood of other Hanifin-Rajka criteria, including pruritus, flexural dermatitis, chronic dermatitis, ichthyosis, nipple eczema, hand/foot dermatitis, immediate skin reactivity, subcapsular cataracts, cutaneous infections, pruritus when sweating, intolerance to wool/lipid solvents, environmental/emotional factors worsening AD, or white dermatographism.

A recent systematic review found differences of AD characteristics by study region.[1] Flexural involvement was less commonly reported in India, America and Iran. East Asian studies reported more erythroderma, truncal, extensor, scalp, and auricular involvement. Southeast Asian studies reported more exudative eczema, truncal involvement, lichenification and prurigo nodules. Studies from Africa reported more papular lichenoid lesions, palmar hyperlinearity, ichthyosis, and orbital darkening.

CONCLUSIONS

Our results further indicate there are racial differences of AD characteristics within the same region. These differences may be attributable to population-differences of genetics, environmental exposures, skincare practices, etc. Future research is needed to understand the mechanisms and treatment responses of these heterogeneous AD presentations.

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Is Beta-Alanine a Potential Therapy for Idiopathic Aquagenic Pruritus?

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Aquagenic pruritus (AP) is a skin condition that manifests as an acute itching sensation following water exposure. Many patients report that their AP symptoms are so severe that they actively avoid water-based activities, including showering and swimming, and that they experience significant depreciation of the quality of life. The pathophysiology of idiopathic AP is poorly understood, posing a challenge for treatment. Thus far, treatments for idiopathic AP have had varying efficacies and limited clinical evidence. One therapeutic option rising in popularity in online patient forums is beta-alanine (bAla), but it requires further investigation on its mechanisms, safety, and efficacy before physicians can recommend it for AP.

Many patients report that their idiopathic AP is refractory to the most common anti-pruritis medications. Antihistamines are effective in only some patients for symptom prevention or decreasing severity.[1] Other pharmaceuticals that have been studied with mixed success include analgesics, selective serotonin reuptake inhibitors, opioid receptor antagonists, alpha interferon 2b, propranolol, cholestyramine, and clonidine.[1] Clearly, many options have been tried, but these studies have yet to show significant therapeutic effects in a large clinical study.

bAla is a non-essential amino acid sold over the counter as an athletic performance-enhancing supplement.[2] Current medical literature that reports the effective use of bAla for AP is limited to a single 2021 case report on an adolescent male with refractory idiopathic AP.[2] bAla is worthy of investigation as a treatment for AP because it has few adverse effects (namely temporary paresthesia and flushing[2]) and it is low cost and accessible.

bAla's exact antipruritic mechanisms are unclear, but the difference in acute and chronic itch pathways and therapeutic targets may explain why AP patients have varying success with anti-itch treatments. Based on the current understanding of the itch-anxiety cycle, bAla's therapeutic effects for AP may be through its anxiolytic-like effects or by increasing carnosine, a free-radical scavenger and organic pH buffer with anti-inflammatory and antioxidative properties.[3] This is thought to be because of bAla signaling through MrgprD receptors in a histamine-independent itch neural circuit.[2] Glutamate release by MrgprD-expressing neurons may help suppress mast cell hyperresponsiveness and skin inflammation, which could be a neuroimmune connection in cutaneous immune homeostasis.[4] This pathway may connect the roles of mast cells in AP pathophysiology and the paradoxical pro- and anti-pruritic effects of bAla.[5] bAla is suspected to suppress the AP itch through desensitization of pruritic pathways, in a manner similar to topical capsaicin, which elicits similar initial paresthesia followed by longer-term pain and pruritus alleviation.[2] Although bAla appears promising, its reported efficacy is still limited to patient testimonies. With increased controlled studies and peer-reviewed publications, bAla could be a pivotal success in AP relief.

AP support groups have been sharing anecdotal success with bAla whose anti-inflammatory and antioxidative properties may result in a disturbance in the anxiety-itch cycle.

Idiopathic AP is a skin disorder that manifests as severe itching, without any visible skin changes, following water exposure. Many patients suffer from AP refractory to front-line anti-itch therapies. AP support groups have been sharing anecdotal success with bAla whose anti-inflammatory and antioxidative properties may result in a disturbance in the anxiety-itch cycle. AP patients are advocating for further research on bAla's clinical use, which requires a greater understanding of the pathophysiology of AP and bAla's cellular mechanisms. With increased research, bAla has the potential to become a highly effective AP treatment, giving patients hope that they can finally return to an itch-free life.

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The Evolution of Ancient Heliotherapy to Modern Phototherapy

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Numerous ancient texts verify Ancient Indian and Egyptian healers as the first photo biologists. Heliotherapy, or the therapeutic use of sunlight, was the treatment of choice for skin conditions such as vitiligo. The Ebres Papyrus, an Egyptian text and one of the oldest maintained medical documents dating 1550 BC, lists the use of natural sunlight after topical application of Bishop's weed, found along the Nile Valley, or parsley, to induce skin pigmentation. Similarly, Atharvaveda, an ancient sacred text from India dating 1400 BC, also writes of vitiligo treatment, but with the use of direct sunlight in the form of sun-worshiping prayer and the application of the Psoralea corylifolia plant. It wasn't until 1947 that the active ingredients 8-methoxypsoralen (8-MOP) and 5-methoxypsoralen (5-MOP) were isolated from these plants and used in modern photochemotherapy as photosensitizers for patients with vitiligo and psoriasis.

Various ancient cultures worshiped sun gods and believed that the sun had the ability to bring forth health and heal disease. Herodotus, known as the "Father of History," correlated sun exposure and skull strength. In 525 BC, he remarked that the skulls of Egyptians are "so tough that it is hardly possible to break them with a stone. I was told … that the reason was that the Egyptians shave their heads from childhood so that the bone of the skulls is indurated by the sun...". The ancient Egyptian city of Heliopolis, or 'City of the Sun', was known for its healing temples that housed light rooms. It was believed that each color of the spectrum held differing therapeutic properties. Patients were 'color diagnosed' and prescribed the associated colored room. Gemstones were situated near windows so the entering sunlight would illuminate the room with a specific light spectrum. For example, rubies were used to create the red-lit treatment room. Other ancient cultures also appraised the ruby gemstone. Indian Vedic texts state that the ruby signifies the blood of the Vedic demon Vala, and reflects human blood circulation. Ruby was also thought to increase the body's temperature and decrease inflammation.

While ruby's use in heliotherapy vanished during the Middle Ages, it made a significant reappearance within the scientific community in 1960; this time, in Theodore Maiman's lab for the creation of the first modern laser. While Maiman's colleagues believed gas mediums were more promising, Maiman was familiar with the ruby's emission properties and successfully developed the first solid-state laser with the ruby as the medium. The continuous pulse ruby laser was the first to be used in medicine. After refinement to a pulsed laser, the Q-switched ruby laser is commonly used in dermatologic practice. Spurred by Maiman's discovery, other investigators then explored the application of different gemstones as laser mediums. Garnets were used in 1964 to create the neodymium-doped yttrium aluminum garnet (Nd: YAG) laser, Alexandrite for the alexandrite-chromium doped chrysoberyl laser in 1974, and sapphire for the Titanium Sapphire laser (Ti:Al2O3) in 1982. Each of these lasers have unique applications. The alexandrite and Nd: YAG lasers, like the ruby laser, have dermatologic applications in the treatment of telangiectasias, tattoo pigment removal, and more. From heliotherapy to modern phototherapy, we should note the importance of these precious gemstones, and how the sun, ironically, has helped bring these therapeutic components to light.

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Transcriptome Analysis of Epicardial Adipose Tissue and Myocardium in Differential Body Mass States

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Heart disease is currently the leading cause of death in the United States, and a major risk factor for cardiac disease is obesity. Prior studies have shown links between epicardial adipose tissue (EAT) on the heart and cardiomyopathies and arrythmias.[1] However, the molecular mechanisms for these connections remain poorly understood. In addition, transcriptome expression profiles of the EAT are not well-characterized with respect to sex and total EAT coverage. This study examines the differential gene expression and molecular pathways in the EAT and proximal myocardium of the left ventricle in individuals while comparing features such as sex and total epicardial adiposity coverage.

Human donor hearts (n=40) were acquired from local hospitals through the Washington Transplant Regional Community organization. Tissue samples from the ventricle epicardial adipose tissue and the underlying myocardium were collected from the donor hearts and processed. High-throughput RNA sequencing was conducted to analyze the expression profiles and used several tools for pathway analysis based on enrichment of disease and biological states.

Results show significant differences in gene expression and pathway regulation among the different comparison groups. Compared to the myocardium, the EAT returned more significantly differentially expressed genes. Obese epicardial adipose coverage was linked to an uptick in immunological response and pathways indicative of a pro-inflammatory state. In addition, EAT coverage was shown to affect males in the study more than females. This study demonstrates the utility for EAT coverage as a novel clinical marker for heart disease.

Results show significant differences in gene expression and pathway regulation among the different comparison groups. Compared to the myocardium, the EAT returned more significantly differentially expressed genes.

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Analysis of Electronic Health Record Data Identifies Features Associated With Future Genetic Evaluation

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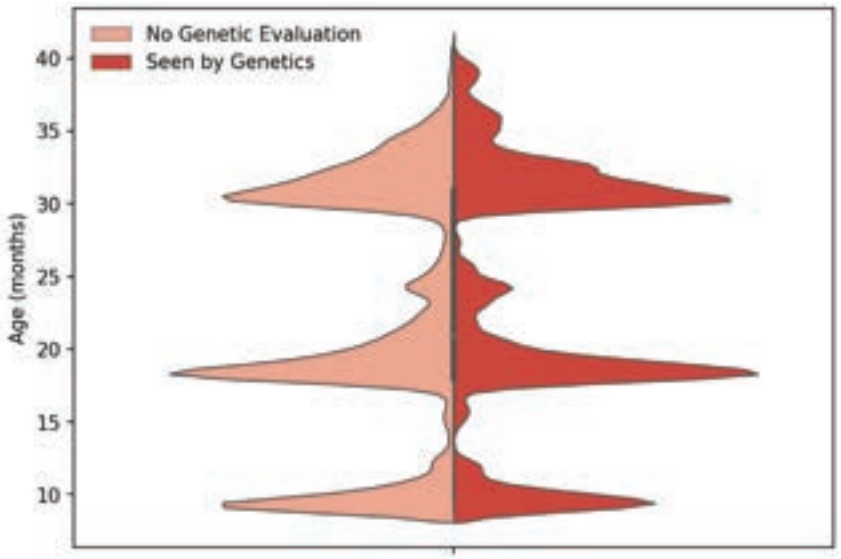


FIGURE: Age and genetic evaluation distribution.

Distribution of age shows clusters that correlate with 9-month, 18-month, and 30-month-old well-child visits.

Neurodevelopmental syndromes represent a large percentage of rare diseases which present clinically in the primary care setting, but may not be fully recognized as having a genetic etiology.[1] Pediatricians are the first care providers to screen for possible developmental delays, and early identification of developmental delays allows for timely interventions to maximize developmental outcomes.[2,3] Currently, the recommended workup involves stepwise evaluations for treatable inborn errors of metabolism, Fragile X repeat expansions, large chromosomal copy number variants, and molecular sequencing panels or exome sequencing to evaluate for monogenic neurodevelopmental disorders.[4,5] Automated evaluation of the data generated by primary care providers in standardized, age referenced screening batteries in conjunction with observation and parent/caregiver histories can suggest earlier referral for children with initial signs of neurodevelopmental disorders. Our analysis of primary care electronic medical record data identified features that are strongly correlated with eventual genetic evaluations.

Retrospective patient-level data was obtained from electronic health records, extracting International Classification of Diseases (ICD) codes, number of encounters, Ages & Stages Questionnaire (ASQ) scores, newborn screening results, biometrics (height, weight, and head circumference) and medications. These records reflect five years of data from the Goldberg Center's primary care records cross-referenced with genetics and neuro-genetics records over the same period. Point biserial correlation coefficients were calculated for each feature and the outcome of genetic evaluation for seven–11-month, 16–20-month, and 28–32-month-olds.

In the study, 25,281 records were accessed, with 11,045 meeting the inclusion criteria for analysis. For infants between seven and 11 months old at the time of visit, referrals (0.259, p=0.00), number of medications (0.192, p=0.00), number of abnormal ASQ domains (0.181, p=0.00), and number of associated ICD codes (0.176, p=0.00) were the highest correlated features with future genetic evaluation. Among 16- to 20-month-olds, abnormal ASQ gross motor score (0.303, p=0.00), number of departments seen (0.285, p=0.00), and number of abnormal ASQ domains (0.260, p=0.00) were the highest correlated features. The strongest correlations seen in the 28- to 32-month-old group included number of departments seen (0.376, p=0.00), abnormal ASQ gross motor score (0.325, p=0.00), number of encounters (0.320, p=0.00), and number of abnormal ASQ domains (0.304, p=0.00). No significant differences were seen between genders.

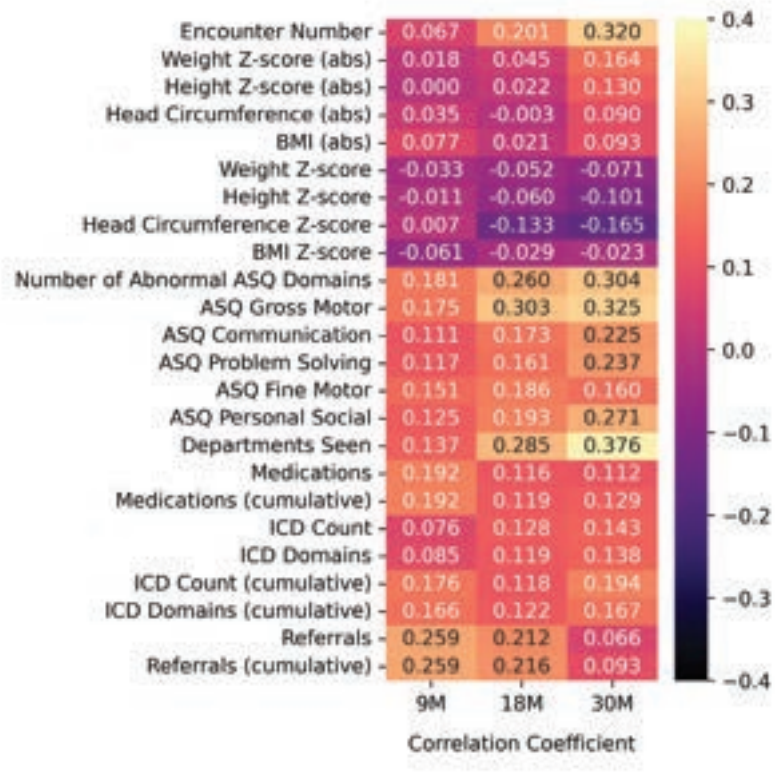
The features identified through this analysis indicate that abnormal ASQ screening results and frequent encounters with medical services are associated

with future genetic evaluation. Several features also demonstrated stronger correlation over time, suggesting that the persistence of neurodevelopmental delay is an indicator for referral to genetics. However, the stronger correlation can also be explained by the clinical difference between a delay at seven months and a delay at 30 months; an abnormal gross motor score at seven months is less clinically significant than one at 30 months, wherein the impetus for a genetic screening is stronger.

The relationship between these variables will be used to develop and train a machine-assisted algorithm that can identify patients in need of genetic testing and evaluation. Further investigation is needed to elucidate associations with other outcome variables related to neurodevelopmental delays and underlying genetic conditions. Machine-assisted referral recommendations may lead to earlier diagnoses; however, additional socioeconomic barriers may delay genetic evaluation including availability of specialists, variable insurance reimbursement for genetic testing, family understanding of the extent of delays, and family ability to divert time and funds toward a diagnostic odyssey.

TABLE: Point biserial correlation of features with genetic evaluation.

Correlation coefficients between features extracted from electronic medical record and genetic evaluation.



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COVID-19 Pancreatitis in a Vaccinated Patient

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Case reports from the early stages of the pandemic have brought to light the extrapulmonary manifestations of SARS-CoV-2 (COVID-19). While the most common etiologies of acute pancreatitis (AP) are alcohol ingestion or gallstones, it is estimated that up to 10% of cases are of an infectious etiology, with viruses being the largest contributor.[1] Here we report a case of COVID-19-associated acute pancreatitis in a fully vaccinated patient.

CASE PRESENTATION

A 58-year-old male with a past medical history of hypertension and one-week prior discharge from a neighboring hospital for acute pancreatitis and COVID-19, presented to the emergency department with nausea, vomiting, and abdominal pain. The patient had been tolerating a slow advance of oral intake with small meals; however, had been experiencing five to six episodes of non-bilious, non-bloody vomiting a day for two days. The patient had been vaccinated against COVID-19 and received his second dose more than two weeks before admission.

A computerized tomography (CT) scan of the abdomen/pelvis from the admission a week prior showed AP with surrounding inflammatory standing. There was no evidence of pancreatic necrosis.

On presentation, the patient was afebrile, normotensive, tachycardic to 104 beats per minute. Physical exam was notable for a soft abdomen with diffuse tenderness and guarding in the epigastric region. An abdominal ultrasound showed biliary sludge without cholelithiasis. The pancreas was not well visualized by ultrasound, although it appeared normal to the examiner. The patient's lipase was found to be elevated to 434 Units per liter. COVID-19 test was negative.

Treatment consisted of supportive care including morphine, lactated ringers, sucralfate, and famotidine. By day three of hospital stay, the patient was discharged with scheduled follow-up.

DISCUSSION

The diagnosis of AP was made for this patient based on a recent discharge of AP, abdominal pain consistent with AP and an elevated serum lipase. While the lipase was not at the level consistent with a diagnosis of pancreatitis established by the Atlanta criteria, the clinical picture is such that another diagnosis is unlikely.[2] Alcohol and gallstones are two of the most common causes of AP but were ruled out as etiologies of this patient's presentation. The patient reported no history of alcohol consumption, and had no gallstones visualized on ultrasound.

Up to 17% of patients diagnosed with COVID-19 develop some form of gastrointestinal symptoms.[3] These can range from mild diarrhea, abdominal pain, nausea, vomiting and rarely pancreatitis. Unlike other cases of COVID-19 related AP, this patient was fully vaccinated more than two weeks prior and had minimal respiratory symptoms.

The most common viral etiologies of AP are Coxsackie virus, CMV, HIV, HSV, mumps, varicella-zoster virus.[1] An observational study of 12 hospitals in New York City found a point prevalence of 0.27% of pancreatitis among patients hospitalized with COVID-19.[4] Interestingly, there have been several case reports of COVID-19 associated AP that did not meet the full Atlanta criteria for pancreatitis.[5]

This case contributes to the growing body of evidence regarding the association of COVID-19 infection and AP. To our knowledge, this is the first described case of a patient vaccinated against COVID-19 to develop AP.

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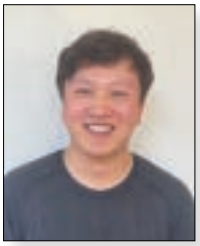
Smoking and Type 2 Diabetes Mellitus Risk in NAFLD Patients: A Longitudinal Cohort Study

Jeffrey Wang, MSI



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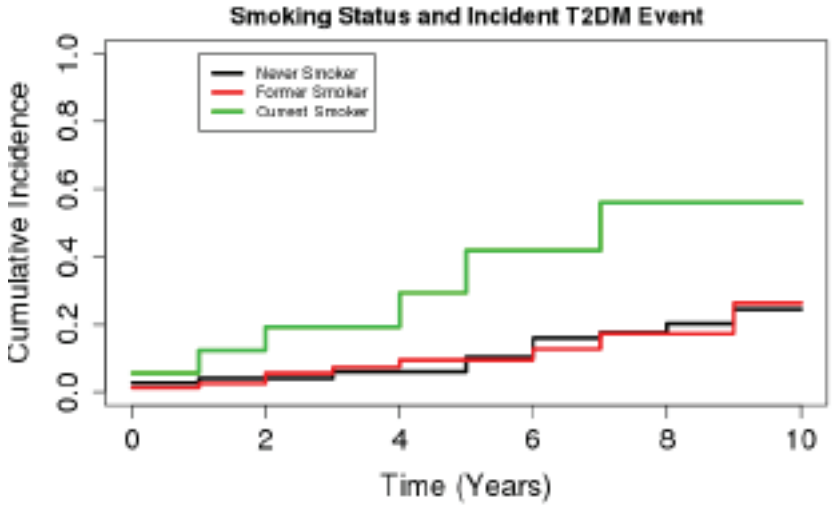

FIGURE 1: Cumulative incidence curve depicting the time to T2DM event between never-smokers, former-smokers, and current-smokers.

Log rank test (p=0.03)

FIGURE 2: Cumulative incidence curve depicting the time to T2DM event between ever-smokers and never-smokers.

Log rank test (p=0.4)

Non-alcoholic fatty liver disease (NAFLD) remains one of the most prevalent chronic liver diseases in the United States and globally. Type 2 diabetes mellitus (T2DM), also with a rising burden, is closely linked to NAFLD. Tobacco use may also be associated with T2DM; however, the synergistic impact of NAFLD and tobacco use on the incidence of T2DM is unknown.

OBJECTIVE

This study explores the temporal relationship between cigarette smoking and T2DM in a cohort of NAFLD patients.

DESIGN

A longitudinal cohort study was conducted to explore the effects of smoking

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on incident T2DM in adults with NAFLD. A total of 279 adults with biopsy-proven NAFLD without baseline T2DM were included. The primary exposure status was categorized as either never-smoker or ever-smoker, while secondary exposure status was further stratified into never-smoker, former-smoker, or current-smoker. The primary outcome was the development of T2DM. Furthermore, a cox-proportional hazard analysis was performed to demonstrate associations between tobacco consumption and incident T2DM.

RESULTS

Compared with never-smokers, ever-smokers had an increased risk of T2DM with an adjusted hazard ratio (aHR) of 1.48 (95% CI: 0.74 – 2.97). Secondary analysis using the stratified exposure status showed elevated hazard ratios for current smokers [aHR 2.79 (95% CI: 1.09, 2.79)] and former smokers [aHR 1.10 (95% CI: 0.49, 2.51)], respectively, compared to never smokers. In addition, the non-parametric Kaplan Meier survival curve also demonstrated a significantly shorter time to the development of T2DM (log-rank test p=0.03) among current smokers, while the time to develop T2DM in former smokers was not significantly different from that of non-smokers.

TABLE: Adjusted cox proportional hazard model showing the effect of tobacco use on incident T2DM in NAFLD patients

Characteristic	HR1	95% CI1	p-value*
Smoker Status			
Never Smoker	–	–	
Former Smoker	1.10	0.49 2.51	0.8
Current Smoker	2.79	1.09 7.19	**0.033**
1HR = Hazard Ratio, CI = Confidence Interval			
*Adjusted model			

CONCLUSION

The risk of T2DM among adults with NAFLD increased in a stepwise manner from never-smokers to former smokers, with the highest incidence in current cigarette smokers. Further studies are needed to determine if smoking cessation programs can decrease the risk of T2DM in adults with NAFLD.

Blood RNA Biomarkers Distinguish Immune Responses to COVID-19 Viremia Versus Comorbid Infections

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While the COVID-19 syndrome is triggered by infection and expansion of the SARS-CoV2 virus, secondary co-infections and superinfections have been shown to contribute to morbidity and mortality.[1] In a prior study, our group identified several biomarkers of COVID-19 infection and severity via whole blood RNA sequencing (RNAseq).[2] This identified activators of specific cell states and can be utilized to distinguish immune responses to COVID-19. In the present study, we sought to validate five of our previously identified RNA biomarkers for viral, bacterial, and biofilm infections in patients with COVID-19 infections.

This was a prospective, observational study approved by the IRB of The George Washington University (#NCR202539). Patients admitted to The George Washington University Hospital Intensive Care Unit (ICU) of age 18 or older and who had obtained a positive test for SARS-CoV-2 were eligible for inclusion in this study. The study was conducted from January to February 2022, during the Omicron wave of the COVID-19 pandemic. After providing informed consent, subjects (n=20) received a venous blood draw into Tempus Blood RNA tubes (ThermoFisher), which were then stored at -80° C. Subject blood samples were used for RNA purification and droplet digital PCR (ddPCR) quantification of five novel RNA biomarkers[2] for viral (IFI27, RSAD2), biofilm (ALPL, IL8RB/CXCR2), and bacterial (DEFA1) infections. RNA biomarkers were expressed as a percentage of actin B (ACTB) copies for analysis. Subjects' SARS-CoV-2 viral titers were analyzed in parallel by ddPCR for SARS-CoV2 sequences (BioRad, EUA).

Sequential organ failure assessment (SOFA) is a tool used clinically to identify organ failure and mortality risk. Higher SOFA scores have been associated with an increased risk of mortality in COVID-19 patients.[3] Among the RNA biomarkers analyzed, ALPL, a biofilm marker, was noted to have a moderate positive correlation (Pearson's, r=0.48) to SOFA score. Clinical marker lactate dehydrogenase (r=0.68) showed a high positive correlation with SOFA score, followed by neutrophil count (r=0.39) and BMI (r=0.34), which had moderate positive correlations. These markers may be able to predict poor outcomes of COVID-19. Notably, SARS viral titer was not associated with SOFA score (r= -0.07). However, RNA biomarkers of viral infection IFI27 (r=0.72) and RSAD2 (r=0.42) were positively correlated with SARS-CoV-2 viral titer, suggesting that the host immune response is proportional to the viremia of COVID-19. Taken together, these data suggest that blood RNA transcripts involved in the host immune response can indicate the presence and severity of infection, including unexpected comorbidities. Furthermore, these biomarkers can distinguish between viremia, biofilms, and other types of infections that may undermine recovery from COVID-19.

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The Effects of Prenatal Adversity and Neonatal White Matter Microstructure on Child Language Skills at Age Two

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Neighborhood disadvantage and lower household incomes are associated with well-established impairments on language development, which predict academic difficulties throughout school.[1,2] These language delays are observable by age two, indicating that before this time-point, life adversities may be silently affecting the development of brain regions involved in language. Of interest are three white matter tracts implicated in early language learning: the corpus callosum (CC), inferior fronto-occipital fasciculus (IFOF), and uncinate (Unc).[3,4] However, no prior study has examined how prenatal adversities, particularly social adversity and maternal psychosocial stress, may affect the development of these neural pathways and downstream language abilities.

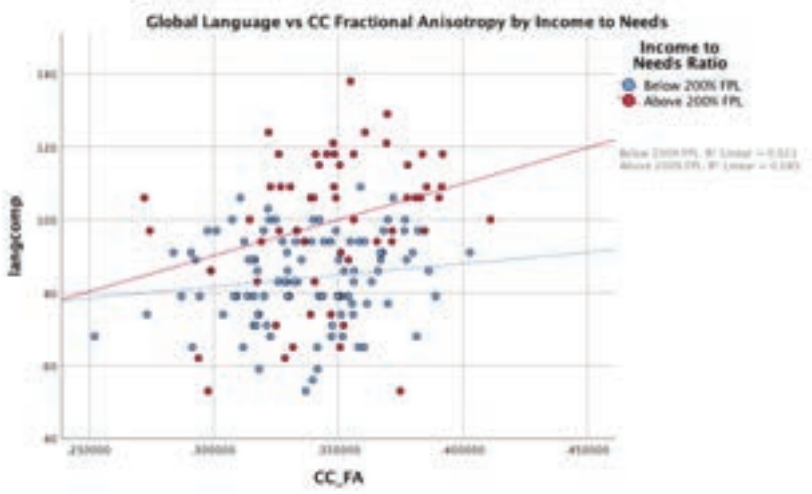

FIGURE: Global Language vs CC Fractional Anisotropy by Income to Needs

SAMPLE

A longitudinal cohort of 160 healthy term-born (>36 weeks gestation) neonates were recruited from the Early Life Adversity and Biological Embedding study, which oversampled urban Saint Louis families in poverty through the March of Dimes 1000 Women Cohort. Complete data sets were required for inclusion in analyses.

METHODS

Structural equation modeling was used to create two latent constructs of prenatal adversity. The first, "social disadvantage", is a composite of neighborhood disadvantage, family income, insurance status, maternal education, and the USDA Health Eating Index5. The second, "maternal psychosocial stress", models maternal depression (Edinburgh Postnatal Depression Screen), stress (Cohen's Perceived Stress Scale), life adversities (Stress and Adversity Inventory), and perceived discrimination (Everyday Discrimination Scale). At birth, diffusion MRI assessed development of white matter microstructure. At subsequent two-year follow-up assessments, child receptive, expressive, and overall language abilities were evaluated (Bayley Scales of Infant and Toddler Development). Stepwise linear regression models assessed the independent and interactive effects of prenatal adversities and neonatal white matter microstructure on children's language outcomes at age two years after adjustment for child sex, gestational age, and postmenstrual age at scan.

RESULTS

Prenatal social adversity (p=.000) and maternal psychosocial stress (p=.002) predicted significantly lower language scores by age two, particularly in receptive skills. However, in a joint model, only the effects due to social adversity (p=.000) were significant. Regarding models with neonatal white matter microstructure, IFOF and Unc were not

predictive of language scores. However, lower CC fractional anisotropy (FA) predicted significantly lower language scores (p=.019) independently of social disadvantage (p=.000). This trend held in a joint model, indicating a possible significant interaction between the maturity of neonatal CC myelination and prenatal social disadvantage on year two language skills. To visualize this relationship, a moderation analysis was conducted after dichotomizing families' income into above and below 200% the federal poverty line (see Figure 1). Although the interaction term was not significant (p= .11), it appears that higher CC FA is more protective of language skills amongst neonates experiencing less social adversity.

DISCUSSION

This study suggests that prenatal social disadvantage and immature neonatal CC myelination are strong predictors of language delays by age two, especially in receptive skills. Although there was no significant interaction between prenatal adversity and neonatal white matter microstructure on year two language skills, it is possible that myelination of CC white matter may be more underdeveloped in infants experiencing higher degrees of social disadvantage. Future studies are needed to support or refute this claim. Nonetheless, by continuing to explore how prenatal adversities affect neonatal brain development, future studies will continue to identify specific neurological markers of early language skills to allow clinicians to intervene before delays develop.

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Screening for and Assessing Adolescent Mental Health Through the Measurement of Mental Health among Adolescents at the Population Level Initiative

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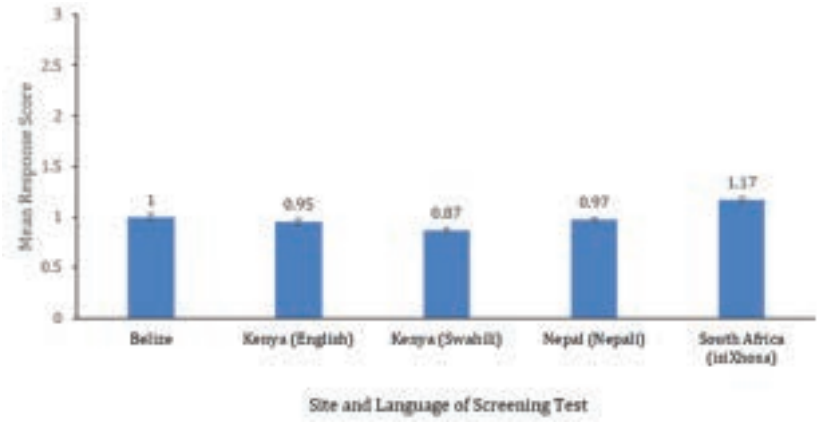

FIGURE: Mean response scores ± standard error of mean of MMAP01. A sample of the data for MMAP01 across the four sites.

There is an extensive history of various screening and diagnostic tools used in the assessment of psychiatric ailments such as major depressive and anxiety disorders. However, there is currently a gap in validated mental health tools and literature within adolescent populations, particularly across different cultures in low and middle-income countries. Further, there are few interventions validated to effectively prevent depression and anxiety among such populations. The present study aims to develop and pilot-test a depression and anxiety screening tool as part of the Measurement of Mental Health among Adolescents at the Population level (MMAP) initiative.

Adaptation and validation of our MMAP tool involved both quantitative and qualitative methods, including statistical analysis and clinical validation of measurements of depression, anxiety, and suicidality. Tests such as PHQ-9, GAD-7, KSADS, and RCADS were administered among adolescent populations in Nepal, Kenya, South Africa, and Belize. These screening tools have been historically validated for assessing depression and anxiety symptoms. Symptoms are screened for via survey questions such as "[In the past two weeks] How often was it hard for you to have fun," and "How often have you had trouble relaxing?"

Data were collected from the four population sites, and a harmonized data set was created . We assessed the specific wording of each of the test's screening items, pinpointing the specific phrasing of symptom descriptions that held the most validity. From here, a new scale with a list of symptom items was developed. These 29 items included descriptions regarding symptoms of both depression and anxiety, such as "Low energy," "Depressed mood," and "Nervous." The mean scores of each of these MMAP items was scored and recorded (Figure 1).

This new MMAP tool will be statistically run against PHQ-9 and GAD-7 items to assess for rates of true positives, true negatives, false positives, and false negatives. Currently, this data analysis is being performed. Once this is complete, the research team will present the new MMAP tool to the United Nations International Children's Emergency Fund (UNICEF). A pilot evaluation will be implemented in the form of diagnostic interviews conducted by mental health professionals across different countries, languages, and socioeconomic backgrounds. The psychometric validity will be assessed from the pilot test data, and once validated, the tool will be ready for field implementation across a spectrum of countries, languages, and demographics. The end result will be a rigorously validated mental health screening tool that can assess for mood disorders among adolescents of varying backgrounds. The outcomes of this project will thus be critical in furthering equitable mental health care on an international scale.

Assessing the Association Between Amyloid Imaging and Cognitive Change in a Cohort with Racial and Ethnic Diversity

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TABLE 1: Baseline Sample Characteristics

	Non-Hispanic (NH) White	NH Black	Hispanic
N	81	20	18
N (%)	68.1%	16.8%	15.1%
Variable	Mean (SD)	Mean (SD)	Mean (SD)
Age at Scan	72.9 (6.2)	71.4 (7.1)	69.2 (5.8)
Male (%)	44.5%	55%	44.5%
Education*	17.1 (2.5)	14.7 (2.9)	14.2 (4.3)
Years of Follow Up	5.1 (2.8)	5.1 (2.0)	4.4 (2.7)
Diagnosis (%)			
Cognitively Normal	69.1%	65.0%	55.6%
Impaired non-MCI	0.0%	10.0%	0.0%
MCI	21.0%	20.0%	44.5%
Dementia due to AD	6.2%	5.0%	0.0%
Other	3.7%	0.0%	0.0%
CDR-Global Score	0.2 (0.2)	0. (0.3)	0.2 (0.3)
Amyloid Positive* (%)	32.1%	15.0%	0.0%
Tracer Used (%)			
Amyvid	29.6%	70.0%	77.8%
Neuroceq	70.4%	30.0%	22.2%

Previous research has shown that amyloid is limited in specificity, sensitivity, and reliability as a biomarker for predicting the trajectory of cognitive decline.[1,2] Racial disparities may exist in using biomarkers such as amyloid in assessing cognition in underrepresented groups.[3] Few clinical studies have examined neuroimaging biomarkers and longitudinal cognitive data in underrepresented diverse groups in Alzheimer's Disease (AD).

The Alzheimer's Disease Research Center at the Icahn School of Medicine at Mount Sinai (MSADRC) has a sizable cohort of diverse participants who have undergone longitudinal amyloid-PET imaging, clinical characterization of cognitive status, and neuropsychological testing. In a prior study,4 the MSADRC assessed amyloid status in non-Hispanic White, Hispanic, Black, Asian, and other research participants. Participants completed the Unified Data Set (UDS) and amyloid imaging from 2011–19. The UDS, administered to participants annually, includes a neuropsychological battery that assesses how memory disorders affect cognitive abilities. Amyloid images, as measured by positron emission tomography, received a clinical read by a neuro-radiologist. The study assessed data from a sample of 186 participants. Results showed that the rate of amyloid positivity was lower in minority cohorts despite poorer cognitive performance.

This study aimed to assess whether results of amyloid imaging predict different cognitive trajectories, measured by change in clinical diagnosis and neuropsychological scores in cognition over time, in cohorts with racial and ethnic diversity.

METHODS

Data were selected from the MSADRC's original sample. To assess amyloid status and cognitive change over time, only participants who completed two or more annual cognitive assessments were included. The current study includes data from a sample of 119 participants. For all participants, if multiple brain images had been collected, the clinical read of the first image was used. Primary outcomes were baseline to last visit change in: (1) Clinical Dementia Rating (CDR) Global Score and (2) clinical diagnosis. Race was self-reported by participants at their baseline visit, using categories: Non-Hispanic (NH) White, Non-Hispanic (NH) Black, Hispanic, Asian and Other. The relationship between primary outcomes and ethnicity, and the relationship between primary

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outcomes and amyloid positivity for the total sample and ethnic subsamples were assessed. Nonrandom associations were tested using Fisher's exact test. Distribution of demographic variables across ethnic groups was assessed using Kruskal-Wallis tests.

RESULTS

Baseline analysis revealed a significant difference in amyloid positivity across ethnic groups ($p<0.01$) (Table 1). There was an association between change in CDR Global Score and ethnicity, with NH White participants worsening more than other groups ($p<0.05$) (Table 2). There was no association between deterioration in clinical diagnosis and ethnicity. Results showed a relationship between amyloid status and change in CDR Global Score, with amyloid positive participants showing higher rates of worsening ($p<0.001$) (Table 2b). Similarly, amyloid status was found to be associated with deterioration in diagnosis ($p<0.05$) (Table 2). Within subsamples, amyloid status and change in CDR were associated for both NH White (p .004) and NH Black participants ($p<0.001$) (Table 2). Amyloid status and deterioration in diagnosis were associated for NH white ($p<0.05$), but not NH Black (p 0.284) (Table 3). Association among the Hispanic group was not assessed because the subsample only has negative scans.

CONCLUSION

These preliminary results suggest differences in rate of cognitive decline by ethnicity and amyloid status. Race and ethnicity are social constructs without biological basis. Therefore, to improve understanding of AD overall, these differences must be further explored, and more complex etiologies of cognitive decline considered.

TABLE 2: Relationship between ethnicity and key outcome measures

Outcome	Non-Hispanic (NH) White	NH Black	Hispanic	P Value
Worsening of CDR Global Score by 0.5 or more (Baseline to Most Recent Follow Up Visit)	28.4%	15.0%	11.1%	.041
Deterioration in Clinical Diagnosis	14.8%	10.0%	5.6%	.647

TABLE 3: Relationship between amyloid status and key outcome measures in total sample and by ethnic subsample

Ethnicity: Total	Amyloid Status		P Value
	Positive	Negative	
Worsening of CDR Global Score by 0.5 or more	58.5%	12.2%	< .001
Deterioration in Clinical Diagnosis	27.6%	7.8%	.009
Ethnicity: NH White			
Worsening of CDR Global Score by 0.5 or more	53.8%	16.4%	.004
Deterioration in Clinical Diagnosis	26.9%	9.1%	.047
Ethnicity: NH Black			
Worsening of CDR Global Score by 0.5 or more	100%	0%	< .001
Deterioration in Clinical Diagnosis	33.3%	5.9%	.284

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Cognitive and Psychological Findings in COVID-19 Survivors

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The experience of persons living with COVID-19 brain fog is similar to cognitive loss in late life, where persons are unable to manage executive tasks of living, perform cognitively in the workplace, and often require support from family to meet basic needs.[1,2] Many individuals require prolonged absences or reduced work schedules for months at a time. The clinical course of COVID-19-associated brain fog is not yet described, and this work will contribute to the necessary knowledge to help care for individuals suffering from this condition. Combined with the profound public health implications of COVID-19, this research begins to fill gaps in knowledge about chronic cognitive symptoms associated with the novel COVID-19 pandemic.

A retrospective chart review of persons presenting to The GW Medical Faculty Associates' interdisciplinary COVID clinic reporting symptoms of "brain fog" was evaluated. They were subsequently referred for an abbreviated neuropsychiatric symptom battery prior to further dedicated memory clinic evaluation. Patients seen in person and via telehealth from Jan. 8, 2021, through May 11, 2021, were reviewed. Eighteen people were evaluated for this study and those with known cognitive disorders were excluded.

Outcome measures were based on the results of a cognitive battery which included a prospective memory test, Hopkins Adult Reading Test Form A, Hopkins Verbal Learning Test-Revised, Trial Making Test Part A and B, Letter and Pattern Comparison Test, Digit Span, Clock Drawing, Hopkins Verbal Learning Test-Revised (HVLT-R) 20-minute Delayed Recall and Recognition, and Verbal Fluency Test. Additionally, PHQ-9, PCL, and GAD questionnaires were administered for major depressive disorder, post-traumatic stress disorder (PTSD), and general anxiety disorder, respectively.

Data was reviewed for clinical patterns associated with brain fog in the post-acute COVID-19 syndrome. In evaluating GAD scores, 50% of patients reported at least mild anxiety, with additional difficulty in the ability to get along with other people. Of the patients who had PHQ scores, 61.1% had scores consistent with mild depression. Of that group, 63.6% of patients had scores consistent with moderate depression where counseling, follow-up, or pharmacotherapy was indicated. Additionally, 33.3% of patients presented with an HVLT-R Retention of less than 90%. Upon interview, patients' stories were notable for profound depression, anxiety, sense of trauma, and overwhelming difficulty with resuming work. A comprehensive analysis of the neuropsychiatric panel of tests obtained by these individuals is pending. However, preliminary results do show an impact interfering with returning to daily tasks at work. Many patients took a leave of absence due to slowing of speech, significant time increase in email writing due to scrutiny over word choice, and concentration difficulties. Patients were often left exhausted by the cognitive overdrive, amplifying existing or new anxiety, depression, sleep disturbances, and/or PTSD. Conceptualizing thoughts, stumbling over words, and delivering responses in a delayed and fragmented manner were common features of the brain fog observed. In particular, symptoms related to language and speech trended amongst all patients.

Additional research is warranted to better understand COVID-19 brain fog, how it is associated with specific signs and symptoms, and its evolution in patients. Further studies should also focus on patient backgrounds that may contribute to differences in symptomology, including those with prior experiences with brain fog.

Conceptualizing thoughts, stumbling over words, and delivering responses in a delayed and fragmented manner were common features of the brain fog observed.

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The Impact of a Culinary Medicine Curriculum on Gestational Diabetes for Expectant Mothers

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Gestational diabetes mellitus (GDM) is the most common complication of pregnancy and is associated with an increased risk for Type 2 diabetes.[1] The rate of GDM continues to increase across all groups, with the increases being most dramatic amongst racial and ethnic minority populations.[2] An estimated 25% of infants born to individuals with GDM had an adverse outcome, including preterm birth, growth abnormality, and neonatal intensive care unit (ICU) admission.[1] Further, perinatal health is profoundly impacted by maternal diet, and healthier consumption habits improves outcomes for both mothers and infants. There is a need for actionable, culturally appropriate, real-world guidance on food education as medicine practices to help expectant mothers translate dietary research into practical daily habits. The Culinary Medicine Program (CMP) at the George Washington University (GW) has deployed an innovative virtual nutrition education model used by over 60 academic medical centers that addresses nutrition knowledge, food security, health, and socialization for diverse populations.

This project will assess the impact of a free, virtual, five-session, hands-on Health Meets Food cooking series on expectant mothers' dietary habits, attitudes, and competencies (DACs). These DACs include diabetic control, pregnancy outcomes, understanding and adoption of the tenets of a healthy Mediterranean diet, changes in cooking habits, as well as food security status. This will be conducted as a randomized controlled trial of patients at risk for or diagnosed with GDM who are attended to at a Washington, D.C., clinic. There will be 40 participants in the investigation arm, participating in the five-session Health Meets Food course held by the CMP at GW, and 40 participants in the control arm, receiving traditional clinical education.

The topics of the sessions include "Introduction to the Mediterranean Diet: Breakfast," "Nutrition in Pregnancy: Lunches and Snacks," "Meal Planning: Dinners," "Post-Delivery," and "Lifecycle." Participants will learn to cook delicious recipes and basic nutrition concepts such as building healthy menus, eating on a budget, meal planning, and how to cross-utilize leftovers. The first three sessions will be held synchronously over Zoom and the last two sessions will be delivered asynchronously. This model minimizes barriers to accessibility while offering a platform providing inclusive and culturally considerate programming to underserved populations. The additional asynchronous modules and resources create an environment for life-long healthy eating. Participants will complete a 30-minute module and quiz prior to each session. During the 90-minute session, participants will prepare different recipes and engage in discussion with co-participants regarding topics discussed in the respective module for each session.

All study participants will take the baseline Health Meets Food validated Cooking for Health Optimization with Patients (CHOP) questionnaire at the time of enrollment. The questionnaire will be provided via Qualtrics. At the end of session five, study participants in both the control and investigation arms will repeat the CHOP questionnaire. Participants will also be contacted to complete the CHOP questionnaire again three months after the conclusion of the Health Meets Food program. The survey responses will be used to measure the magnitude of change in DACs between the investigative and control groups. The outcomes of this project will inform the feasibility of culinary medicine programming as an effective tool for improving nutrition and health outcomes in pregnant parents and newly born infants using a virtual model.

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Correlation of Non-Invasive Hemoglobin Measurement with Bleeding During Cesarean Delivery: The PPHgb Study

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Early recognition of postpartum hemorrhage (PPH) and decision to transfuse is challenging. Non-invasive hemoglobin measurement (SpHb) offers point of care hemoglobin measurements that may demonstrate acute changes in blood loss for early intervention.

OBJECTIVES

Our primary objective was to assess the association between clinically meaningful change in SpHb from the start of surgery and the decision to intervene. Our secondary objective was to compare the pre and postoperative SpHb with standard laboratory hemoglobin (Hgb).

METHODS

This was a prospective, observational study of 40 women during non-urgent cesarean delivery (CD) at George Washington University Hospital from 2020-2022. We included women 18-50 years old with CD at >34 weeks. Logistic regression compared those with >20% decrease from first SpHb after the start of surgery and odds ratio (OR) and 95% confidence intervals (CI) were calculated for receiving interventions. Pre and postoperative SpHb and Hgb values were compared using t-tests.

RESULTS

Mean age of participants was 34.7 years. Eight women received intervention to reduce bleeding during CD, which included more than the two standard doses of oxytocin, misoprostol, carboprost, methergine, and/or tranexamic acid. Seven women progressed to PPH, three with early intervention for bleeding. Women with >20% decrease in SpHb from the start of surgery compared to those without >20% decrease had an OR of 4.17 (95%CI: 0.77 - 25.28) for receiving intervention during CD. Mean preoperative SpHb (14.3 g/dL) was 2.6 g/dL (95% CI: 1.9 - 3.3) higher than the mean preoperative Hgb (11.8 g/dL), ($p< 0.001$) and mean postoperative SpHb (13.4 g/dL) was 3.6 g/dL (95%CI: 2.9 - 4.2) higher than postoperative Hgb (10.1 g/dL), ($p< 0.001$).

CONCLUSIONS

Our data suggest that hemoglobin measures collected continuously during surgery may provide earlier indication for intervention than pre and postoperative lab measurements. Pre and postoperative comparison of Hgb and SpHb were clinically and statistically significant, suggesting that device hemoglobin may not be reflective of the current gold standard hemoglobin value.

Retrospective Review Differentiating Pediatric Lichen Sclerosus and Vitiligo

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Lichen sclerosus (LS) and vitiligo present similarly with white discoloration in the anogenital region. The persistence of depigmentation after symptom resolution in LS and the potential co-existence of vitiligo with symptomatic dermatoses can introduce diagnostic challenges. Vitiligoid LS is an LS variant reported in darker skin tones. It resembles vitiligo clinically but is symptomatic and histologically consistent with LS.[1] This introduces further diagnostic challenges in darker skin tones. Lichen sclerosus must be treated aggressively to prevent sequelae such as permanent scarring and vulvar squamous cell carcinoma, making an accurate diagnosis crucial.[2,3]

OBJECTIVE

To review cases from a multidisciplinary vulvar dermatology clinic to identify symptoms and exam findings that can help differentiate LS and vitiligo at the time of initial clinic visit.

METHODS

Data were retrospectively extracted from 98 patients with a diagnosis of LS (80) or vitiligo (18) seen at a vulvar dermatology clinic over a 6.8-year period. Descriptive statistics and Z-tests were used for data analysis.

RESULTS

Pruritus, constipation, and dysuria were the most common symptoms experienced by both LS and vitiligo patients. Symptoms were experienced more frequently by LS patients, but only pruritus reached statistical significance ($p=0.040$). Lichen sclerosus patients had exam findings including petechiae, erosions, fissures, hyperkeratosis, adhesions, clitoral hood involvement, and symmetry more frequently, but only epidermal atrophy ($p=0.047$) and figure-of-8 hypopigmentation ($p=0.036$) reached statistical significance. Lichen slerosus and vitiligo were misdiagnosed as one another 15 times. 46.7% of these misdiagnoses were made in African Americans, who comprise 38.8% of all patients.

CONCLUSIONS

There were fewer symptom and exam finding differences between vitiligo and LS than expected. The relatively small number of vitiligo patients and the commonality of symptomatic vulvovaginitis and constipation in prepubertal females may be confounding and partially explain these results. Additionally, prior treatments can alter the presentation of these conditions. Treatment of LS with topical steroids can result in a clinical presentation that mimics vitiligo. More studies are needed to differentiate LS and vitiligo, particularly in darker skin tones; these may require analyzing history and exam findings across time to account for evolution as they are treated.

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Acceptability of Intramuscular Injection in Postpartum Hemorrhage Prevention

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Newer research comparing routes of medication administration has extended beyond efficacy as a primary endpoint to incorporate patient preference. However, little is known about the preference of pregnant women toward routes of medication administration, specifically with regard to hemorrhage prevention and control.

OBJECTIVE

To understand the preference of pregnant women for medical interventions to prevent hemorrhage at the time of delivery.

STUDY DESIGN

Surveys were distributed from April to September 2022 using electronic tablets at a single urban center with an annual delivery volume of 3,000 women per year to > 18-year-old women who are either currently pregnant or have been pregnant in the past. Subjects were asked to choose their preferred route of administration from the following options: intravenous (IV), intramuscular (IM), or subcutaneous (SC). The primary outcome was a patient preference towards the route of medication administration during a hemorrhage event.

RESULTS

The study cohort included 300 patients, mostly African American (39.8%), followed by Caucasian (32.1%), with the majority of the participants ranging from 30-34 years of age (31.7%). When asked which method of administration they would prefer to prevent hemorrhage before birth, the results were as follows: 31.1% IV, 23.0% no preference, 21.2% unsure, 15.9% SC, and 8.8% IM. Additionally, 69.4% of respondents reported that they have never declined or avoided IM administration of medication if recommended by their physician. We also found significant associations between race and preferred route (p-value=0.0008) as well as education level and preferred route (p=0.0004).

CONCLUSION

Although some survey participants prefer IV route of administration, 68.9% of subjects were unsure, had no preference, or prefer non-IV routes. This information is helpful particularly in low-resource settings, where IV is not readily available, or in urgent clinical situations where IV is not easily obtainable in high-risk patients.

Developing and Refining a Theory of Change to Improve Time to Antibiotic Administration for Febrile Pediatric Oncology Patients in Real-World Settings

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From May 2019 to November 2020, 23 institutions participated in the first Mexico in Alliance with St. Jude Golden Hour Quality Improvement Collaborative (MAS Collaborative) and successfully reduced the time to antibiotic administration (TTA) in febrile pediatric hematology-oncology patients (fPHOP) from 156.8 minutes to 59.4 minutes and demonstrated improved clinical outcomes. The MAS Collaborative followed the Institute for Healthcare Improvement's Breakthrough Series (BTS) model, which involves using a shared Theory of Change (TOC). This report describes the process followed to develop and refine the TOC, which is currently being used at-scale in the second MAS Collaborative. This report adds to a previously published abstract by publishing additional data about the role of the Plan-Do-Study-Act cycles the teams performed in order to trial specific change ideas and measure their effectiveness.

METHODS

The theory of change was built over the course of four phases: pilot testing, driver diagram refinement, multisite deployment, and consolidation and dissemination. A driver diagram (DD) was used to organize and visualize the TOC. The first version of the TOC was built based on the experience of four institutions that piloted the Golden Hour in Mexico in 2018. It was refined using the input from a multidisciplinary expert panel. The DD was shared by participating institutions and teams used Plan-Do-Study-Act (PDSA) cycles to test and adapt change ideas to their local context. At the end of the first MAS Collaborative, teams reported the change ideas they tested and their degree of belief (low to high) that the change ideas had led to improved outcomes. This information was used to refine the TOC, which was validated with a second expert panel in preparation for the second MAS Collaborative.

RESULTS

The initial DD included five primary drivers, 16 secondary drivers, and 32 change ideas. The primary drivers were effective availability of medications and supplies, dynamic data learning systems, early detection of fever, process reliability, and effective teamwork. The 23 teams tested change ideas for all primary drivers and 34 of the change ideas were reported as having a high degree of belief, suggesting high fidelity in the theory of change. Data collected through the third and final action period showed more than half the teams reported PDSA cycles in six main categories: improving medication availability in point-of-care areas (52%), improving data analysis (52%), promoting early fever detection (57%), standardizing PHO patient care processes (65%), reducing laboratory sample processing time (57%), and providing effective training (70%). Based on the feedback from participating teams, two secondary drivers were added to the DD for the second MAS Collaborative: 1) promoting wellbeing and resilience and 2) promoting early detection of fever at home. A refined and robust TOC is currently being used for the second MAS Collaborative.

CONCLUSIONS

The multiphase process followed to develop the TOC was key to the success of the first MAS Collaborative. Contrary to more prescriptive approaches to project implementation, the inherent flexibility of this TOC allowed teams to operate with a greater sense of agency, developing, adapting and testing implementing changes. This TOC provides practitioners with practice-based evidence to reduce TTA and improve clinical outcomes for children with cancer in resource-limited real-world settings in the context of the second MAS Collaborative and beyond.

Relationship Between Young Age (40–49) and Breast Cancer Prognostic Factors at Diagnosis: An Argument for Annual Screening

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Younger women who develop breast cancer are more likely to be diagnosed with breast cancer at a more advanced stage with a larger tumor size and/or spread to lymph nodes, as well as a more biologically aggressive profile, yielding an overall poorer prognosis compared to older women.[1] Yet, multiple conflicting published recommendations on screening mammography exist for this age cohort. Breast cancer screening interval recommendations for women ages 40–49 years old vary between annual and biennial.[2] Ideally, the screening interval should be shorter than the lead time for cancer detection.[3] Younger women are more likely to have aggressive tumors with a shorter lead time (1.7 years) compared to women 50–59 (3.3 years).[4] As a result, younger women who undergo biennial versus annual screening are more likely to have larger tumors, positive lymph nodes and a later stage of disease at presentation.

METHODS

Data were extracted from 740 patients over a 5 year period at an academic hospital center. The pathology reports of the resected breast cancer specimens were examined to determine the histopathological features of disease including size, grade, and the presence of lymphovascular invasion, histological subtype, hormone receptor status, and nodal status. Any participant with documented high risk breast cancer mutations was removed. Racial differences in the distribution of the demographic and clinical characteristics were compared using chi-square tests for homogeneity of proportions. The method of detection was attributed to screening or symptomatic if the abnormality was palpated.

TABLE: Invasive breast cancer (excluded DCIS) comparison of 40–49-year-old cohort compared to 50-74 cohort.

	Age cohort				
	40–49 years old		50–74 years old		p-value
Tumor Characteristics	No.	%	No.	%	
Total	98	22.58	336	77.42	
Screen-detected	42	41.84	182	54.17	0.044*
Triple negative	18	18.37	35	11.63	0.034*
HR + /HER2-	65	66.32	257	76.49	0.044*
HER2 enriched	6	6.12	9	2.68	0.021*
LVI	17	17.35	55	16.37	0.111
Lymph node positive	23	23.47	50	14.88	0.041*
Interval cancer rate	31	31.60	42	12.40	0.021*

*denotes statistical significant ($p \leq 0.05$)

HR = hormone receptor; LVI = lymphovascular invasion; Minority is defined as patients self-identifying as Black, Asian, American Indian, or Native Hawaiian.

RESULTS

When comparing 40–49 years to 50–74 years in our participants the average size, grade or stage of the invasive breast cancer did not differ. However, the breast tumors in younger women were less likely to be detected via screening mammography (p=0.044, table). Those

When comparing 40–49 years to 50–74 years in our participants the average size, grade or stage of the invasive breast cancer did not differ.

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same tumors were also more likely to present with factors predictive of an aggressive tumor such as having positive lymph nodes (p=0.041, table), being a triple negative tumor (0.034) or HER2 enriched (p=0.021). Invasive breast cancers in older women were more likely to present with favorable luminal-A tumors (p=0.044).

CONCLUSIONS

The results of this retrospective cohort study provided further confirmation of the value of screening mammography in detecting small, localized breast cancers among younger women in their forties. Efforts to limit screening among women aged 40-49 years old who have elevated risk would miss the benefits of early detection of breast cancers among women in this age group.[5]

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X285K HOXB13 Binds Androgen Receptor within Nucleus but Possibly to a Lesser Extent than WT HOXB13 as Assessed by PLA Assay

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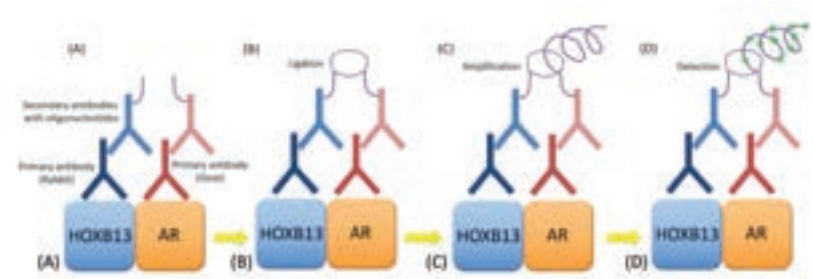

FIGURE: Protein Ligation Assay Protocol
(A) Proteins are first incubated with primary antibodies from different species. Primary antibodies are then incubated with secondary antibodies with probes which contain oligonucleotide tails. (B) Ligase is added which forms circular DNA from the two oligonucleotide tails which links the two protein/antibody complexes. (C) Polymerase is added to amplify the circular DNA sequence. (D) Complementary oligonucleotide sequences coupled to fluorochromes (GFP) bind to respective regions of the amplified DNA, which can then be visualized under microscopy.

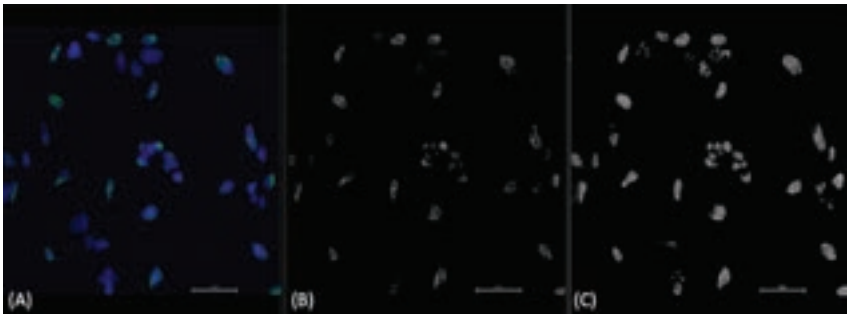

FIGURE 2: ImageJ Analysis
(A) A merged image (blue=DAPI stained nuclei, green=PLA signals). (B) Images were separated by color. Image from green channel (i.e., PLA signal) is shown. (C) Auto local threshold (Bernsen, radius 1) was applied to each PLA image (green). Particles were analyzed by ImageJ software to quantify the number of PLA signals per image. PLA signals were divided by the number of cells per image. Scale bars: 50 um.

Prostate cancer (PCa) is known to be more prevalent among men of African descent, compared to white individuals.[1] While it is currently unclear as to why Black men are more affected by PCa, the reasons are likely multifaceted involving multiple factors including social determinants of health. Recently, a new HOXB13 variant, X285K, has been identified among men of West African descent with PCa.[2] The X285K variant has a single base deletion in its stop codon (c.853delT), which results in an extension by 96 amino acids at the C-terminal end. Although the relationship is multifaceted, it is well established that HOXB13 interacts with androgen receptor (AR) which plays a pivotal role in PCa pathogenesis.[3] However, little is known about how this specific variant (X285K) may impact HOXB13's function endogenously. In the current study, we hoped to address two important parameters involving X285K: (1) determine if X285k HOXB13 binding was increased in androgen rich environments (R1881), (2) compare WT HOXB13 to X285K HOXB13 to assess any potential differences in terms of binding to AR. We hypothesize that the extended amino acid tail on X285K HOXB13 may disrupt AR binding, resulting in a weaker PLA signal intensity.

METHODS

LNCaP95 (PCa cell line) Tet-ON stable lines which inducibly express WT or X285K HOXB13 together with RFP-tagged HOXB13 shRNA have been generated and cultured in RPMI media containing 10% charcoal stripped FBS (Figure 1). 20 ng/mL Doxycycline (Dox)

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and 1 nM R1881 (synthetic androgen) were added to media at various time points prior to PLA (24 hr, 48 hr, 72 hr). Primary antibody concentrations were as follows: (1) Goat-derived anti-AR antibody (Invitrogen, PA1-9005) 1:100, (2) Rabbit-derived anti-HOXB13 antibody (CST 1:200, 90944). PLA was performed in accordance with manufacturer's protocol.4 Images were captured using EVOS and ISIS fluorescence microscope following PLA. ImageJ was utilized to quantify PLA signal (Figure 2). Welch's T tests were performed to compare means of PLA signal between X285k Dox+R1881+ and WT Dox+R1881+, as well as X285k Dox+R1881+ and X285k Dox+R1881-.

RESULTS

X285k displayed decreased PLA signal density at 24 hrs (69.38 vs. 91.43, p=.004), 48 hrs (48.97 vs. 82.27, p=.022), and 72 hrs (79.62 vs. 109.36, p=.004) compared to WT. Furthermore, addition of synthetic androgen (R1881) increased PLA signal density for X285k at 24 hrs (69.33 vs. 29.15, p=.008), 48 hrs (48.97 vs. 6.75, p=.005), and 72 hrs (79.62 vs. 41.06, p=.002), suggesting that X285k HOXB13 binding is enhanced upon androgen stimulation.

CONCLUSION

The current study indicates that X285K HOXB13 variant protein interacts with androgen receptor (AR) protein in prostate cancer cells. X285k binds AR within the cell nucleus as assessed by PLA, as is the same for WT HOXB13. X285k HOXB13 binding to AR was enhanced upon androgen stimulation. The current study also suggests X285k may bind to AR to a lesser extent than WT. This difference, if confirmed, may be explained by the extended amino acid tail of X285k potentially limiting AR access to HOXB13. However, this relationship has never been documented before and therefore warrants future investigation given the critical role of both HOXB13 and AR in PCa development.

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Efficacy of Influenza Vaccine on T-cell Response in Recipients of CAR-T Therapy for Leukemia

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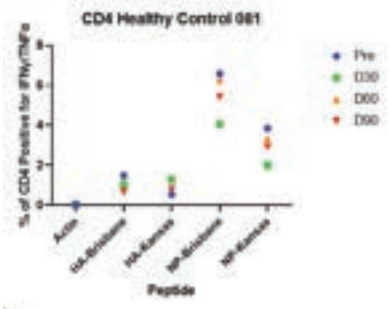

FIGURE 1: Healthy Control % IFN-γ+/TNF-α+ CD4+/CD8+ cells. Percent of double positive (IFN-γ/TNF-α) cells stimulated and expanded with 2019 influenza vaccine peptides (HA-Brisbane, HA-Kansas, NP-Brisbane, and NP-Kansas). The CD4+ and CD8+ responses for healthy control 081 at four time points (Pre-vaccine, Day +30, Day +60 and Day +90) are shown.

Chimeric antigen receptor-modified T-cell (CAR-T) therapies are gaining wider use in pediatric leukemia patients. Depletion of the immune system, specifically B-cells, following CAR-T therapy leaves patients immunocompromised and susceptible to post-therapy infections, including influenza infection. A recent study evaluating antibody responses to influenza vaccine following CAR-T therapy showed only a partial vaccine response.[1] However, these studies did not analyze cellular responses to vaccination, which is well described after influenza vaccine, and could provide additional protection. This study aimed to assess the T-cell response in an established cohort of CAR-T recipients who received the 2019-2020 influenza vaccine.

T-cells were isolated following a 10-day micro expansion by stimulating thawed peripheral blood mononuclear cells with peptide libraries encompassing four proteins from the 2019-2020 influenza vaccine: Hemagglutinin-Kansas (HA-Kansas), Hemagglutinin-Brisbane (HA-Brisbane), Nucleoprotein-Kansas (NP-Kansas), and Nucleoprotein-Brisbane (NP-Brisbane). Cellular immune response was evaluated using flow cytometry identifying IFN-γ+/TNF-α+ activated influenza-specific T-cells.

Pre-vaccine and post-vaccine cells from one healthy control and three post-CAR-T patients were stimulated using 2019 influenza vaccine peptides. Healthy control cells were analyzed at four timepoints including pre-vaccine, day 30, day 60, and day 90. ELISpot and flow cytometry analysis revealed a robust CD4+ T-cell pre-vaccine response to NP-Brisbane (mean 6.58% IFN-γ+/TNF-α+) and NP-Kansas (mean 3.86%) followed by waning responses over the course of 90 days. The HA-Kansas response followed an expected pattern with the number of specific CD4+ T-cell responses to the peptide increasing from pre-vaccine (mean 0.55% IFN-γ+/TNF-α+) through day 60 (mean 1.36%), before waning at day 90 (mean 0.80%). Percentage of influenza activated CD8+ T-cells remained below 1% for all peptides. Post-CAR-T cohort samples included cells from two timepoints, pre-vaccine and post-vaccine. Participant HiC001 presented as an outlier among the CAR-T cohort, but like healthy control 081, with robust pre-vaccine CD4+ responses to both nucleoprotein peptides (mean 14.93% IFN-γ+/TNF-α+) that waned post-vaccine. Participants HiC002 and HiC004 displayed increased IFN-γ/TNF-α+ CD4+ activity to NP-Brisbane (mean 3.05%) and NP-Kansas (mean 1.74%) in post-vaccine cells. HiC004 is the only CAR-T sample in which a robust post-vaccine IFN-γ/TNF-α+ CD4+ response to HA-Kansas (6.65%) was observed. Consistent with healthy control 081, all post-CAR-T samples produced less than 1% IFN-γ/TNF-α+ CD8+ T-cells across all peptides.

CAR-T therapy increases a patient's risk of post-therapeutic infection, including influenza. Using T-cell assays, we identified a CD4+ population response in CAR-T therapy patients to multiple peptides from the 2019 influenza vaccine. Preliminary data suggests a more robust CD4+ than CD8+ population response. However,

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a positive CD8+ response cannot be ruled out. Reactivity to nucleoprotein peptides was generally stronger compared to hemagglutinin peptides. Robust responses to nucleoproteins in the pre-vaccine cells suggest a possible role of recent influenza infection or sustained immune response from the previous year's vaccine. This should be further explored via comparison of sequencing to the 2018 influenza vaccine. This research is a preliminary step in determining the benefit of vaccination for T-cell immunity in immunocompromised individuals receiving CAR-T therapy. Next steps include expanding sample sizes of the current cohorts, as well as including samples from a cohort of patients vaccinated prior to CAR-T therapy.

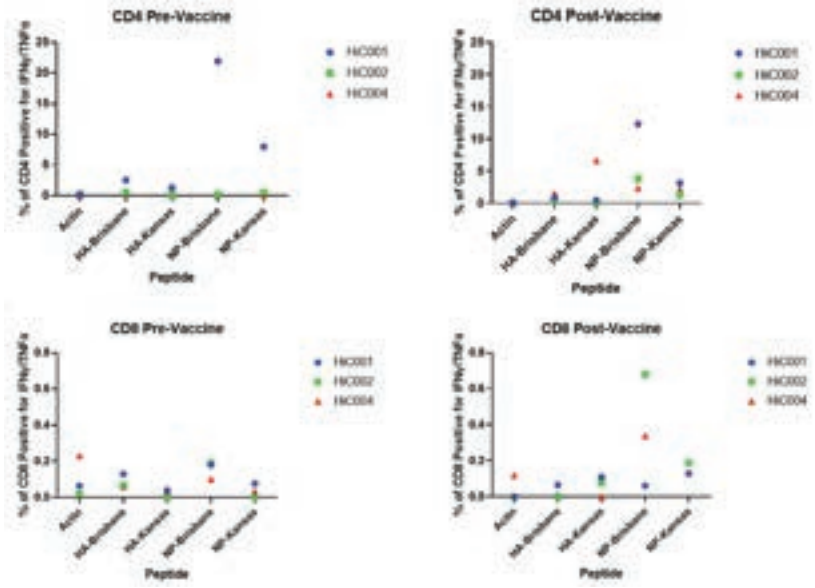

FIGURE 2: CAR-T % IFN-γ+/TNF-α+ CD4+ and CD8+ cells. Percent of double positive (IFN-γ/TNF-α) cells stimulated and expanded with 2019 influenza vaccine peptides (HA-Brisbane, HA-Kansas, NP-Brisbane, and NP-Kansas). The CD4+ and CD8+ responses for three CAR-T patient samples at timepoints pre- and post-vaccine shown.

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Assessing the Efficacy of a Tumor-Specific Vaccine, Anti-pd-1, and Decitabine in a Syngeneic Murine Model of Glioma: A Preclinical Trial

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Despite the revolution in immunotherapy over the past decade, brain malignancies remain relatively insensitive to immune checkpoint blockade and other immune-based approaches. Traditionally thought to be due to CNS immune privilege,[1] many reports have thought immunotherapy would never show efficacy in brain cancers. However, there have been recent reports of tumor-associated antigen and tumor-specific antigen T-cells generated in cancer models, some with spontaneous immune clearance, implying a potential for immunotherapy in brain cancer.[2,3] Of even more interest, many brain cancers may contain environments that, with the correct therapeutic combinations, could elicit an antitumor immune response. In this experiment, we sought to target a tumor-specific antigen (Trp2) with a vaccine in combination with immunotherapy and an epigenetic therapy. By this combination, we hypothesized increased immune infiltration and significant anticancer effects, potentially outlining a new therapeutic avenue for glioma treatment.

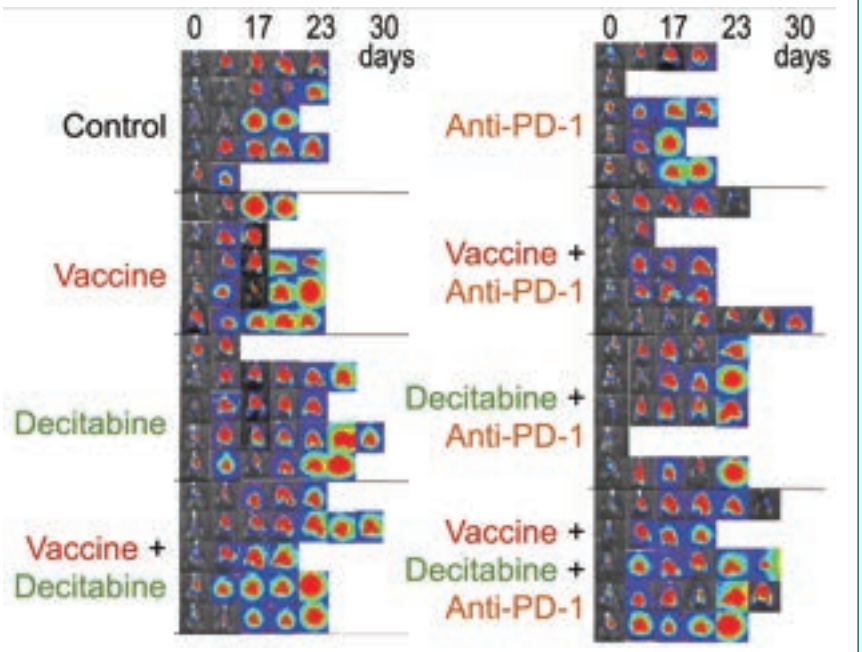

FIGURE 1: Bioluminescence of glioma-harboring mice was monitored twice a week by IVIS 200 Bioluminescence/Fluorescence (Xenogen, 2013)

RESULTS

Based on previous in vitro experiments proving GL261-NCI sensitivity to decitabine, we dosed decitabine in vivo in combination with a Trp2-specific anticancer vaccine, and anti-PD-1. Tracking the BLI over the experiment demonstrated a trend of the treatment groups dosed with decitabine to trend toward later increase in signal (Figure 1). Keeping this data, the Kaplan-Meier curves generated showed an increase in survival in the treatment groups dosed with decitabine. Figure 2d shows an increase in survival by 50% in the decitabine-only group as compared to control. Cementing this trend further, Figure 2d shows all groups dosed with decitabine demonstrated an increase in survival ($p=0.0006$). However, the anti-Trp2 vaccine and anti-PD-1 groups show no survival benefit unless dosed with decitabine.

DISCUSSION

Taken together, this data would imply GL261-NCI in vitro sensitivity and a survival benefit in our in vivo glioma model. However, mechanisms of resistance of the vaccine and anti-PD-1 are yet to be determined. Currently, we are evaluating these mechanisms via CyTOF, particularly looking at exhaustion signatures and other anti-inflammatory signatures that may be playing a role in our traditionally immune cold

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microenvironment. We will also be evaluating the microenvironment with IHC to determine how the tumor cells are directly contributing to the suppression of the immune system.

Further, we hope to optimize our in vivo model, as we believe too many cells were injected initially. The timeline of this experiment may have contributed to a poor response in the anti-Trp2 vaccine, as the tumors may have grown faster than the immune system could handle. We are planning more experiments with different cell lines and fewer initially injected cells to understand how decitabine can contribute to tumor control in these models. This is of particular importance because GL261 sensitivity in vivo to anti-PD-1 has been demonstrated before.

Ultimately, we hope to demonstrate decitabine's role and importance as a potential therapy for glioma.

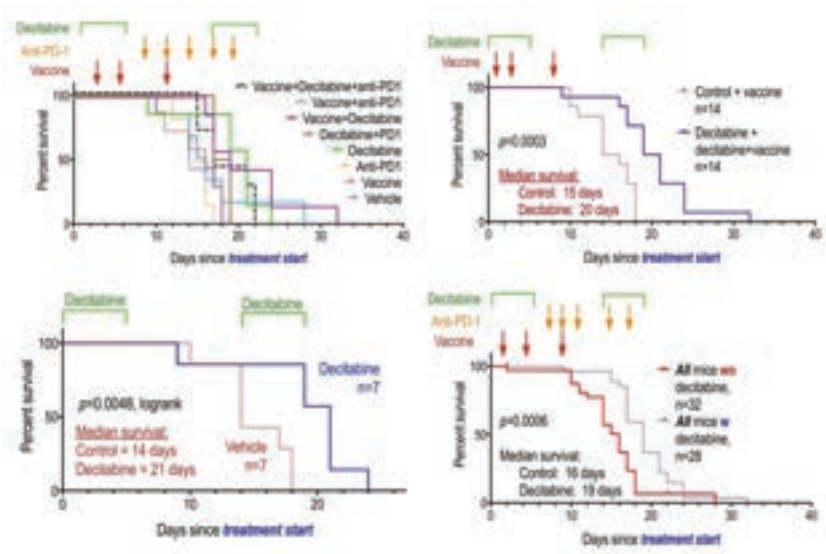

FIGURE 2: Kaplan-Meier curves of (a) all experimental groups (b) vehicle + vaccine vs decitabine + vaccine (c) decitabine vs vehicle (d) all mice dosed without decitabine vs all mice dosed with decitabine.

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Evaluating the Prognostic Utility of the Hematopoietic Cell Transplantation Comorbidity Index (HCT-CI) in Children and Young Adults with Relapsed Refractory B-cell Acute Lymphoblastic Leukemia (r/r B-ALL) Prior to CAR T-cell Therapy

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Despite the clinical efficacy of chimeric antigen receptor (CAR) T-cells in children and young adults (CAYA) with relapsed/refractory (r/r) B-ALL—many of whom have had extensive prior therapy—there is limited understanding of how baseline comorbidities associate with outcomes. In patients, including children, undergoing allogeneic hematopoietic stem cell transplant (HCT), the hematopoietic cell transplantation-specific comorbidity index (HCT-CI) is a validated tool for prognostication of post-transplant non-relapse mortality and survival based on a set of pre-transplant comorbidities; increasing scores are associated with worse outcomes.1 To date, there is no tool which helps to predict CAR T-cell outcomes as informed by baseline comorbidities.

TABLE 1: HCT-CI In Relation to Outcomes

HCT-CI in Relation to Outcomes						
		All Patients (n=119)	HCT-CI 0 (n=20)	HCT-CI 1-2 (n=40)	HCT-CI 3+ (n=59)	p
Any CRS	Yes	96	15	31 50		0.28
	No	23	5	9 9		
CRS by Max Grade	0	23	5	9 9		0.37
	1	45	8	13 24		
	2	30	5	10 15		
	3	17	2	6 9		
	4	4	0	2 2		
Complete Response	Yes	82	16	27 39		0.29
	No	36	4	12 20		
	Median OS		14.6 mos (95% CI:9.9-38.7)	18.8 mos (95% CI: 7.3-27.4)	12.2 mos (95% CI: 7.9-14.9)	0.39
	2yr CIR		49.3% (95% CI: 19.9-73.4%)	64.6% (95% CI: 41.9-80.3%)	61.6% (95% CI: 42.2-76.2%)	0.36

OBJECTIVES

To evaluate the use of HCT-CI for prognostication of outcomes following CAR T-cells.

METHODS

The HCT-CI score was retrospectively determined for 119 patients with r/r B-cell ALL treated on one of three Phase I CAR trials at the National Cancer Institute (NCT01593696, NCT02315612, NCT0344839) through 12/31/2020. A score for each of the comorbidities included in the HCT-CI was applied to every patient using data collected prior to the start of lymphodepleting chemotherapy. Scores were analyzed with respect to outcome measures including cytokine release syndrome (CRS), complete response (CR), median overall survival (OS), and cumulative incidence of relapse (CIR).

RESULTS

Among the 119 patients, the median age was 15.4 (range, 4.4-30.7) and median number of prior cycles of therapy (excluding HCT) was five (1-14). The median HCT-CI score was two (range, 0-7), with 49.6% of patients having a score > 3. Each patient had a median of one comorbidity (range, 1-3), with hepatic and pulmonary systems predominantly contributing

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to the HCT-CI scores. There was no association between HCT-CI and CRS incidence (p=0.28), CRS max grade (p=0.37)), CR (p=0.29), median OS (p=0.39), nor 2-year CIR (p=0.36) (Table 1, Figures 1&2), and scores did not differ between trials (p=0.21).

CONCLUSION

Despite the important role of HCT-CI in predicting post-HCT outcomes, it lacked prognostic utility in CAYA with r/r B-ALL undergoing CAR T-cell therapy. Nonetheless, integrating comorbidities with known determinants of response and toxicities (ie. disease burden) may be important in predicting outcomes, especially considering the substantial baseline profiles of these patients. Efforts to generate and validate a CAR Comorbidity Index using such a set of pre-CAR characteristics and risk factors are underway.

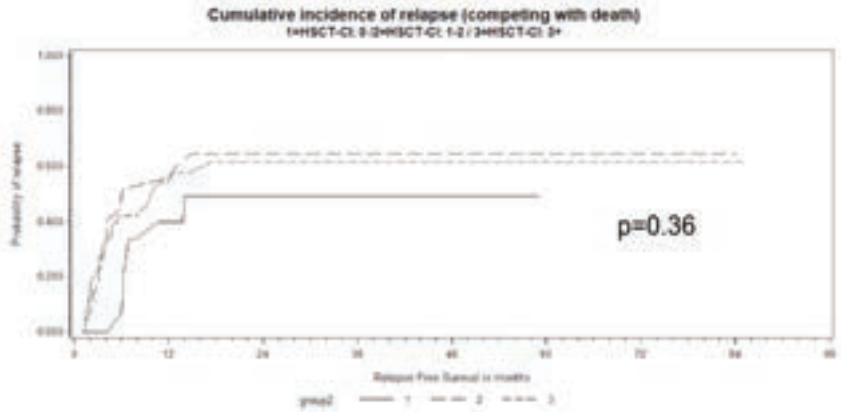

FIGURE 1: Overall Survival by HCT-CI Figure 2: Cumulative Incidence of Relapse by HCTCI.

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Comparing Treatment Options for High-Risk Prostate Cancer Patients: An NCDB Analysis of Outcomes

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The current standard therapy for high-risk prostatic adenocarcinoma is either radical prostatectomy (RP) or the combination of radiotherapy (XRT) with androgen deprivation therapy (ADT). We analyzed the National Cancer Database (NCDB) to compare patient characteristics and survival outcomes between treatment options to determine if there is an optimal strategy.

METHODS

Within the NCDB, men with high-risk prostate cancer, defined by the National Comprehensive Cancer Network, were identified from January 2010 to December 2016. These individuals received either RP or XRT + ADT as their initial treatment course. XRT + ADT was defined as beam radiation to the pelvis with ADT initiated within 90 days. Clinical, demographic, and pathologic characteristics were obtained. Survival analysis was performed using Cox Proportional Hazards Model and the Kaplan-Meier Method. A multiple logistic regression model was used to predict receipt of secondary therapy (adjuvant or salvage) among RP patients.

RESULTS

A total of 58,415 men were analyzed; 63% underwent RP first and 37% underwent XRT + ADT first. In a multivariable logistic regression model predicting treatment, the XRT + ADT group was more likely to have higher PSA, higher clinical stage, and higher Gleason score (all $P < 0.001$). Median follow-up was 3.33 years. Survival analysis showed that the RP group fared better (96.6% OS at median follow-up versus 90.1%), even while controlling for patient demographics and disease characteristics. The resulting hazard ratio for the XRT + ADT group compared to RP was 2.0 (95% CI 1.90 – 2.17, $P < 0.001$). Within the RP group, 5,273 (9%) received secondary therapy (XRT ± ADT) with a median time of 3.3 months from date of surgery.

CONCLUSIONS

These findings suggest that while each modality has its own risks and benefits, RP provides better survival outcomes over XRT + ADT when used as the primary definitive treatment course in well-selected high-risk patients.

Valproic Acid Induced Cervical Tremor in a Pediatric Patient

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Valproic acid is primarily used to treat disorders ranging from epilepsy, migraines, and seizures to bipolar, mood, and anxiety disorders.[1] With utility in the pediatric and adult populations, the safety profile of Valproic acid has been studied to characterize its major adverse effects. The drug is accompanied by a black box warning for life-threatening hepatotoxicity, teratogenicity, and pancreatitis, and indicates that patients in the pediatric population are at an increased risk of developing such complications.[1-2]

As with other psychopharmacologic agents, such as lithium and antidepressants, a drug-induced tremor has also been associated with Valproic acid.[3] Studies suggest that chronic Valproate use induces an enhanced physiologic tremor in about 10% of patients, with most of these tremors appearing within a month of Valproic acid initiation.[4-5] One study aimed to prove an association between plasma Valproate level and tremor severity, suggesting tremors may be more apparent with dosages of Valproic acid exceeding 750mg daily.[5] There have been repeat studies to establish the relationship between Valproic acid and tremors, yet it is still poorly understood.

This case report concerns a cervical tremor that emerged after initiation of Valproic acid in a pediatric patient, a group more susceptible to medication side effects, and that ceased only with discontinuation.

CASE

Manny is a 17 year old male with a past psychiatric history of bipolar 1 disorder who frequently presents after marijuana usage. During this admission, an isolated head tremor was noted without extremity tremors. There was unclear cause of head tremor. Benztropine was tried with minimal response. As his long-term medication regimen consisting of lithium and paliperidone did not appear effective in managing his mania, Valproic acid was started. More traditional routes to control his mania like increasing antipsychotic dose were not pursued as he is sensitive to medications, evidenced by his history of neuroleptic malignant syndrome one year prior. Valproic acid was tapered down which was accompanied by gradual improvement in his head tremor.

DISCUSSION

It is well documented that Valproate is associated with dose-dependent side effects, like thrombocytopenia. Although there is a well-known relationship between Valproic acid and tremors, medical literature has not yet clarified the character of the tremor in relation to the prescribed dose, with studies lacking particularly within the pediatric population. This case study aims to prove that Valproic-acid induced tremors are also dose-dependent, as evidenced by a 17-year old male.

CONCLUSION/ IMPLICATIONS

With limited medical literature regarding this phenomenon, there is a need to further characterize the tremor associated with Valproic acid pharmacotherapy to better identify at-risk populations, clarify appropriate medication dosages, and understand the implications of chronic therapy with a medication that works so potently on the nervous system.

Studies suggest that chronic Valproate use induces an enhanced physiologic tremor in about 10% of patients, with most of these tremors appearing within a month of Valproic acid initiation.[4-5]

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The Effect of Selective Laser Trabeculoplasty in Patients with Angle Recession Glaucoma: A Case Series

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Selective laser trabeculoplasty (SLT) is a commonly used primary or adjunctive therapy in glaucoma to lower intraocular pressure (IOP). Currently, there is no consensus on whether SLT is safe and effective in decreasing IOP in eyes with ARG.[1,2,3] Our study investigates the pre- vs postoperative change in IOP in a patient's treated and untreated eye within 12 months after receiving SLT.

DESIGN

Patients receiving SLT at the George Washington University Hospital between January 1st, 2008, to January 1st, 2022 were retrospectively queried. Pre- vs post-SLT IOP and the number of medications in each eye were analyzed using a paired samples t-test. Patients were excluded if they did not have SLT done on the eye with ARG, did not have an ARG diagnosis, or received surgery during the 12-month follow-up period. Treatment success was defined as an IOP reduction greater than or equal to 20% of the baseline IOP level after SLT and was calculated at each time point for the untreated eye.

TABLE: Mean IOP values in the untreated contralateral eye within 12 months following SLT

	Number Observed	Mean	Std. Dev	Std. Error	95% Confidence Interval		T-value	P-value
pre-op	125	15.21	3.55	0.32	14.59	15.84		
post-op 6 weeks	125	14.29	3.50	0.31	13.67	14.91	3.33	0.0006
post-op 6 months	125	14.22	3.61	0.32	13.58	14.86	3.09	0.0025
post-op 12 months	125	14.74	3.53	0.32	14.12	15.36	1.59	0.1149

RESULTS

A total of nine cases were included in this study. Cases 5 and 9 were excluded from the t-test at months 6 and 12 (surgical intervention) and month 12 (lost to follow-up), respectively. Mean IOPs for the SLT treated eyes at baseline, 6-week, 6-month, and 12-month visits were 20 ± 6.22 mmHg, 17.39 ± 5.11 mmHg ($P > 0.05$), 17.88 ± 5.93 mmHg ($P > 0.05$), and 17.29 ± 6.62 mmHg ($P > 0.05$), respectively. For the same time points, the mean IOP for the untreated eyes were 15 ± 3.28 mmHg ($P > 0.05$), 16 ± 5.66 mmHg ($P > 0.05$), 13.81 ± 4.29 mmHg ($P > 0.05$), and 14.29 ± 3.77 mmHg ($P > 0.05$), respectively. The number of medications did not change.

DISCUSSION

There was a significant clinical IOP reduction in five ipsilateral eyes and two contralateral eyes within 12 months after SLT. While the average IOP decreased during the 6-week, 6-month, and 12-month follow-up visits post-SLT, this reduction was not statistically significant as a cohort. This study differs from previous research in showing safety and efficacy in decreasing IOP in not only the ipsilateral eye but also the contralateral eye after SLT. This study's population also improves on the previous study's external validity. There were nine patients (previously 41) who had diverse backgrounds (African American (66.7%), Caucasian (22.2%), Hispanic/Latino (11.1%) — previously unreported[1]).

CONCLUSION

SLT can produce a greater than 20% decrease in IOP in an eye with ARG for up to one year after treatment. SLT can also produce a greater than 20% decrease in IOP in the untreated eye.

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Selective Laser Trabeculoplasty in a Pediatric Juvenile Open-Angle Glaucoma Patient on Maximum Glaucoma Medications: Case Report

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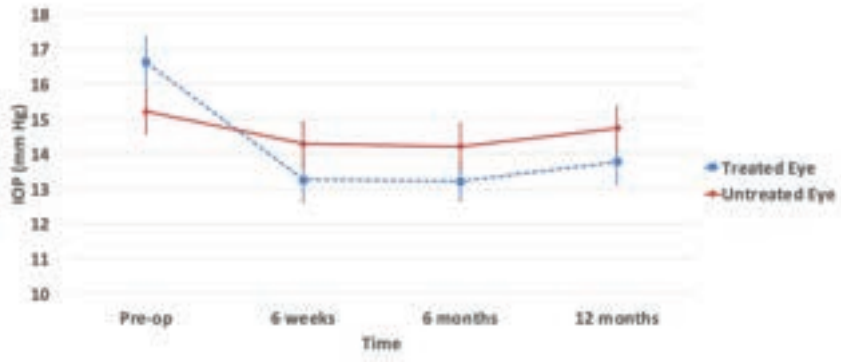

FIGURE: Mean IOP in the treated and untreated eye within 12 months following SLT with 95% confidence intervals.

Juvenile open-angle glaucoma (JOAG) is a severe form of glaucoma that is often refractory to medication and requires surgery. To lower intraocular pressure in glaucoma patients, selective laser trabeculoplasty (SLT) is used as a primary or adjunctive therapy. Currently, there is no literature on the effect of SLT on pediatric JOAG patients using maximum antiglaucoma medications.[1,2,3] We describe a pediatric JOAG patient on maximum glaucoma medications who responded well to bilateral SLTs.

DESIGN

A retrospective case report was conducted on a patient who visited the GW Medical Faculty Associates Department of Ophthalmology between Jan. 1, 2020 to Jan. 1, 2022, and received bilateral SLT. Visual field testing and optical coherence tomography were collected before and after the procedure. The percent change in intraocular pressure (IOP) and the number of medications over 12 months were calculated. Treatment success was defined as greater than or equal to 20% decrease in post-operative IOP as compared to pre-operative.

RESULTS

A 14-year-old female with a one-year history of bilateral JOAG on four antiglaucoma medications received sequential bilateral SLTs 6 weeks apart. Prior to SLT, a visual field exam showed a superior nasal step OD (MD -5.21, PSD 4.62) and superior and inferior nasal steps OS (MD -8.93, PSD 4.57). Optical Coherence Tomography (OCT) revealed average retinal nerve fiber layer (rNFL) thickness of 70 microns OD and 64 microns OS. The preoperative IOP in the right eye was 15 mmHg. The postoperative IOP and percent decrease was 13 mmHg (13%) at one week, 12 mmHg (20%) at six weeks, 12 mmHg (20%) at three months, 10 mmHg (33%) at six months, and 10 mmHg (33%) at 12 months. The preoperative left eye IOP in the left eye was 14. The postoperative IOP and percent decrease was 11 mmHg (21%) at one week, 11 mmHg (21%) at six weeks, 13 mmHg (7%) at three months, 12 mmHg (14%) at six months, and 11 mmHg (21%) at 12 months. Medications did not change in the course and visual field tests and OCT revealed no changes.

This study demonstrates that SLT may be viable as an adjunct therapy for pediatric JOAG patients on maximum medications prior to surgical intervention.

DISCUSSION

The patient experienced a successful

decrease in IOP after SLT (IOP reduction > 20%) at six weeks (20% OD and 21% OS), 3 months (20% OD), six months (33% OD), and 12 months (33% OD and 21% OS). To our knowledge, this study reports the first effect of SLT in a pediatric JOAG patient on maximum medications as previous reports included patients without medications[1,3] or were adults on maximum medications.[2] This study demonstrates that SLT may be viable as an adjunct therapy for pediatric JOAG patients on maximum medications prior to surgical intervention.

CONCLUSION

SLT is a safe and efficacious treatment for pediatric JOAG patients as an adjunct therapy with maximum medications.

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Social Determinants of Health Disparities Increase the Rate of Complications After Total Knee Arthroplasty

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The incidence of both total knee arthroplasty (TKA) and revision TKA has been increasing since the 1990s.[1,2] The current rise in TKA and the need for revision is expected to generate an economic burden of $13 billion annually by 2030.[3] Previous studies have investigated outcomes of TKA outcomes using surrogates for social determinants of health disparities (SDHD).[4] The Centers for Disease Control and Prevention defines SDHD as particular conditions where people are born, live, learn, work, play, worship, and age; that affect their health, functioning, and quality-of-life and may increase the risk for other medical conditions and were added to the International Classification of Disease (ICD) 10th edition as Z-codes, these include economic, social, education, health care, and environmental factors.[5] No studies using ICD codes have assessed outcomes with these new ICD Z-codes. We aim to investigate the association between SDHD, identified through this novel methodology, and postoperative complications following TKA.

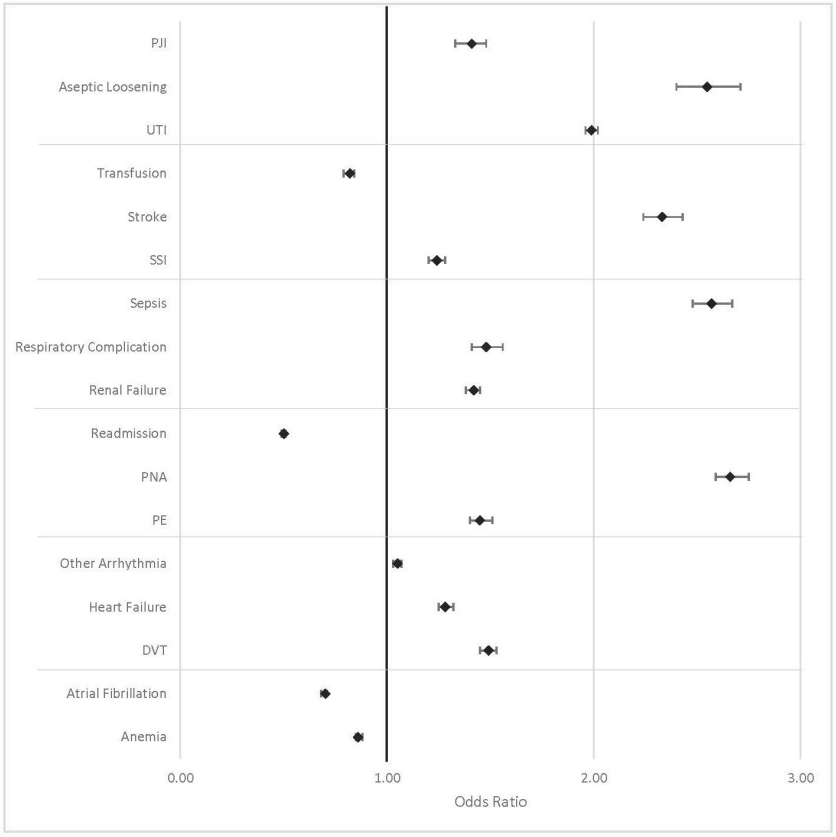

FIGURE: Forest plot of multivariable analysis of 90-day medical and 2-year surgical complications after TKA for patients with SDHD with odds ratio and 95% confidence interval.

PJI – periprosthetic joint infection, UTI – urinary tract infection, SSI – surgical site infection, PNA – pneumonia, PE – pulmonary embolism, DVT – deep vein thrombosis

METHODS

Using a national insurance claims database, a retrospective cohort analysis was performed. Patients were selected using CPT and ICD codes for primary TKA between 2010-2018. Patients were stratified into two groups using ICD codes, those with SDHD and those without. Comorbidities, demographic, 90-day medical and 2-year surgical complications were analyzed using univariate analysis. Significant complications ($p<0.05$) were analyzed using multivariable logistical regression with significant ($p<0.2$) comorbidities and demographic data being controlled for through univariate analysis.

RESULTS

997,812 patients were included, of which 69,179 (6.93%) patients had SDHD and 928,633 (93.07%) patients did not. Patients with SDHD were more likely to be younger ($p<0.001$), male ($p<0.001$) and generally had a higher

prevalence of comorbidities (Table). Complications were more common, and the length of stay was longer in patients with SDHD. In patients with SDHD, multivariable analysis found decreased rates of readmission (OR: 0.50), anemia (OR: 0.86), atrial fibrillation (OR: 0.70), and blood transfusion (OR: 0.82) within 90-days, with increased rates of DVT (OR: 1.49), heart failure (OR: 1.28), PE (OR: 1.45), pneumonia (OR: 2.66), renal failure (OR: 1.42), respiratory complications (OR: 1.48), sepsis (OR: 2.57), SSI (OR: 1.24), stroke (OR: 2.33), and UTI (OR: 1.99). Surgical complications within two years were significant for aseptic loosening (OR: 2.55) and periprosthetic joint infection (OR: 1.41) (Figure).

CONCLUSION

Using ICD Z-codes may be a viable option to screen patients with SDHD, who from this study experience disparate rates of medical and surgical complications as well as the length of stay, but lower rates of readmission and blood transfusion. Care should be taken to ensure that SDHD are considered preoperatively and addressed if possible. Further work is needed to clarify which specific ICD Z-codes are most relevant and whether this can be applied across other procedures and disciplines to improve efforts in targeting high-risk patients to improve patient outcomes.

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TABLE: Demographic and comorbidity univariate analysis between patients with SDHD and without before TKA. P-value <0.2 bolded and considered significant, which were controlled for in the multivariable analysis.

		Control		Presence of SDHD		
	Total	n	%	n	%	P-value
Total	997812	928633	93.07%	69179	6.93%	
AGE						
Mean		65.77		64.51		<0.001
Std. Dev.		8.59		9.60		
SEX						
Male	367677	349073	37.59%	18604	26.89%	<0.001
Female	630135	579560	62.41%	50575	73.11%	
COMORBIDITIES						
Alcohol Abuse	5393	4450	0.48%	943	1.36%	<0.001
Anemia – Blood Loss	13623	11374	1.22%	2249	3.25%	<0.001
Anemia - Deficiency	69543	57672	6.21%	11871	17.16%	<0.001
Arrhythmias	172737	154847	16.67%	17890	25.86%	<0.001
CHF	57675	51256	5.52%	6419	9.28%	<0.001
CKD	68337	59436	6.40%	8901	12.87%	<0.001
Coagulopathy	55658	47860	5.15%	7798	11.27%	<0.001
COPD	183198	163359	17.59%	19839	28.68%	<0.001
Depression	169741	146687	15.80%	23054	33.33%	<0.001
Diabetes Mellitus	228950	206928	22.28%	22022	31.83%	<0.001
Drug Abuse	22628	18021	1.94%	4607	6.66%	<0.001
Fluid/Electrolyte Disorders	118634	102738	11.06%	15896	22.98%	<0.001
HTN	543920	501269	53.98%	42651	61.65%	<0.001
Hypothyroidism	174359	154440	16.63%	19919	28.79%	<0.001
Liver Disease	65174	55906	6.02%	9268	13.40%	<0.001
Lymphoma	6511	5797	0.62%	714	1.03%	<0.001
Metastatic Cancer	9555	8275	0.89%	1280	1.85%	<0.001
Nonmetastatic Cancer	93845	84430	9.09%	9415	13.61%	<0.001
Obesity	57083	41761	4.50%	15322	22.15%	<0.001
Other Neurological Disorders	26533	22813	2.46%	3720	5.38%	<0.001
Paralysis	6377	5419	0.58%	958	1.38%	<0.001
Psychoses	13684	11255	1.21%	2429	3.51%	<0.001
PUD	3362	2367	0.25%	995	1.44%	<0.001
Pulmonary Circulatory	22728	19605	2.11%	3123	4.51%	<0.001
PVD	100879	89374	9.62%	11505	16.63%	<0.001
RA/CV	91482	80323	8.65%	11159	16.13%	<0.001
Smoking	72904	63482	6.84%	9422	13.62%	<0.001
Valvular Disease	102974	91960	9.90%	11014	15.92%	<0.001

SDHD – Social Determinants of Health Disparities, % - prevalence, SD – Standard Deviation, CHF – congestive heart failure, CKD – chronic kidney disease, COPD – chronic obstructive pulmonary disease, HTN – hypertension, PUD – peptic ulcer disease, PVD – peripheral vascular disease, RA/CV – rheumatoid arthritis/collagen vascular disease

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Benefits of Using 3D-Printed Cutting Guides in Medial Closing-Wedge Distal Femoral Osteotomy

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Patients with osteoarthritis are at risk for developing severe valgus deformities that require surgical treatment. Several surgical options are available, one of them being Medial Closing Wedge Distal Femoral Osteotomy (MCWDFO). Recent advancements in technology such as the use of 3D-Printed Cutting Guides (3D-PCG) offer exciting opportunities for surgeons to improve patient outcomes. The aim of this study is to determine whether the use of 3D-PCG can significantly improve surgical outcomes in MCWDFO.

METHODS

A meta-analysis was conducted using data collected through the PubMed database (Figure 1). All patients who underwent MCWDFO as well as MCWDFO with 3D-PCG to correct valgus deformities since the year 2000 were identified. Data collected include Technical Success Rate (TSR), Major Adverse Event Rate (MAE), pre- and post-operational anatomical Lateral Distal Femoral Angle (aLDFA), post-operational Tibiofemoral Angle (TFA), Surgical Time, number of fluoroscopic images taken, and post-operational Weight Bearing Line (WBL) between using a 3D-PCG or not. TSR was defined by successful completion of the surgery to fix and remove the severe valgus deformity while MAE was defined as complications during the surgery that were life-threatening or resulted in unexpected hospitalization. The incidence of TSR and MAE were evaluated with univariate and multivariate analyses where appropriate.

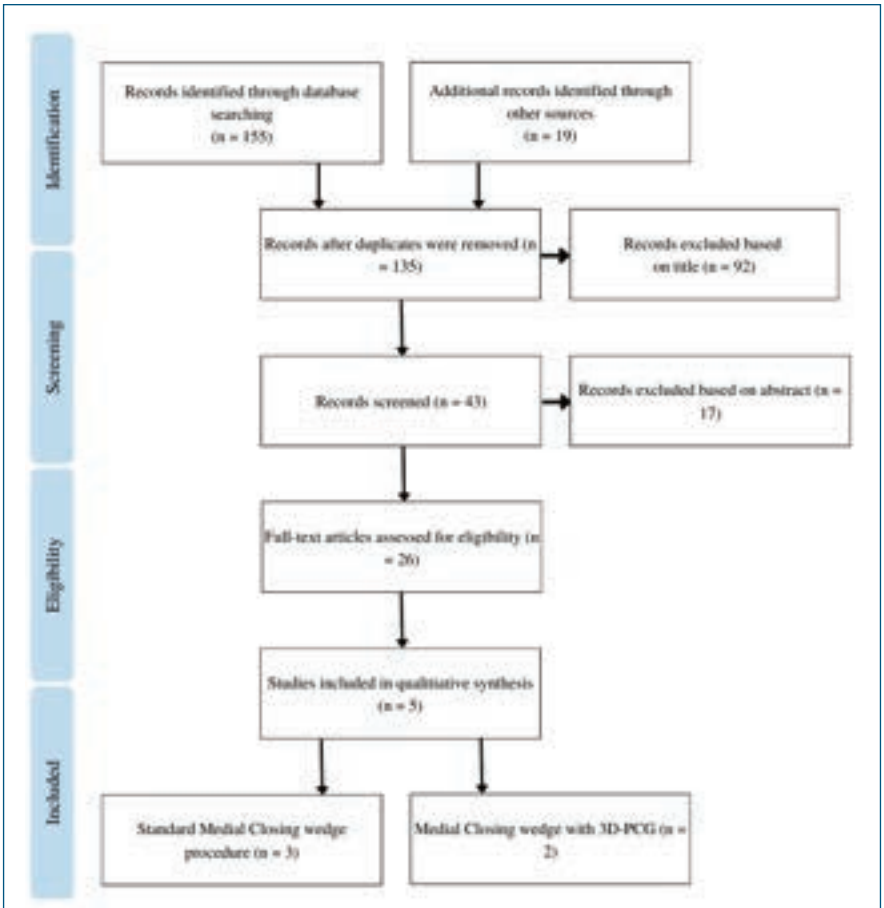

FIGURE 1: Systematic review flow diagram.

RESULTS

There was no significant difference in TSR[1,2,3,4,5] and MAE[1,2,3,4,5] between groups and, on average, surgeons that performed a traditional MCWDFO were able to do better than their 3D-PCG counterparts when it came to achieving an optimal post-surgical aLDFA[1,2,4] and WBL.[1,3] The use of 3D-PCG did, however, yield a 19.5% decrease in time spent in the operating room as well as an 82.42% decrease in the amount of radiation that the patient received.[3]

CONCLUSION

The use of 3D-PCG to aid an MCWDFO does not provide significant benefits in terms of promoting TSR, mitigating MAE, and improving other surgical

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outcomes (aLDFA, TFA, WBL). While it doesn't provide significant surgical outcome benefits, the use of 3D-PCG significantly minimizes the radiation that the patient receives during the operation as the amount of time spent in the operating room. As such, using a 3D-PCG might allow surgeons to see more patients daily. Further research, however, is needed to determine the long-term effects of using a 3D-PCG in correcting osteoarthritis induced severe valgus deformities.

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Peripheral Nerve Blocks Associated with Reduced Hospital Length of Stay and Increased Likelihood of Home Discharge After Pilon Fracture Fixation

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Peripheral nerve blocks have been increasingly incorporated into post-operative multimodal pain control regimens, mainly in the context of arthroplasty, because of their capacity to allow earlier mobilization and shorter hospital length of stay (LOS).[1] Following surgical treatment of tibial plafond (pilon) fractures, early mobilization may prevent post-operative stiffness, post-traumatic arthritis, deep vein thrombosis, and pulmonary complications.[2] The goals of this study are to examine the impact of peripheral nerve blocks on hospital length of stay and location of discharge after operative treatment of pilon fractures.

METHODS

Patients who sustained pilon fractures from 2010 to 2020 were identified through the PearlDiver Database using current procedural terminology and international classification of disease codes. These patients were stratified based on whether or not they had received a peripheral nerve block. Patients were additionally stratified according to the type of fracture (open versus closed) and type of peripheral nerve block (sciatic versus femoral). Discharge locations were stratified into home versus secondary facilities including acute rehabilitation centers, skilled nursing facilities, and long-term care facilities. Univariate analysis was conducted on demographic characteristics, comorbidities, and discharge location using Pearson chi-square analysis or analysis of variance (ANOVA). If a postoperative outcome was significant on univariate analysis ($p < 0.05$), a multivariable analysis using logistic regression was conducted to adjust for demographics and comorbidities ($P < .2$) as possible risk factors.

TABLE 1: Demographics and comorbidities amongst patients with pilon fractures

	Control		Peripheral Nerve Block		
	n	%	n	%	P-value
Total	15264		3678		
Age	47.314		46.982		<0.001
Charlson Comorbidity Index	1.579	0.01%	1.469	0.04%	<0.001
Congestive Heart Failure	1584	10.38%	263	7.15%	<0.001
Valvular Disease	1823	11.94%	371	10.09%	0.002
Pulm Circ Disorders	839	5.50%	168	4.57%	0.027
Peripheral Vascular Disease	2103	13.78%	432	11.75%	0.001
Hypertension	4851	31.78%	1086	29.53%	0.009
Paralysis	563	3.69%	78	2.12%	<0.001
Other neurological disorders	1741	11.41%	361	9.82%	0.006
Chronic Kidney Disease	1693	11.09%	332	9.03%	<0.001
Deficiency anemia	2029	13.29%	431	11.72%	0.012
Drug abuse	2751	18.02%	760	20.66%	<0.001
Depression	5609	36.75%	1445	39.29%	0.004
Smoking	3847	25.20%	1069	29.06%	<0.001
Diabetes Mellitus	3053	20.00%	652	17.73%	0.002

RESULTS

In total, 16,204 patients sustained pilon fractures (2,313 open and 13,891 closed). 3,433 patients received a sciatic nerve block and 2,981 received a femoral nerve block. Demographic information is displayed in Table 1. Univariate analysis demonstrated that all patients with a pilon fracture who received any peripheral nerve block had

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TABLE 2: Univariate analyses comparing (A) LOS and (B) Rates of home discharge

LOS	Time (Days)	SE	Time (Days)	SE	P-value	Time (Days)	SE	P-value
All Fractures	7.059	9.931	6.021	5.885	**<0.001**	6.205	5.964	**<0.001**
Closed Fracture	6.637	10.076	5.800	5.543	**<0.001**	5.465	5.861	**<0.001**
Open Fracture	9.124	9.157	7.599	7.033	**0.0322**	8.595	7.395	**<0.001**
Rate of Discharge	**n**	**%**	**n**	**%**	**P-value**	**n**	**%**	**P-value**
All Fractures	1796	11.77%	334	9.73%	**0.003**	291	9.76%	**0.002**
Open Fracture	326	14.09%	61	9.69%	0.1427	48	11.48%	0.1765
Closed Fracture	1591	11.45%	278	9.76%	**0.007**	203	9.53%	**0.010**

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shorter LOS compared to those who did not ($p<0.001$; Table 2). Additionally, univariate analysis demonstrated that patients with pilon fractures who received any form of peripheral nerve block were more likely to be discharged to home ($p<0.001$; Table 2). When stratified into open vs. closed fractures, patients with a closed pilon fracture who received a peripheral nerve block were more likely to be discharged home ($p<0.001$; Table 2). Multivariable analysis confirmed that patients with closed pilon fractures who received a peripheral nerve block had a higher likelihood of being discharged home ($p<0.001$).

CONCLUSION

Among patients with pilon fractures, those with perioperative nerve blocks had a shorter LOS. Additionally, patients with closed pilon fractures that had a perioperative nerve block were more likely to discharge to home. Orthopedists should consider peripheral nerve blocks during the operative treatment of pilon fractures, as reducing LOS and need for skilled rehabilitation prevents adverse health outcomes and reduces health care costs. Randomized trials and prospective studies must be conducted to support these results.

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COVID-19 induced Hepatitis and Cholestasis in a Pediatric Patient

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In the years since the World Health Organization declared SARS-CoV2, coronavirus disease 2019 (COVID-19) as a pandemic, we are still elucidating the extent of the extrapulmonary manifestations of the virus. Of the COVID-19 pediatric hepatitis case reports that do exist, presentations range from fulminant liver failure to a mild elevation in transaminases without synthetic dysfunction.[1,2] Here we report the case of a patient who had acute-onset infectious hepatitis with synthetic dysfunction and transaminitis in the setting of COVID-19 infection.

CASE PRESENTATION

A previously healthy 4-year-old boy presented with one week of abdominal pain, recurrent non-bloody, non-bilious emesis, three days of acholic stools, dark urine, scleral icterus, without any changes in mentation. Physical exam showed scleral icterus, jaundice, a diffusely tender abdomen with a palpable liver edge.

Initial laboratory values showed aspartate aminotransferase (AST) of 5,442 unit/L and alanine aminotransferase (ALT) of 3,313 unit/L, total bilirubin of 5.6 mg/dL, direct bilirubin 4.5 mg/dL, alkaline phosphate of 331 unit/L, gamma-glutamyl transferase (GGT) of 266 unit/L. Complete blood count and basic metabolic panel were within normal limits.

Laboratory testing was positive for COVID-19, adenovirus, and human herpesvirus-6 (HHV-6) but negative for Cytomegalovirus, Epstein–Barr virus, Herpes simplex virus, and enterovirus. Hepatitis A, B, C serologies were negative. Anti-LKM, Anti-actin, and antinuclear antibodies (ANA) were negative. Alpha-1-antitrypsin phenotype and ceruloplasmin were normal. Acetaminophen and aspirin levels were undetectable.

A liver biopsy showed moderate active hepatitis with mixed inflammatory infiltrates, moderate hepatocanalicular cholestasis, and scattered single cell necrosis. Adenovirus immunostaining and copper and iron staining were negative. No obvious cholangitis was seen, although focal venulitis and ductular proliferation was noted.

Treatment was supportive with Vitamin K supplementation and maintenance intravenous fluids.

At the time of discharge, the patient's transaminitis, elevated GGT, direct bilirubin level, and INR had all improved. Clinically, the patient demonstrated increased energy and activity levels, and only trace scleral icterus. The patient was seen at an outpatient clinic 26 days after discharge with labs showing an AST of 63 units/L, down from a peak during admission of 5,442 units/L.

DISCUSSION

The definition of acute liver failure is an INR ≥ 1.5 with altered mental status, or an INR ≥ 2.0 regardless of mental status.[3] This patient's hospital course was notable for a rapid rise of INR to 1.6 with stable mental status; therefore, he did not meet the criteria for acute liver failure.

The most likely etiology of this patient's acute hepatitis and cholestasis was determined to be COVID-19 infection. Although adenovirus testing was positive, adenovirus-associated acute hepatitis is most commonly seen in transplant recipients and chronically immunosuppressed patients.[4]

Here we report the case of a patient who had acute-onset infectious hepatitis with synthetic dysfunction and transaminitis in the setting of COVID-19 infection.

Additionally, the quantitative viral load was low on presentation and decreased to undetectable levels when patient's symptoms peaked. Negative liver adenovirus immunostaining confirmed that the initial low level of adenovirus likely represented a resolving infection. Although HHV-6 viral load was 170 copies, HHV-6 commonly causes symptomatic infection in liver transplant patients and with viral loads greater than 7,000 copies.[5]

There is no consensus for the treatment of COVID-19 hepatitis in pediatric patients. In this case, COVID-19 hepatitis without liver failure was treated with supportive care.

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Functional Outcomes of Pediatric Craniopharyngiomas in Relation to Resection Approach

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Craniopharyngiomas (CP) account for 6-8% of intracranial neoplasms in pediatric patients.2 Although CP are histologically benign, their proximity to critical suprasellar structures and propensity for recurrence create morbidity.[1,2] The most common long-term consequences of craniopharyngiomas include panhypopituitarism, visual impairment, hypothalamic obesity, and cognitive impairment.[2] However, outcomes vary based on tumor size, location, and treatment approach.3 Although endonasal approaches are increasingly preferred, practice patterns in pediatric skull base surgery are varied.[3,4,5] The relationship between surgical approach and functional outcomes related to morbidity in pediatric populations remains understudied. The aim of this study was to examine outcomes as they relate to surgical approaches for pediatric craniopharyngioma resection at Children's National Hospital (Children's National) in Washington, D.C.

METHODS

We retrospectively reviewed the electronic medical records of pediatric patients who underwent procedures related to a diagnosis of craniopharyngioma at Children's National from 2002 to 2020. Inclusion criteria consisted of patients less than or equal to 21 years of age at the time of presentation, resection of a new or recurrent craniopharyngioma at Children's National, with follow-up data available.

RESULTS

The study included 33 patients, and the mean follow up was 51 months (range 1 to 204 months). The mean age at presentation was 8 years, ranging from 1 to 17 years. 73% (n=24) were male and 27% (n=9) were female. The most common presenting symptoms were headaches, visual disturbances, and emesis. 96% (32/33) had suprasellar extension: suprasellar (n=15), intra-suprasellar (n=11), and suprasellar with 3rd ventricular involvement (n=6). All subtyped tumors were adamantinomatous (n=22). 30 were operated through a frontotemporal craniotomy or its variants, one through bifrontal approach and two through the extended endonasal approach. Additional radiation therapy was used in 48% (n=16): proton beam (n=5), gamma knife (n=2), IMRT (n=8), and multiple modalities (n=1). Overall visual acuity improved in 53% (n=10) of patients and worsened in 21% (n=4). Hormonal outcomes (DI, hypothalamic and pituitary deficiencies) improved in 0% of patients and worsened in 35% (n=7). Cognition improved in 43% (n=6) and worsened in 7% (n=1). Hydrocephalus improved in 85% of patients (n=11).

DISCUSSION

Craniopharyngioma treatment is associated with high morbidity. Although anatomic factors guide approach selection, these data provide a baseline for a predominantly transcranial frontotemporal approach-based case series. Additional factors to consider include location, tumor characteristics on imaging, and role of adjuvant radiation. Frontotemporal craniotomies were associated with a 50% rate of visual improvement, serving as a baseline for comparison with upcoming pediatric endoscopic endonasal approach series.

Craniopharyngioma treatment is associated with high morbidity. Although anatomic factors guide approach selection, these data provide a baseline for a predominantly transcranial frontotemporal approach-based case series.

CONCLUSION

This 20-year series of predominantly transcranial approaches to pediatric craniopharyngioma provides a baseline

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for comparison in the modern era. Visual outcomes should be a particular focus of analysis in upcoming studies.

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Words Matter: The Effects of a Quality Improvement Intervention on Stigmatizing Language in Pediatric Primary Care Weight Management and Diet Related Chronic Disease Documentation

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TABLE: Operational definition of stigmatizing language as evaluated in the charts reviewed.

	If present code "yes"	If present code "no"
Diagnosis	• Morbid Obesity • Extreme Obesity	• Obesity • Severe Obesity • Class I/II/III Obesity
Review HPI and Treatment section for patient first language	• __ obese patient	• Patient with obesity
Physical Exam	• Obese within general appearance or abdominal exam • Buffalo hump	• Specific descriptors of atypical adiposity (ie, prominent central or facial adiposity) • Dorsocervical adiposity
Follow Up	• Weight check	• Nutrition check • Goal check

Weight stigma remains prevalent within health care. A 2017 American Academy of Pediatrics (AAP) policy statement outlined the detrimental impact of stigma in its many forms, including harmful language used by providers. In the context of the Cures Act, which grants patients unprecedented access to their health records, practices must ensure that destigmatizing language is used to promote positive health outcomes.

OBJECTIVE

To reduce stigmatizing language in clinical documentation through educational and electronic health record (EHR) interventions in the context of a clinical quality improvement (QI) initiative.

METHODS

A comprehensive QI project focused on improving the diagnosis and management of pediatric obesity was conducted at primary care centers affiliated with Children's National Hospital in Washington, D.C. Two health centers in Washington, D.C. were identified for targeted interventions. Seventeen pediatricians from these centers were selected for monthly chart review conducted at baseline, during the 12-month initiative, and six months post-intervention. The project included the development of clinical algorithms, enduring educational materials, monthly coaching sessions, and EHR changes. Employing empathetic language was incorporated into the project's key drivers. While patient-first language was emphasized throughout, additional interventions targeted clinical documentation: 1) ICD code changed to "severe obesity" from "morbid obesity" in the EHR, 2) documents disseminated outlining specific antiquated exam terminology, 3) and removal of "weight check" for follow up visits.

As patients push for increased transparency from their clinicians, we need our written language to reflect the same person-first language that we are striving for within clinical encounters.

RESULTS

A significant decrease in the use of stigmatizing language (Table 1) was noted across both outpatient clinics. At baseline, 40% of all charts of patients

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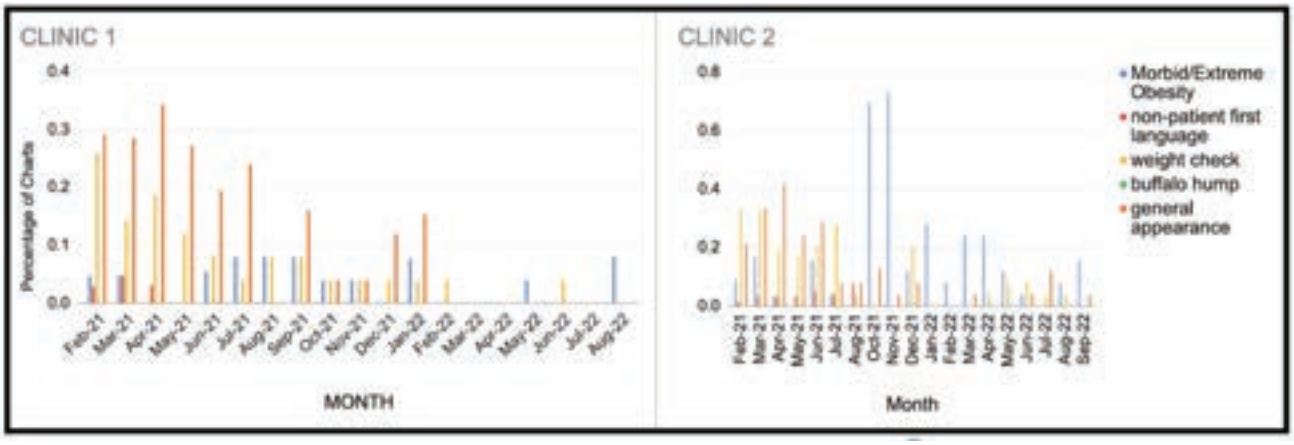

FIGURE: Breakdown of stigmatizing language used at target health centers.

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with obesity included stigmatizing language. This number dropped by 20% and was sustained after the intervention. The terms "weight check" and "obese" within the general appearance section of the physical exam, and "buffalo hump" reached near zero and were sustained six months post-intervention (Figure). Improvements in all metrics were seen, with the only deviation being an increase in the use of inappropriate body mass index (BMI) coding during the six- to ninth-month period of intervention, isolated to a single provider.

CONCLUSION

This intervention demonstrates that replicable education interventions and institutional support in removing stigmatizing language from the EHR can significantly improve the use of patient sensitive language. As patients push for increased transparency from their clinicians, we need our written language to reflect the same person-first language that we are striving for within clinical encounters.

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Evidence-Based Digital Interventions for Adolescents with ADHD: Stakeholder-Generated Solutions to Optimize Engagement and Implementation in School Settings

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Despite evidence demonstrating the effectiveness of behavioral/organizational skills interventions for adolescents with attention deficit hyperactivity disorder (ADHD),[1] this demographic demonstrates poor treatment utilization, express limited motivation for treatment, and struggles to engage in behavioral skills interventions compared to younger children.[2] Access to and uptake of these interventions continue to be limited, and minoritized families of low socioeconomic status experience significant barriers to treatment engagement.[3,4] There is a critical need for identifying strategies to improve quality of care and reduce treatment disparities in adolescents, thereby decreasing negative long-term patient outcomes associated with ADHD. The proposed study used a stakeholder-centered, theory-driven, empirical approach for optimizing treatment for ADHD by engaging key adolescent, parent, and school/community stakeholders in the iterative, co-development of a technology-enhanced intervention that targets skills acquisition/utilization. ATOM (Advanced Tools for Organization Management) was developed facilitating a user-centered design with iterative stakeholder input collected via focus groups/interviews, and formative usage evaluation. The data were collected by the ADHD & Learning Differences Program under the directorship of Melissa Dvorsky, PhD, with funding from the National Institutes of Health (NIMH # K23MH122839; https://theatom-program.com). Participants included adolescents (N=26; Mage=12.4 years 50% female), parents (N=16), teachers (N=8), and providers (N=8). This study included mixed method results such as analyses of focus group themes (coded using rapid qualitative analysis) and an open usability trial including collecting stakeholder and user ratings on the System Usability Scale (SUS),[5] which informed the technology design and refinement. Key themes identified from focus group and qualitative interviews emphasized adolescent, family, and provider preferences for features and design of ATOM, including immediate points, in-vivo prompts for skills, and interactive rewards (see summary of key themes and exemplar quotes in Table). Results from extended usability testing found high usability (SUS scores ranging from Ms = 73.0-83.7) across informants, and iterative development addressed stakeholders' feedback via enhanced features. ATOM was continuously revised until it met key stakeholders' needs, and ratings suggest high usability (SUS scores > 80). Results highlight the importance of stakeholders input in intervention refinement in order to understand the lived experiences and adequately reduce barriers and promote treatment engagement.

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Sickle Cell Disease Association with Premature Suture Fusion in Young Children

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Sickle cell disease (SCD) leads to the formation of an atypical hemoglobin tetramer with a reduced capacity to carry oxygen. Although the correlation between SCD and craniosynostosis (CS) has been mentioned, these are mostly small series or case reports.[1] This article aimed to study any correlation between these entities in a large pediatric population.

METHODS

Head CT scans of SCD patients from 0 to 8 years of age who required a CT for issues unrelated to their head shape between 2012 and 2020 were retrospectively reviewed. Patients with a known history of CS or any CS-related syndrome, hydrocephalus, shunt placement, history of cranial surgery, or any reported cerebral or cranial shape abnormality were excluded.

RESULTS

Ninety-four CT scans were analyzed. The mean age at imaging was 4.48±2.30 years. CS prevalence in this cohort was 19.1%. Analysis between independent variables and patients with +CS showed that SCD-associated vasculopathy, first-degree relatives with SCD, and the use of folic acid had a statistically significant association with CS development.

CONCLUSIONS

Approximately 20% of pediatric patients with SCD developed CS. This association was higher in those patients who had a family history of SCD, used folic acid, and had SCD-associated vasculopathy. While the clinical impact of these findings needs more extensive study, centers that manage patients with SCD should be aware of the relatively high concordance of these diagnoses, vigilantly monitor head shape and growth parameters, and understand the potential risks associated with unidentified or untreated CS.

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Using Steroids to Improve Outcomes in Rhabdomyolysis in Pediatric Patients

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Rhabdomyolysis is a complex medical condition leading to the disruption of skeletal muscle integrity. As a result, there is an inflammatory, self-sustaining myolysis cascade that causes the destruction of the muscle fibers and releases the muscle contents into the bloodstream and extracellular space, leading to elevated creatine kinase (CK). Patients experience significant muscle pain, and there is a risk of kidney injury and death.[1,2,3] Risk factors for rhabdomyolysis include trauma, excessive heat and dehydration, medication effects (including anesthesia), and genetic factors. Available therapies for rhabdomyolysis are not curative but are aimed at addressing the triggers, managing symptoms, and are limited to intravenous fluids and supportive care until the resolution of the episode. The goal of rhabdomyolysis management is to maintain adequate fluid resuscitation and prevent acute kidney injury. Some patients have recurrent rhabdomyolysis and face exercise restrictions and other limitations. There is a significant unmet need for optimized treatment, and our teams have extensively reviewed the literature and have proposed new treatment considerations.

CASE REPORT

We report a case of a 13-year-old female with a history of rhabdomyolysis in 2019 (with CK of 300,000) presenting with bilateral upper extremity pain, severe and cramping in nature. Genetics were consulted during admission, and acylcarnitine profile, Free/Total Carnitine, and urine organic acids returned as normal excluding fatty acid oxidation defects. Her CK levels remained refractory to adequate IVF treatment. Off-label use of dexamethasone per the genetics team was provided (16 mg PO for five days) and her CK levels dropped from 144,910 to 79,125 upon her first dose. Her CK levels continued to drop to 12,920 at discharge (within three days of treatment).

DISCUSSION

Limited case reports for rhabdomyolysis have mentioned the adjunct addition of steroids in some cases, as seen in inflammatory myopathies, and protocols have been suggested but not standardized.[4] Corticosteroids are well known for their widespread anti-inflammatory effects on multiple systems throughout the body. They suppress neutrophil migration, decrease transcription of inflammatory mediators, and decrease capillary permeability, all of which decrease the overall inflammatory load.[5] The process of rhabdomyolysis is postulated to have an associated inflammatory component, specifically due to the release of inflammatory mediators from dying myocytes.[5] Therefore, our hypothesis is that the use of adjunct steroids offers the potential to reduce rhabdomyolysis episode duration, symptomatology, and other disease risks.

CONCLUSION

Continued research in rhabdomyolysis therapy is needed. This case report highlights considering the addition of dexamethasone to current treatment protocols for idiopathic rhabdomyolysis, but further studies are needed. Our team is now commencing a ten-year retrospective chart review of the natural history of rhabdomyolysis and has been selected to receive funding from Cures Within Reach for a clinical trial comparing dexamethasone plus standard therapy versus standard therapy alone in rhabdomyolysis patients.

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Investigating the Effects of Cardiopulmonary Bypass on Structural Networks of the Neonatal Piglet Brain Using Connectome Analysis

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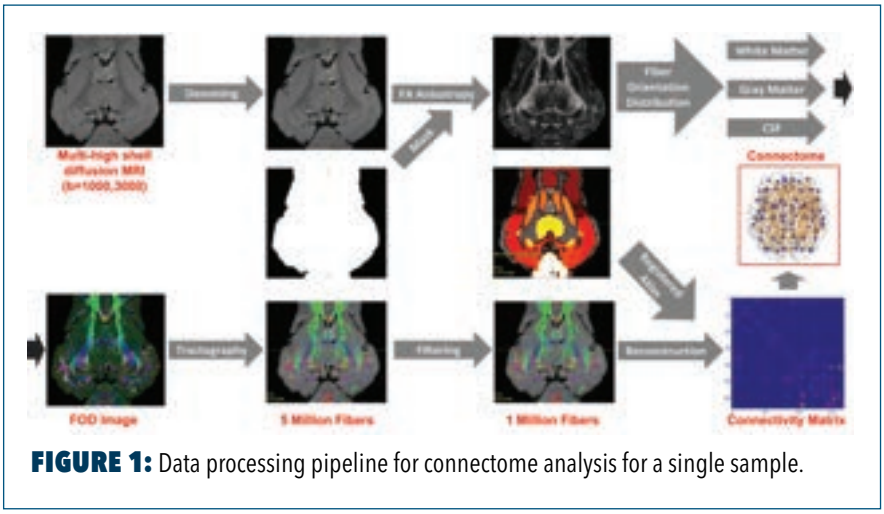

FIGURE 1: Data processing pipeline for connectome analysis for a single sample.

Newborns and infants with congenital heart disease (CHD) are now living longer and healthier because of the advancement in surgical techniques and medical care. Though neonatal cardiac surgery using cardiopulmonary bypass (CPB) is required for newborns with complex CHD, it can cause systemic inflammatory responses and reperfusion/reoxygenation injury, leading to delays in neurodevelopment.[1] While cellular analysis is commonly used in detecting microstructural changes to study brain development and abnormalities, it is often limited to whole-brain analysis. Connectome analysis, on the other hand, is considered an efficient and unbiased method to quantitatively investigate whole-brain development, neurodevelopmental disorders, as well as the effects of an intervention.[2] This study aims to investigate the impact of CPB on the neonatal piglet brain using structural connectome and network analysis.

Healthy two-week-old Yorkshire piglets were designated for one of two groups: no intervention (control) and CPB surgery via ascending aortic perfusion with right atrial drainage (CPB). High-resolution diffusion tensor images (DTI) were collected from each of the piglets four weeks post-treatment. Tractography was performed on denoised DTI scans to reconstruct whole-brain fibers using MRtrix3 software.[3] To expedite this 8-hour-per-sample process, a pipeline was created using Children's National Hospital's High-Performance Computing (HPC) cluster to compute samples in parallel. Whole-brain fibers were then registered to an in-house 3D piglet brain atlas with 68 individual regions to generate brain connectivity matrices (Figure 1). The resulting matrices were analyzed using graph theory by the MATLAB Brain Connectivity Toolbox for global, intermediate, and local characteristics.[4] Global characteristics such as clustering coefficients, small-world indices, global efficiency, local efficiency, and network density were extracted. These global characteristics of the brain networks were also compared against a thousand random networks to evaluate biological relevance.

We found that the global clustering coefficients differ significantly between the random and biological networks in both the control ($p<0.001$) and CPB datasets ($p<0.0001$). We compared the global and local efficiency of our samples' biological networks to random networks and a rigid lattice. Similar to the clustering coefficient, both global and local efficiency followed the expected trend which suggests the high capacity for exchanging information in the brain networks. In terms of intermediate measurements, there was no significant change between the rich club coefficients between the two conditions. Local measurements showed that there was more dynamic activity in the following regions in normal groups compared to the CPB group: basal ganglia, hippocampus, visual cortex, and frontal cortex.

With these findings, connectome analysis can be established as an unbiased approach to observing whole-brain connectivity and development which can leverage scientists' insights into experimental design when studying neurodevelopment. Since mesenchymal stromal cells derived from bone marrow (BM-MSC) can indeed mitigate the impact of inflammatory and oxidative stresses by inhibiting microglia activation, our team has

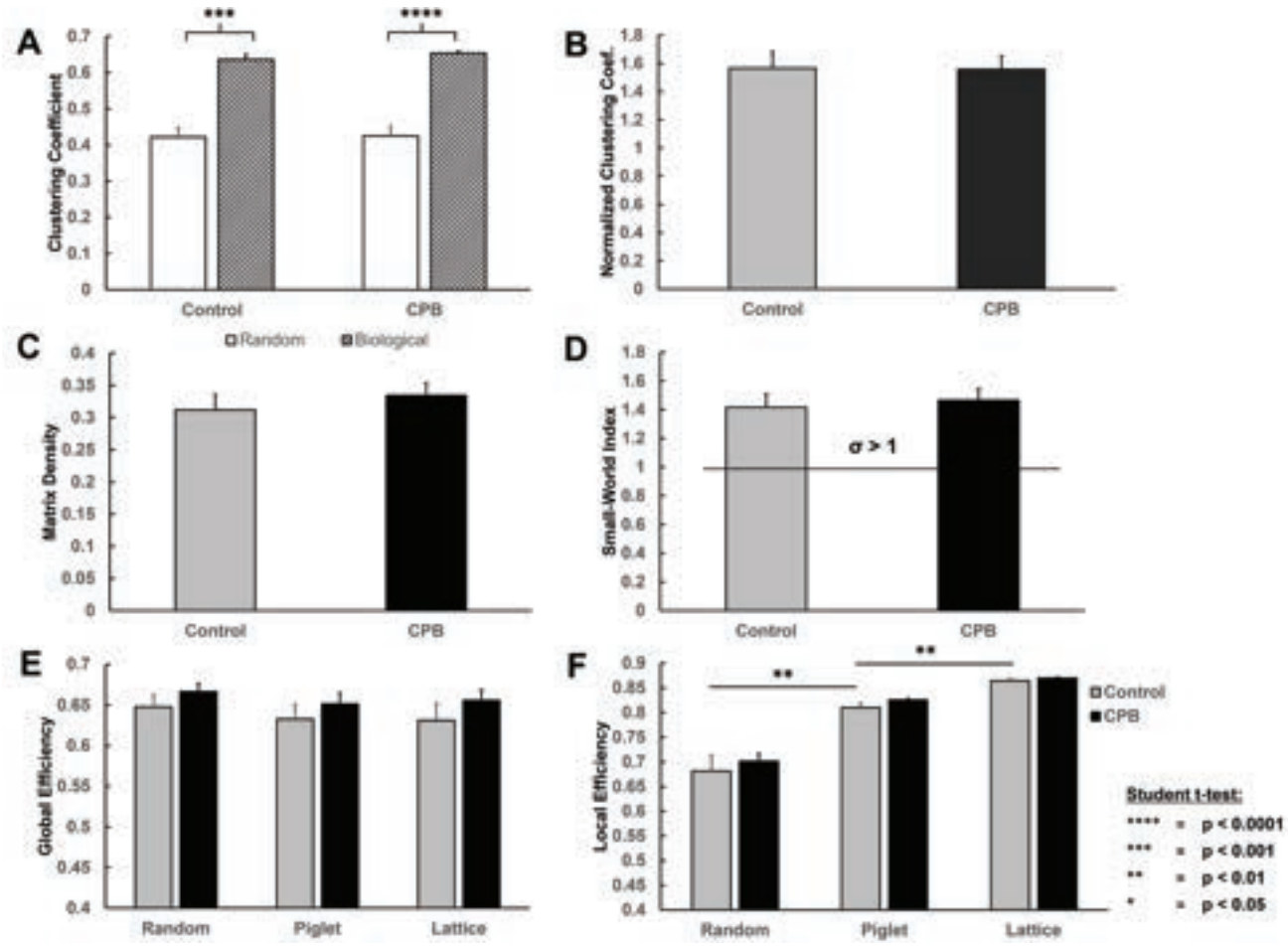

FIGURE 2: Bar graphs showing A and B) significant difference between random and biological brain networks in clustering coefficient (CI). C and D) matrix density and small-world indices. E and F) distribution of global and local efficiency reflecting expected trends (Global = Random > Piglet > Lattice; Local = Random < Piglet < Lattice).

also performed intra-arterial infusion of these cells in the CPB group. Future work will include further local network analysis to investigate the effects of BM-MSC on brain connectivity during CPB surgery.

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Performance of a Highly Accurate Prostate Cancer Algorithm on MR Image Data From a Different Institution: Do the Results Hold Up?

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Machine learning (ML) algorithms are gaining broad applications in oncologic imaging, including prostate cancer (PCA).[1] This has produced an increase in ML-associated research, most of which reports high diagnostic accuracy of algorithms in image analysis.[2-3] However, many of these algorithms are developed using only a single institution's data, with little research investigating multi-institutional datasets. The purpose of this project was to determine the accuracy of a highly effective prostate-cancer ML algorithm, trained and tested on image data from a single institution, then tested on image data from a different institution.

METHODS

The National Cancer Institute (NCI) & International Society of Optics and Photonics (SPIE) hosted the ProstateX Challenge in 2017, which provided a database of MR imaging for the development of ML algorithms.4 The most successful algorithms from the challenge were able to predict clinically significant prostate cancer (csPCA), with AUC and Accuracy over 0.9 and 90% respectively. In collaboration with our biomedical engineering department, we developed a residual neural network (ResNet) like those from the challenge. Axial T2 and ADC MRI image data from ProstateX was used to train and optimize the algorithm. Common ML testing and augmentation techniques were used, including 5-fold cross-validation, training set augmentation with image rotation, and preweighted imageNet weights. The ResNet was initially tested with ProstateX T2 and ADC imaging to assess its accuracy. Our institution (GW Hospital) was the "new" image data used to test ResNet. The differences between ProstateX and our institution's data are in Table 1. There was a total of 330 ProstateX images (254 benign, 76 csPCA) and 41 total GW images (two benign, 39 csPCA) used.

TABLE 1: Prostate X and GW Hospital Image Data

	Prostate X	Local Institution
Source:	Radboud UMC, Netherlands (The Cancer Imaging Archive[5])	George Washington University Hospital, Washington DC
Lesions:	330 (204 patients)	41 (41 patients)
mpMRI exams:	3T Siemens, Ø endorectal coil 3.6 mm thick slices Axial, Sag, Cor T2 small FOV DWI @ b = 50, 400, 800 Dynamic contrast-enhanced	3T Siemens, Ø endorectal coil 3 mm thick slices Axial, Sag, Cor T2 small FOV DWI @ b = 50, 800, 1400 Dynamic contrast-enhanced
Image analysis:	Axial T2 Axial ADC	Axial T2 Axial ADC
Pathology results:	Transrectal MR-guided biopsy	Prostatectomy: surgical pathology
csPCA:	≥ Gleason Grade 2 (GS 3+4)	≥ Gleason Grade 2 (GS 3+4)

RESULTS

After testing on ProstateX image data, our algorithm was shown to perform similarly to the most successful challenge algorithms (AUC 0.9, Accuracy 90%) at predicting csPCA. However, when testing on "new" GW image data the algorithm performed very poorly with AUC and Accuracies of 0.15 and 12.5% for T2, and 0.31 and 60.9% for ADC. In addition, we have preliminary data showing that after further training on combined ProstateX and GW data, the algorithms' performance began to approach ProstateX performance as evidenced in Table 2.

CONCLUSION

There are a few limitations present that could have impacted the performance of the algorithm. First, the GW dataset was much smaller (41 vs 344) with fewer benign lesions. The two institutions also used different biopsy methods (ProstateX MRI guided vs GW Surgical pathology). Finally, differences between the institutions' pathology interpretation of biopsy results can also be a limiting factor affecting the results. This study illustrates that highly

accurate algorithms trained on data from a single institution can underperform when using image data from a "new" institution. Differences in the MR scanners and image parameters likely account for discordant results. Variability in pathologist interpretation could also account for differing performance between institutions. Future efforts into ML algorithm development will require training using diverse multi-institutional image data. This has already spurred the field of federated learning, which seeks to bring together multi-institutional anonymized image data for ML algorithm development. Concepts such as federated learning will be essential in the development of further medical-based ML algorithms.

TABLE 2: ResNet Algorithm Training/Testing Data

Training:	ProstateX		ProstateX		ProstateX & GW	
Testing:	ProstateX		GW		GW	
	T2	ADC	T2	ADC	T2	ADC
AUC:	0.81	0.92	0.15	0.31	↑↑	↑↑
Accuracy:	96.0%	93.4%	12.5%	60.9%	↑↑	↑↑

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Magnetic Resonance Imaging vs. Inferior Petrosal Sinus Sampling in the Diagnosis of Pituitary Adenoma Induced Cushing's Disease

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Cushing's Disease (CD) is defined by hypercortisolism secondary to adrenocorticotropic hormone (ACTH) overproduction by a functioning pituitary adenoma. Two to three million new cases of endogenous hypercortisolemia (Cushing's Syndrome) are reported each year, 70% of which are due to CD.[1] The overall prevalence of CD is estimated to be higher due undiagnosed cases.[1] Current diagnosis of CD involves identifying abnormal plasma levels of ACTH and cortisol followed by imaging studies to confirm the ACTH-secreting tumor; however, imaging modalities have historically faltered in reliably visualizing small pituitary tumors. In cases highly suspicious for CD but without an identifiable pituitary adenoma on Magnetic Resonance Imaging (MRI), Inferior Petrosal Sinus Sampling (IPSS) can be used. This technique can localize the adenoma for surgical planning and exclude an ectopic, extra-adrenal source of ACTH production. This review article compares MRI and IPSS in the detection and localization of ACTH-secreting pituitary adenoma.

MATERIALS AND METHODS

A literature review was done using the PubMed database to compare the sensitivity of MRI to IPSS. Results from five studies were compiled and reviewed based on inclusion criteria. Between the five studies, a total of 392 cases were imaged or sampled. Of these cases, 309 were analyzed with MRI, while 83 were analyzed by IPSS.[1,2,3,4,5]

RESULTS

Of the 309 patients that were analyzed using MRI, the location of the tumor was accurately identified 230 times (sensitivity=74.4%). IPSS analysis correctly identified the location of the tumor 75 of 83 times (sensitivity=90.4%) which is significantly superior compared to MRI (p=0.00194).[1,2,3,4,5]

[P]atients with suspected CD, but a negative MRI result, a subsequent IPSS procedure should be the gold standard to confirm or exclude the presence of an ACTH-producing adenoma.

CONCLUSION

IPSS has a improved sensitivity for assessing pituitary adenoma location when compared to MRI; however, due to its procedural invasiveness, IPSS is considered a second line diagnostic measure when MRI is non-diagnostic.[1,2,3,4,5] In conclusion, patients with suspected CD, but a negative MRI result, a subsequent IPSS procedure should be the gold standard to confirm or exclude the presence of an ACTH-producing adenoma.

CLINICAL RELEVANCE STATEMENT

This review compares the sensitivity of Magnetic Resonance Imaging to Inferior Petrosal Sinus Sampling in the diagnosis of Pituitary Adenoma induced Cushing's Disease, and shows that IPSS is superior.

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Magnetic Resonance Imaging vs Transient Elastography in Assessing Pediatric Non-Alcoholic Fatty Liver Disease

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Non-alcoholic fatty liver disease (NAFLD) stands as the most common chronic liver disease in the pediatric population and is increasing in prevalence alongside the childhood obesity epidemic. Lab tests and biomarkers alone provide low sensitivity and specificity for pediatric NAFLD, while the most stringent diagnostic method of liver biopsy is invasive and expensive. Thus, non-irradiating, non-invasive imaging modalities are the ideal approach for diagnosing and staging NAFLD in pediatric patients. Presently, ultrasound is not sensitive enough to detect liver steatosis below 33% of hepatocyte involvement. As a result, magnetic resonance imaging (MRI) and transient elastography (TE) are promising diagnostic options for identifying and quantifying liver steatosis in pediatric NAFLD patients. This review article will compare MRI to TE to determine which method offers higher sensitivity for NAFLD diagnosis in children.

MATERIALS AND METHODS

A PubMed database literature review was performed to compare the sensitivity of MRI to TE in diagnosing pediatric NAFLD. Results from five studies were compiled based on predetermined inclusion criteria. Between the five studies, a total of 480 cases were imaged. Of these cases, 224 were analyzed with MRI, while 256 were analyzed by TE.[1,2,3,4,5]

RESULTS

Of the 224 NAFLD pediatric patients analyzed using MRI, the calibrated MRI fat fraction measurements produced an average sensitivity of 64.9%.[1,2] Of the 256 pediatric patients assessed using TE techniques, measurements for hepatic steatosis demonstrated an average sensitivity of 81.1%.[3,4,5] Thus, TE shows significantly superior sensitivity compared to MRI in pediatric NAFLD diagnosis ($p < 0.00001$).

CONCLUSION

The childhood obesity epidemic coupled with rising rates of pediatric NAFLD poses a need for accessible and noninvasive diagnostic technologies. This review suggests that TE offers greater sensitivity than MRI for NAFLD, with the convenience of a bedside imaging technique. Additionally, the less lengthy scan is of particular advantage in the pediatric population who may have difficulty complying with awake MRIs. More research should be done to determine the differences in specificity, exam time, and cost.

CLINICAL RELEVANCE STATEMENT

This review shows that in pediatric Non-Alcoholic Fatty Liver Disease, the quantification of liver steatosis is more sensitive when Transient Elastography is used over Magnetic Resonance Imaging.

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Thirty Day Complication Rates After Gender-Affirming Bottom Surgery: An Analysis of the NSQIP Database from 2010–20

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Gender-affirming surgeries (GAS) are a rapidly growing and changing field within plastic surgery. In particular, gender-affirming bottom surgeries (GABS) play a central role in treating gender dysphoria and significantly improve the quality of life in terms of both mental and sexual health for transgender and nonbinary (TGNB) patients.1-4 Like with any procedure, however, complications may arise from GABS. With more than 1.3 million adults in the United States who are part of the TGNB community, characterization of how to better offer specialized care for TGNB patients is necessary.5 While there are several reports on the various complications that may arise from GABS procedures, how demographics and clinical history affect the outcomes of GABS remains unknown. To bridge this gap, this study aims to analyze and determine the incidence and risk of 30-day postoperative complications in patients undergoing GABS from 2010 to 2020 using the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database.

METHODS

Using the American College of Surgeons-National Surgical Quality Improvement Program (NSQIP) database, we identified patients undergoing gender affirmation surgery using Current Procedural Terminology (CPT) codes included in male to female (MtF) and female to male (FtM) bottom surgery. The cases were further filtered by International Classification of Diseases Ninth and Tenth Revisions (ICD 9 and ICD 10 codes) for gender identity disorder and transexualism. Our clinical outcome measures consisted of postoperative complications, unplanned reoperation related to principal operative procedure, and 30-day readmission rates. Multivariate analysis was performed using IBS's SPSS statistical system to identify risk factors for increased 30-day postoperative complications.

RESULTS

The total number of GABS from 2010 to 2020 was 1809. Overall 30-day complication rate was 7.5%. Unplanned reoperation was the most common complication (2.8%) with 50 cases of one or more unplanned reoperations. Patients 36 and older were at greater risk for readmission (OR = 1.91, p =0.03) and wound complications (OR = 1.83, p =0.02). Non-insulin dependent diabetes was a risk factor for reoperation (OR= 3.80, p = 0.04). Black or African race was a risk factor for readmission (OR= 2.10, p= 0.05) and unplanned reoperation (OR= 2.25, p =0.03).

CONCLUSIONS

Black or African American patients were at significantly higher risk of postoperative wound complications than any other race or ethnicity. Besides race, age was found to be an important factor for readmission and developing postoperative wound complications. As GABS advances, this information will improve our understanding of associated risk factors and relevant post-operative complications. Physician awareness of risk factors and social determinants of health will help improve postoperative care education and patient compliance.

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Reducing Length of Stay following Autologous Breast Reconstruction via Combined Nerve Block-ERAS Protocol? A Systematic Review and Meta-Analysis

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Reducing length of hospital stay (LOS) and narcotic usage following autologous breast reconstruction has been shown to reduce postoperative complications, and lead to an increased rate of recovery. Previous studies support the use of Enhanced Recovery After Surgery (ERAS) protocols as well as nerve blocks to reduce LOS and lower narcotic usage. However, the additive effectiveness of both methods is not well understood. This systematic review and meta-analysis explores current pain management methods following autologous breast reconstruction to assess best methods of practice.

METHODS

A comprehensive literature search was conducted in October 2021 using publications extracted from Pubmed, Scopus, and Cochrane Library. Eligible studies were published on or after 2000 and had data reporting LOS, postoperative medications, narcotic usage measured in morphine milligram equivalents (MME). The criteria used were those described in the PRISMA Declaration for performing systematic reviews.

RESULTS

The initial search yielded 301 results. After screening, 20 studies were included. Of those 20, 9 implemented ERAS protocols and 11 used nerve blocking techniques. Implementation of ERAS protocols had a shorter LOS (4.5:5.85, p=0.0047) than non-ERAS postoperative methods. Implementation of nerve blocks, most commonly a Transverse Abdominis Plane block (TAP block), also showed reduced LOS (3.36:4.475, p=0.0254) and narcotic usage than the lack thereof.

CONCLUSIONS

Existing findings suggest ERAS protocols and nerve blocks reduce LOS following autologous breast augmentation. Furthermore, a combined intervention using both may have an additive effect in reducing LOS. Further studies analyzing the effects of a combined nerve block-ERAS protocol are needed to reliable assess the potential synergistic effects of the two components.

Wound Disruption Causing Increased Reoperation Rates in Transfeminine Bottom Surgery? An Analysis of the NSQIP Database from 2010–20

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Gender affirmation surgery (GAS) has gained traction in recent years due to increased societal acceptance of transgender individuals and its shown therapeutic benefits for male-to-female (MtF) transgender patients.[1,2] Specifically, transgender women report having transfeminine bottom surgery at varying rates from 5–13%, and an additional 45–54% report the desire for bottom surgery in the future.[3] Unfortunately, the literature is sparse on the causes of common postoperative complications and re-operation rates post-bottom surgery. So far, wound dehiscence, delayed wound healing, postoperative bleeding, infections, as well as urethral strictures and neovaginal stenosis, have been identified as the known complications of vaginoplasty.[4,5] The ability to objectively evaluate surgical outcomes of MtF bottom surgery remains an important step towards improving care for MtF transgender patients undergoing GAS. Our study aims to evaluate the postoperative complications with potential risk factors and re-operation rates following MtF surgery, with the ultimate goal of improving surgical outcomes in the MtF transgender population.

TABLE: Multivariate Regression Analysis Results when adjusted for age, race, BMI, smoking status, and diabetes

Variable tested	Odds Ratio	Significance
Wound Disruption	73.9	< 0.001
Chronic Steroid Use	11.6	0.045
Operation Time	1.3	0.038
Bleeding Transfusion	6.4	0.05
History of Hypertension	0.7	0.711
Superficial SSI	3.1	0.494
Deep SSI	1.2	0.909

METHODS

The American College of Surgeons-National Surgical Quality Improvement Program (NSQIP) databases from 2010 to 2020 were utilized to identify patients undergoing GAS with the relevant CPT codes. The cases were further filtered by ICD-9 and ICD-10 codes to further specify patients specifically undergoing GAS. Multivariate regression analysis was performed to identify risk factors for unplanned reoperation using the IBM SPSS statistical system (IBM Corp, NY). A risk-adjusted multivariate regression analysis controlling for BMI, age, race, smoking status, and diabetes was also performed to identify other risk factors using odds ratio (OR).

RESULTS

Of the 651 MtF bottom surgeries from 2010–20, over one-fifth of the total number of surgeries were performed in 2018 alone. For those who underwent at least one unplanned reoperation, the average age at the time of the initial surgery was 41 [23-65] and with a mean BMI of 30.2. The adverse event that posed the highest risk for reoperation in this study was wound disruption/dehiscence (OR=73.85, p<0.001) (Table 1). Those who had a wound disruption were 73.85 times more likely to have an unplanned reoperation compared to those who had no wound disruption (p= <0.001). History of steroid use for a chronic condition (OR=11.56,p=0.05) and longer operation times (OR=1.27,p=0.04) were also shown to be risk factors. Patients who needed a red blood cell transfusion intraoperatively or 72 hours postoperatively were 6.40 times more likely to undergo an unplanned reoperation compared to those who did not need a transfusion (p=0.05). Superficial and deep surgical site infections and

a history of hypertension did not pose a risk of having an unplanned reoperation.

CONCLUSION

Our results show that wound disruption/dehiscence constitutes the highest risk factor for an unplanned reoperation following MtF surgeries, along with the long operative times, bleeding requiring intra/post-operative blood cell transfusion, and history of steroid use for a chronic condition (Table). This suggests that the choice of appropriate surgical technique, minimizing blood loss and operation length as much as possible, and postoperative wound care are crucial in decreasing unplanned reoperation following MtF surgeries. These matters along with preoperative evaluation of patients for history of chronic steroid use can aid plastic surgeons to minimize the risk of complications and improve surgical outcomes in the MtF transgender population.

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An Atypical Presentation of Ruptured Appendicitis Discovered during Cesarean Delivery

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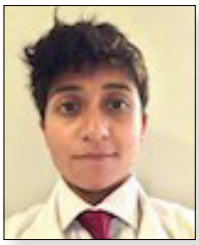

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A 23-year-old G2P1001, Hispanic, female patient, who was 36 weeks pregnant with a singleton fetus, presented to the labor & delivery triage unit with complaints of constant, generalized lower abdominal and back pain accompanied by nausea and vomiting for 12 hours. The patient denied loss of fluid, vaginal bleeding, fever, or chills. She reported good fetal movement and endorsed an uncomplicated pregnancy with standard prenatal care. Her gynecological history was negative for STIs or pelvic inflammatory disease. Prior pregnancy was uncomplicated and resulted in term spontaneous vaginal delivery. Medical history was noncontributory with regards to this pregnancy. She denied drinking, tobacco use, and drug use.

Vitals were significant for tachycardia at 118 bpm on admission and were otherwise within normal limits. On external fetal monitoring, fetal heart tones were classified as Category 1 tracing and reactive. The abdomen was gravid and non-tender to palpation, with the absence of palpable masses, bruising, or trauma. The cervix was closed, 50% effaced, with no evidence of blood or discharge in the vaginal vault. Tocometry ruled out labor as the cause of pain. Subsequently, maternal fetal medicine was consulted due to suspicion of concealed placental abruption. Ultrasound revealed a cephalic fetus with a normal amniotic fluid index and an intact, posteriorly placed placenta without evidence of placental abruption. Biophysical profile was 8/8. Urinalysis and CBC showed expected changes of pregnancy.

Patient was started on IV hydration, made NPO, and was continued on monitoring. The patient's pain worsened despite pain management and began to localize around the periumbilical region. The fetus was noted to become tachycardic and developed occasional late decelerations. Nonreassuring fetal heart strip resulted in the collective decision to deliver the patient via emergent C-section. After delivery of the neonate, the right-side of the round ligament was found to have purulent, foul-smelling fluid and was hyperemic in nature. After anteversion of the uterus, the appendix was revealed to be enlarged, encased in rind, and perforated. General surgery was consulted in the OR and performed an open appendectomy through the Pfannenstiel incision. Pathology collection and gross inspection at the time of surgery confirmed a diagnosis of ruptured appendicitis with peritonitis. Patient was managed post-operatively with pain control, IV hydration, and Zosyn but was noted to have persistent hypotension and fever. She was admitted to the ICU for concerns of sepsis and placed on IV fluids. Blood cultures revealed no growth after 48 hours. Blood pressures stabilized and the patient was discharged on post-operative day 4 on oral Augmentin. She reports full recovery upon follow-up call three weeks later.

Differential diagnoses for this patient included obscured placental abruption. While this patient did not present with any risk factors for placental abruption, this diagnosis was important to consider because it can prove fatal for mother and fetus if it remained undetected. Ultrasound by maternal fetal medicine was done to rule out this condition, and continuous monitoring aided in assessment of fetal status. Variable decelerations could indicate cord compression, but the development of late decelerations indicate placental insufficiency and along with tachycardia, fueled the collective decision to proceed to delivery via C-section. This unique and unusual presentation highlights the importance of considering appendicitis in pregnant individuals, as it can lead to perforation, peritonitis, and threatening of fetal status, as evidenced by this patient.

This unique and unusual presentation highlights the importance of considering appendicitis in pregnant individuals, as it can lead to perforation, peritonitis, and threatening of fetal status, as evidenced by this patient.

Delaying Surgery in Favorable-Risk Prostate Cancer Patients: An NCDB Analysis of Outcomes

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Concern for overtreatment in very low-, low-, and favorable intermediate-risk prostate cancer has promoted a more conservative approach through active surveillance (AS). Data from the National Cancer Database (NCDB) was analyzed to determine if delaying radical prostatectomy greater than six months is associated with increase in the rate of secondary treatment (adjuvant or salvage) and/or adverse pathology at radical prostatectomy.

METHODS

Within the NCDB, 40 to 75 year-old men with very low-, low-, and favorable-intermediate risk prostate cancer, defined by the National Comprehensive Cancer Network, were identified from January 2010 to December 2016. These individuals received radical prostatectomy either before or after six months following diagnosis. Clinical, demographic, and pathologic characteristics were obtained. Adverse surgical outcomes were defined as pT3-4N0-1. Multiple logistic regression models were used to predict delay in treatment, adverse surgical outcomes, and receipt of secondary therapy. Survival analysis was performed using a Cox Proportional Hazards Model and the Kaplan-Meier Method.

RESULTS

Of the 95,425 patients that met inclusion criteria, only 5,776 patients received surgery six months after diagnosis. The median time of delay was 7.4 months compared to 2.3 months in the immediate treatment group. Delaying surgery had no statistically significant impact on adverse surgical outcomes, regardless of risk category. Patients who had delayed surgery, however, were less likely to receive additional therapy (either adjuvant or salvage) (OR 0.64, 95% CI 0.51 - 0.78, $P < 0.001$). Survival analysis showed that both groups fared well, with five-year survival of 97% for both groups. The treatment group was not predictive of survival.

CONCLUSIONS

Delaying surgery more than 6 months following diagnosis showed no impact on adverse surgical outcomes or overall survival. These patients were also less likely to require secondary therapy. The results suggest that even patients who "fail" AS and require subsequent surgery have comparable positive outcomes to those who receive immediate treatment.

Concurrent Abdominal Body Contouring and Hernia Repair is a Safe Choice: An Analysis of the 2015–20 ACS-NSQIP Database

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Abdominal body contouring procedures, panniculectomy and abdominoplasty, aim to ameliorate the shape and appearance of the abdomen after significant weight loss or bariatric surgeries. This is done by removing the large overhanging abdominal panniculus, adipose tissue, and redundant skin by simultaneously tightening the abdominal wall laxity.[1] Many of the patients which undergo these procedures are at a higher risk of having weakened abdominal walls, especially if they have a previous history of obesity.[2] As a result, a significant proportion of these patients can develop abdominal wall hernias intraoperatively or postoperatively.[3] Given the significant co-existing nature of hernias at the time of abdominal body contouring procedures, concurrent hernia repair (HR) with abdominal body contouring (ABD) has been discussed as a strategy.[4,5] Although the purpose of combining these two procedures is to decrease postoperative morbidity, potential risks such as wound complications, infection, venous thromboembolism, and increased operating room and anesthetic time must also be considered. The purpose of this study is to evaluate potential medical and surgical complications following combined abdominal body contouring procedures, with a greater emphasis on cosmetic abdominoplasty, concurrently done with hernia repairs.

METHODS

The American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) was accessed on June 13, 2022, and patients who underwent ABD or ABD-HR between 2015 and 2020 were identified. Given the non-randomized and retrospective nature of this study, a propensity score (PS) matching was used to reduce selection bias by equating groups based on covariates. Bivariate analyses of independent variables were performed using Pearson Chi-Square and Fisher's Exact tests for categorical variables and the Wilcoxon rank-sum test for continuous variables.

RESULTS

Out of the 14,115 patients who were identified in the 2015-2020 ACS-NSQIP databases, 13,634 patients had only ABD, while 481 patients had both ABD-HR. The comparison of unmatched ABD and ABD-HR patient characteristics revealed significant differences in numerous covariates. Following the matching of propensity scores, bivariate analysis for the combination of all hernia types indicated significant differences in longer operative times (mean: 209.6 min) ($P < 0.001$) and longer hospital length of stay (mean: 1.9 days) ($P < 0.001$). The incidence rate of postoperative complications such as wound dehiscence, venous thromboembolism, unplanned return to the operating room within 30 days, sepsis, and other medical complications (pneumonia, pulmonary embolism, postoperative renal insufficiency, UTI, stroke, MI, DVT), displayed no significant differences between the two cohorts. Following a sub-group analysis, which was conducted to examine wound complications more precisely, there was no significant association found between the two groups. When the bivariate analysis was conducted for each type of hernia separately, ABD-VHR, ABD-EHR, and ABD-UHR were also seen to be associated with longer operative times ($P < 0.001$) and longer lengths of hospital stays ($P < 0.001$). All of the other complications mentioned in the combined hernia-type analysis remained the same, and no significant difference was found between the two cohorts.

Our results show no increase in postoperative morbidity when combining ABD and HR compared to ABD alone, suggesting that these procedures can be safely performed concurrently, regardless of the type of hernia.

CONCLUSION

Our results show no increase in post-operative morbidity when combining ABD and HR compared to ABD alone, suggesting that these procedures can be safely performed concurrently, regardless of the type of hernia.

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Influence of Donor Race and Donor-Recipient Race-Matching on Pediatric Kidney Transplant Outcomes

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Racial and ethnic disparities pervade health care delivery and transplant surgery outcomes for adult and pediatric patients.[1] Specifically in the context of kidney transplant outcomes, it is well understood that adult African American/Black (Black) transplant recipients tend to experience worse outcomes including increased graft failure and shorter half-life, as well as for Black pediatric patients, who experience poorer transplant outcomes, including higher rejection rates and higher mortality risk. In kidney transplantation, characteristics of the donor and recipient, including race, are highly relevant because the compatibility between donors and recipients can significantly influence transplant outcomes.[2] Limited research on donor race and race-matching indicates that Black donor race is associated with higher all-cause and cardiovascular mortality and graft loss.[3] Other research though, has indicated that Black and non-Black donors produce similar transplant outcomes in the recipient,[4] and findings about race-matching are inconclusive.[5]

TABLE: Transplant outcomes stratified by donor and recipient race

Recipient races					
	HR (N), CI (N – N), P-value (N)	**White**	**Black**	**Hispanic**	**Asian**
Donor races					
Delayed Graft Function	White (Reference)				
	Black	.86, .48-1.55, 0.62	.91, .58-1.43, 0.68	1.11, .56-2.21, 0.76	0, 0, 0.99
	Hispanic	.62, .35-1.12, 0.11	1, .58, 1.72, 0.99	.80, .49-1.30, 0.37	2.66, .37-19.22, 0.33
	Asian	0, 0, 0.99	.51, .066-3.98, 0.52	.44, .057-3.41, 0.43	.123, .005-3.17, 0.21
Acute Rejection	White (Reference				
	Black	.79, .48-1.32, 0.37	.90, .59-1.35, 0.60	.71, .36-1.42, 0.34	1.80, .44-7.46, 0.42
	Hispanic	1.35, .91-1.01, 0.14	1.24, .77-2.01, 0.38	1.10, .74-1.64, 0.65	.29, .057-1.51, 0.14
	Asian	1.31, .49-3.54, 0.59	1.29, .26-6.5, 0.76	1.21, .34-4.33, 0.77	.94, .12-7.31, 0.96
Graft Failure	White (Reference)				
	Black	.98, .66-1.45, 0.91	1.02, .79-.132, 0.853	1.1, .70-1.73, 0.67	0, 0, 0.98
	Hispanic	1.0, .70-1.42, 0.98	.786, .56-1.10, 0.16	1.07, .80-1.42, 0.67	1.19, .40-3.52, 0.76
	Asian	1.1, .41-2.97, 0.85	.42, .13-1.32, 0.137	.0, 0-1.3E+138, 0.95	1.47, .25-8.64, 0.67
Mortality	White (Reference)				
	Black	.70, .32-1.7, 0.39	.89, .51-1.56, 0.69	1.82, .63-5.24, 0.27	8.33, .29-236, 0.21
	Hispanic	.91, .56-1.81, 0.79	.81, .36-1.81, 0.60	.98, .43-2.21, 0.96	0, 0-5.2E+174, 0.96
	Asian	.001, 0-8.6E+21, 0.81	.54, .07-4.0, 0.55	.006, 0-5.6E+14, 0.80	0, 0-0, 0.98

METHODS

Kidney-only transplant recipients between ages 2–17 from 2000–17 enrolled in the Organ Procurement and Transplantation Network and their associated donors were analyzed. Race was self-reported and categorized

as White, Black, Hispanic, Asian, and Other (includes American Indian/ Alaska Native, Native Hawaiian/ other Pacific Islander, or Multiracial). Multivariable regression models were used to compare outcomes by donor race and donor-recipient race-matched status. The aforementioned categories include both races and ethnicities; for the purposes of this study, donor or recipient "race" will be referred to, with the understanding that some of the race categories are ethnicities, namely, Hispanic. Primary outcomes included delayed graft function (DGF), acute rejection, death-censored graft failure (DCGF), and mortality. Models were adjusted a priori for age, sex, age, body mass index (BMI), and human leukocyte antigens (HLA), as well as dialysis prior to transplant, kidney cold ischemic time, and graft survival time in years for recipients.

RESULTS

Of the total 7,343 recipients, 4,458 (60.7%) recipients received a kidney from a White donor, 1,009 (13.7%) from a Black donor, 1,594 (21.7%) from a Hispanic donor, and 169 (4.1%) from an Asian donor; 4,089 (55.7%) were race matched. No donor races were significantly associated with primary transplant outcomes (all P>.05) (Table 1). However, Asian donor race approached significance for being protective against DCGF (HR=0.56, 95% CI=0.31-1.02, P=0.057). Race-matched status was not associated with DCGF (HR=1.03, 95% CI=.89-1.2, P=.68), mortality (HR=1.1, 95% CI=0.79-1.53, P=0.56), acute rejection at 1 year (OR=0.94, 95% CI=0.77-1.15, P=0.53), or DGF (OR=1.02, 95% CI=.80-1.29, P=0.91).

DISCUSSION

Unlike recipient race, neither donor race nor race-matching appears to be predictors of pediatric kidney transplant outcomes. These findings support the developing movement away from race-based medicine because race is a social construct, rather than a biological attribute. The use of race in medicine has historical ties to disproportionate representation, confounding factors, barriers to care for certain populations, as well as making a fallible assumption that people of certain races are homogenous. This study adds to the limited literature on the influence of donor race on pediatric kidney transplant outcomes and might support the efforts to move away from using race as a foundational consideration in transplant outcomes.

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Simultaneous Free Flap Breast Reconstruction Combined with Contralateral Mastopexy or Breast Reduction: A Propensity Matched NSQIP Study on Postoperative Outcomes

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Simultaneous free flap breast reconstruction combined with contralateral mastopexy or breast reduction can increase patient satisfaction and minimize the need for a second procedure. Surgeon concerns of increases in operative time, postoperative complications, and final breast symmetry may decrease the likelihood of these procedures being done concurrently. This study analyzed postoperative outcomes of simultaneous contralateral mastopexy or breast reduction with free flap breast reconstruction.

METHODS

By using the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database (2010-2020), we analyzed two patient cohorts undergoing (1) free flap breast reconstruction only and (2) free flap breast reconstruction combined with contralateral mastopexy or breast reduction. The preoperative variables assessed included demographic data, comorbidities, and perioperative data. Using a neighbor matching algorithm, we performed a 1:1 propensity score matching of 602 free flap breast reconstruction patients and 621 with concurrent contralateral operation patients. Bivariate analysis for postoperative surgical and medical complications was performed for outcomes in the propensity-matched cohort.

RESULTS

We identified 11,308 cases who underwent microsurgical free flap breast reconstruction from the ACS-NSQIP database from the beginning of 2010 to the end of 2020. A total of 621 patients underwent a free flap breast reconstruction combined with contralateral mastopexy or breast reduction. After propensity-score matching, there were no significant differences in patient characteristics, perioperative variables, or postoperative medical complications between the two cohorts.

CONCLUSIONS

Simultaneous free flap breast reconstruction combined with contralateral mastopexy or breast reduction can be performed in patients with no increase in postoperative complication rates. The combination of these procedures can provide symmetrical, aesthetically pleasing results to breast cancer survivors with minimal complications, reduced costs, and elimination of a second operation.

Trends in Medicare Reimbursement for Transgender Plastic Surgery Procedures

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The goal of this project was to examine trends in Medicare reimbursement rates for transgender plastic surgery procedures from 2007 to 2020.

METHODS

Year to year changes in reimbursement rates were measured for 35 commonly used gender-affirming Current Procedural Terminology (CPT) codes. Reimbursement rates were obtained from January 2007 to January 2020 using the Centers for Medicare & Medicaid Service Physician Fee Schedule (CMS) and adjusted for inflation to 2020 U.S. dollar value.1 The Unadjusted Percent Change in Consumer Price Index (CPI) was calculated using data from the U.S. Bureau of Labor Statistics.2 Reimbursement rates were adjusted for inflation using the CPI for each year, and the average annual and total percent changes in reimbursement rates were calculated using these adjusted prices.

RESULTS

The mean percent change in the reimbursement rates from 2007 to 2020 was +16.01% while the percent change in the Consumer Price Index (CPI) from 2007 to 2020 was +27.45%. Using a two-tailed t test, results indicated that the rate of change in inflation from 2007 to 2020 was significantly higher ($p < 0.0001$) than the change in rate of medical reimbursement for all gender-affirming CPT codes analyzed. After adjusting for inflation, the Compound Annual Growth Rate (CAGR) for each CPT code was also shown to be negative, with an average change of -0.76%. The adjusted total percent change was also calculated at an average of -8.97%.

CONCLUSION

This is the first study evaluating trends in Medicare reimbursement rates for commonly selected gender-affirming procedures in the United States. After adjusting for inflation, Medicare reimbursement rates for all gender-affirming surgeries analyzed declined from the years 2007 to 2020. Using a two-tailed t-test comparison of means, the rate of change in medical reimbursement coverage from 2007 to 2020 was significantly more ($p < 0.0001$) than the change in inflation during that time period. Increased consideration of these trends will be important for U.S. policymakers, hospitals, and surgeons to ensure ease of access to gender-affirming care for transgender individuals.

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Does Innervated Autologous Breast Reconstruction Restore Protective Sensation? A Systematic Review and Meta-Analysis

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Recovery of breast sensation following autologous breast reconstruction represents the next frontier in breast reconstruction and is a growing topic of interest in literature. This systematic review and meta-analysis explores the results of innervated autologous breast reconstruction studies to assess the results of return of sensation.

METHODS

A comprehensive literature search was conducted using publications extracted from Pubmed, Scopus, and Cochrane Library. Eligible studies were published after 2000 and had results measuring breast sensation following innervated and non-innervated autologous breast reconstruction.

RESULTS

The initial search yielded 336 articles. After three stages of screening, 15 studies were included. Of those articles, all 15 reported data on tactile sensation, five on temperature sensation, and four on pain sensation. Eight of the articles that reported data on tactile sensation used the Semmes-Weinstein Monofilament Test (SWMT). Previous literature has shown that scores above 4.56 g/mm2 indicate loss of protective sensation. All eight studies had SWMT values below 4.56g/mm^2 (mean 4.08 g/mm^2) following innervated autologous reconstruction and above 4.56g/mm^2 (mean 4.98 g/mm^2) following non-innervated surgeries. Articles on thermal and pain sensation also discussed greater sensitivity in innervated breasts in comparison to non-innervated breasts.

CONCLUSIONS

Existing findings suggest autologous breast reconstruction with innervation restores protective tactile, thermal, and pain sensation better than techniques without innervation. The aggregated data supports greater incorporation of innervated flaps for breast reconstruction. Future studies with clear SWMT values and standardized thermal and pain scores are needed to further clarify sensory outcomes of innervation in autologous breast reconstruction.

Evaluation of Superior Semicircular Canal Dehiscence Anatomical Location and Clinical Outcomes: A Single Institution's Experience

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Superior semicircular canal dehiscence (SSCD) is becoming increasingly recognized as a pathology underlying various auditory and vestibular complaints. To date, our understanding of the pathology has yet to attribute specific symptoms to the anatomic location of dehiscence in patients with SSCD. This study aims to address this issue by evaluating the relationship between symptomatology and the anatomic location of dehiscence.

METHODS

A single-institution retrospective review of SSCD patients was performed. Information was collected on patient demographics, symptomatology, and anatomic location of dehiscence (Figure 1). High-resolution computed tomography (HRCT) scans of the temporal bones were used to categorize the anatomic SSCD location into one of three groups: anterior limb, apex, and posterior limb. Lastly, we performed statistical analysis to determine the degree of association between each of the various perioperative factors and anatomic SSCD location.

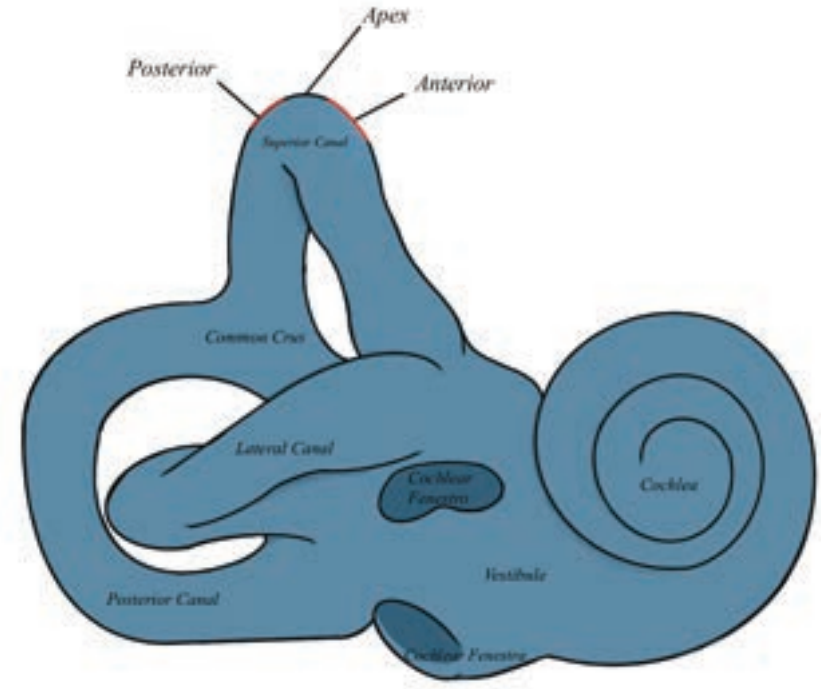

FIGURE 1: An illustration of the inner ear anatomy. This figure was created with Procreate® (Hobart, Australia).

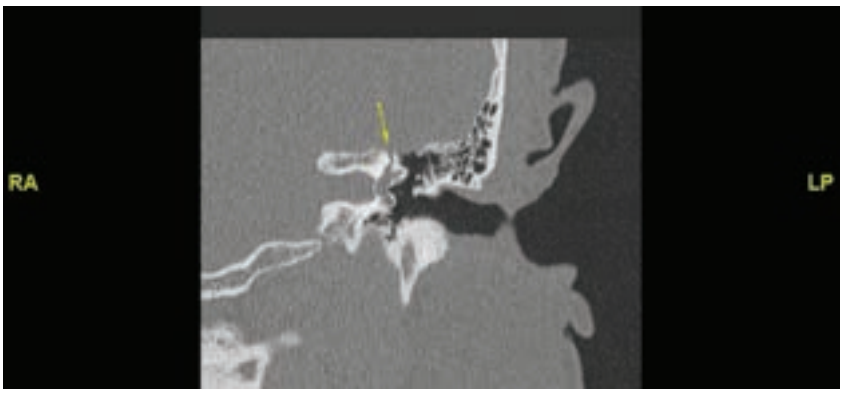

FIGURE 2: HRCT of a left-sided apical SSCD indicated by the yellow arrow.

RESULTS

We studied 54 patients in total (32 female, 22 male). The mean age at diagnosis was 53 years (range: 20-82 years) and mean follow-up length was 5.5 months (range 0.03-27.0). The most common anatomical location of superior semicircular canal dehiscence

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was the apex (Figure 2), which was seen in 68.5% of cases. While preoperative symptomatology was similar amongst the three cohorts, those with apical dehiscences had a significantly higher rate of postoperative improvement of autophony (p=0.03), aural fullness (p=0.03) and tinnitus (p=0.05) as compared to their counterparts.

CONCLUSION

While our results do not support an association between preoperative characteristics — including symptomatology — and anatomic SSCD location, our findings do suggest that apical dehiscences are associated with greater postoperative symptomatic resolution.

To Cut or Tie? A Retrospective Review of Patient-Reported Outcomes Following Postaxial Polydactyly Ligation Versus Surgical Excision

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Interventions for postaxial polydactyly include suture ligation and surgical excision. To date, there is a paucity in the literature reporting the postoperative outcomes of these procedures. Thus, this study sought to compare the long-term complications and patient-reported outcomes between these procedures.

METHODS

A six-question survey was distributed from January 2021 to March 2022 to patients who underwent treatment for type B postaxial polydactyly at a single pediatric institution from 2010 to 2016. The patients were queried about the incidence of sensitivity or pain, keloid healing, and/or persistent presence of bump ("nubbin") at the site of the excised supernumerary digit.

RESULTS

A total of 158 responses accounting for 258 digits were attained, for a response rate of 53%. Seventy-six percent of digits (n=196) were surgically excised whereas twenty-four percent of digits (n=62) were ligated. The median age at excision and survey was 66.5 [41.8, 161.2] days and 8.2 [6.2, 10.3] years, respectively. Patients treated surgically were significantly younger at the time of ligation compared to excision (27.0 vs 66.5 days; $p<0.001$) and survey (5.1 [4.6, 10.1] vs. 8.2 [6.2, 10.3] years; $p=0.004$). While the likelihood of postoperative sensitivity was similar in both groups, a significantly higher incidence of nubbin (48.4% vs. 31.6%, $p=0.016$), and lower incidence of postoperative hypertrophic (19.4% vs. 34.7%, $p=0.023$) was seen in the ligation group. These significant findings were consistent in the adjusted analysis.

CONCLUSION

This study suggests that while surgical excision may be preferable in the treatment of postaxial polydactyly, suture ligation can be used in select cases without increasing the prevalence of long-term pain or sensitivity.

The Impact of Coexisting Substance Use Disorder on Perioperative Outcomes in Patients Undergoing Lumbar Spinal Fusion

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Substance use disorders (SUD) hold a prominent position in global public health concerns and are associated with substantial societal and personal costs. Despite a significant increase in the prevalence of patients with coexisting painful spinal conditions and SUD in recent years, perioperative outcomes and protocols to manage this emerging population are poorly characterized.

OBJECTIVE

This study aimed to explore the impact of comorbid SUD on lumbar spinal fusion outcomes.

METHODS

Medical records for consecutive patients who underwent lumbar spinal fusion were retrospectively reviewed. SUD was defined according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, and identified using the International Classification of Diseases Revision 9 and 10 codes. Variables assessed included patient demographics, intraoperative complications, and postoperative outcomes. Univariate and multivariate analyses were utilized to determine whether patients with a history of SUD differed in perioperative outcomes.

RESULTS

Among the 805 lumbar spinal fusion patients included, 190 (23.6%) had a history of SUD. There was no significant difference in baseline demographics between the two groups. On multivariate logistic analysis, patients with a history of SUD had longer operative time (odds ratio [OR]=1.002, 95% confidence interval [CI] 1.001-1.003, p=0.002), had a higher chance to require admittance to the intensive care unit (OR=1.184, 95% CI 1.091-1.416, p=0.029), and were more likely to get readmitted to the hospital during the 90-day postoperative period (OR=1.275, 95% CI 1.049-1.551, p=0.015).

CONCLUSION

Coexisting SUD in patients undergoing lumbar spinal fusion increased the risk of adverse events. The development of a protocol focusing on patient-led care plans, adequate pain management, and identification of a support network may contribute to better clinical outcomes.

Racial and Ethnic Utilization Differences in Navigated Total Knee Arthroplasty (nTKA): Examining Overall Utilization and Length of Stay

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Racial disparities in medicine involve a complex interplay of implicit bias and structural inequities related to the social determinants of health resulting in minority groups having decreased health at baseline and access to care. With the emergence of these promising technological advances in knee arthroplasty, it is important to examine the equitability and outcomes of this technology in at-risk minority groups. Thus, the aim of this study was to examine racial and ethnic differences in the overall utilization of nTKA compared to TKA and to determine whether there is an association between patient race and length of stay following nTKA. Our hypothesis is that among patients undergoing TKA, African American and Hispanic patients would undergo navigation-assisted procedures at a decreased relative rate compared to Caucasian patients and would also be more likely to experience an extended length of stay following nTKA.

TABLE 1: Characteristics of Patients Undergoing nTKA and Conventional TKA

	nTKA, N=9,860		Conventional TKA, N=368,965		
Characteristics	**N (%)**	**Mean ± SD**	**N (%)**	**Mean ± SD**	**P value**
Age		66.6 ± 9.38		66.8 ± 9.39	P<0.001
Female	6,008 (61)		228,433 (62)		0.050
Hispanic Ethnicity	400 (4.2)		18,137 (5.1)		P<0.001
Smoker	762 (7.7)		29,990 (8.1)		0.151
Diabetes Mellitus	1,608 (16.27)		65,833 (18)		P<0.001
ASA Classification					
1 – No Disturbance	130 (1.3)		5,607 (1.5)		P<0.001
2 – Mild Disturbance	5,040 (51)		180,376 (49)		
3 – Severe Disturbance	4,571 (46)		177,445 (48)		
4 – Life Threatening	105 (1.1)		5,284 (1.4)		
None Assigned	14 (0.14)		237 (0.1)		
COPD	389 (4.0)		12,729 (3.5)		0.008
Congestive Heart Failure	27 (0.27)		1,093 (0.3)		0.686
Previous MI	0 (0)		7 (0.05)		0.571
Hypertension requiring medications	6,505 (66)		240,748 (65)		0.146

ASA, American Society of Anesthesiology; COPD, chronic obstructive pulmonary disease; MI, myocardial infarction

METHODS

Current procedural terminology codes were used to identify adult patients who underwent nTKA from 2015 - 2020 through the National Surgical Quality Improvement Program database. Patient race was categorized as Caucasian, African American (AA), American Indian/Alaskan Native (AI), and Asian. Ethnicity was categorized as Hispanic/non-Hispanic. To limit the influence of confounders

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in the analysis, patient comorbidities including a history of smoking, type II diabetes mellitus, COPD, CHF, MI, angina, transient ischemic attack, peripheral vascular disease, renal failure, or preoperative dialysis were controlled. Patient cohorts were established based on race, Hispanic ethnicity, ASA class, and gender. Patients were excluded if they had non-elective indications for nTKA such as trauma or malignancy. Patients undergoing conventional TKA without navigation were identified as a referent group for calculating incidence rate ratios (IRR). Poisson regression analysis determined incidence rate ratios (IRR) for nTKA:cTKA among minority groups with a Caucasian referent group. The upper 90th percentile of LOS defined patients with extended LOS. The impact of preoperative demographic and medical comorbidities on extended LOS was analyzed using univariate analysis and a multivariate regression model. Significance was set at $p<0.05$.

RESULTS

9,860 patients who underwent nTKA and 368,965 patients who underwent cTKA were included. Overall Prevalence of Navigation-assisted Total Knee Arthroplasty

AA, AI, and Hispanic patients all underwent nTKA at a decreased rate compared to Caucasian patients. AA patients underwent nTKA at an IRR of 0.69 compared to Caucasians (95% CI: 0.63-0.74). AI patients underwent nTKA at an IRR of 0.69 (95% CI: 0.52-0.4). Similarly, Hispanic patients underwent nTKA at a decreased rate compared to Caucasian patients (IRR 0.79, 95% CI 0.72 – 0.88) (Table 2).

TABLE 2: Relative Incidence of nTKA compared to TKA Among Racial and Ethnic Groups

Racial/Ethnic Group	IRR	95% CI
American Indian or Alaska Native	0.69	0.52 – 0.94
Asian	0.86	0.75 – 0.98
Black or African American	0.69	0.63 – 0.74
Hispanic	0.79	0.72 – 0.88

EXTENDED LENGTH OF STAY

Even after controlling for demographics and medical comorbidities, AA patients undergoing nTKA had 1.6 times greater odds of extended LOS (OR 1.6, 95% CI: 1.3-2.0). Similarly, Hispanic patients had 1.5 times greater odds of having extended LOS (95% CI: 1.1-1.9) (Table 3).

CONCLUSION

Among patients undergoing TKA Patients who identify as AA, AI, or Hispanic undergo TKA with navigation assistance at a lesser rate compared to Caucasian patients. Of patients who do undergo nTKA, AA, AI, and Hispanic patients have greater odds of experiencing extended length of stay compared to patients who identify as White. Future research investigating the interplay of race, ethnicity, and social determinants of health should be done to better understand factors influencing extended length of stay following navigated orthopedic procedures and to improve the management of these patients.

The Effects of Attention Deficit Hyperactivity Disorder and Other Psychiatric Comorbidities to Outcomes in Trauma Patients

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Individuals with psychiatric illnesses face higher rates of adverse outcomes in trauma compared to the general population.[1] Studies have examined the relationship between depression, schizophrenia, post-traumatic stress disorder, and other mental disorders with trauma, yet few have examined attention-deficit-hyperactivity disorder (ADHD).[2] ADHD has been suggested to increase the risk of injury, due to a hypothesized inability of patients with ADHD to inhibit their behavioral responses in certain situations.[3] However, the severity and outcomes of injury in trauma patients with ADHD have not been frequently studied. Our study aims to analyze the demographics and traumatic injury characteristics and outcomes of patients with ADHD, while also examining the effects of additional psychiatric comorbidities with ADHD in relation to injury mechanism, severity, and outcome.

TABLE 1: Comparison of ADHD patient demographics to non-ADHD patients

Patient Characteristics	ADHD (n = 73)	Non-ADHD (n = 73)	P-value
Age, median (IQR)	25 (22, 35)	26 (22, 34)	1.00
Sex, n (%)			
Male	48 (65.75%)	48 (65.75%)	1.00
Female	25 (34.25%)	25 (34.25%)	
Race/Ethnicity, n (%)			
White	40 (54.79%)	17 (23.29%)	< 0.01
Black	24 (32.88%)	45 (61.64%)	
Asian	0 (0%)	2 (2.74%)	
Other	9 (12.33%)	9 (12.33%)	
Comorbidity, n (%)			
Dementia	0 (0%)	0 (0%)	(n/a)
Psychiatric	43 (58.90%)	8 (10.96%)	< 0.01
HTN	5 (6.85%)	3 (4.11%)	0.72
DM	3 (4.11%)	4 (5.48%)	1.00
Alcoholism	6 (8.22%)	6 (8.22%)	1.00
Smoker	19 (26.03%)	10 (13.70%)	0.10
COPD	1 (1.37%)	1 (1.37%)	1.00
ISS, median (IQR)	5 (2, 13.5)	4 (1, 8)	< 0.01
GCS, median (IQR)	15 (15, 15)	15 (14.5, 15)	0.10
Hospital LOS (days) median (IQR)	2 (1, 5)	1 (0, 3)	< 0.01
ICU LOS (days), median (IQR)	0 (0, 2)	0 (0, 0)	0.05

ISS: Injury Severity Score; GCS: Glasgow Coma Scale; LOS: Length of Stay; ICU: Intensive Care Unit.

METHODS

A 5-year retrospective analysis was performed using the trauma registry of an urban American College of Surgeons verified level 1 trauma center. Patients with ADHD were separated into ADHD only and ADHD+ (having additional psychiatric comorbidities). These patients were compared to a matched population of patients without ADHD (non-ADHD) and patients with psychiatric disorders, but without ADHD, to analyze their demographics and outcomes. Descriptive statistics were used to analyze the data as appropriate.

RESULTS

Seventy-three patients with ADHD were identified, with 58.9% of the study population having additional psychiatric comorbidities (ADHD+). A majority of patients with ADHD

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were male (65.8%) in this study. At admission, non-ADHD patients had fewer psychiatric comorbidities (11%) compared to ADHD patients (58.9%). The ADHD cohort overall had a significantly higher median Injury Severity Score (ISS) than non-ADHD (5 vs. 4), and longer hospital lengths of stay (LOS) (2 days vs. 1 day) (Table 1). ADHD+ patients had longer hospital LOS compared to patients with ADHD Only (3 days vs. 1 day, p=0.02), but Glasgow Coma Score (GCS) (15 vs. 15, p=0.35) and ICU LOS (0 vs. 0, p=0.08) were not different between the two groups. In the regression analysis, ADHD+ patients had longer hospital LOS compared to patients with non-ADHD and ADHD Only (Table 2).

TABLE 2: Linear regressions to examine the associations of the outcome variables and the diagnoses of ADHD, psychiatric disorders, and both ADHD and psychiatric disorders

	Dependent variable							
	Hospital LOS		ICU LOS		GCS		ISS	
Explanatory variable	Coeff.	p-value	Coeff.	p-value	Coeff.	p-value	Coeff.	p-value
Non-ADHD and Non-PSYCHIATRIC DISORDER (reference)								
ADHD only	1.58	0.14	-0.06	0.89	1.18	0.06	3.34	0.07
PSYCHIATRIC DISORDER only	2.05	0.26	0.38	0.96	1.03	0.33	-1.50	0.62
ADHD+ PSYCHIATRIC disorder	2.98	< 0.01	1.26	< 0.01	0.14	0.80	3.49	0.03

DISCUSSION

Our study shows that young adults are more frequently diagnosed with ADHD than older adults, and that male patients are more commonly affected, in concordance with the existing literature.4 We found that hospitalized trauma patients with ADHD are more likely to have an additional psychiatric comorbidity (ADHD+) compared to trauma patients without ADHD (non-ADHD), also in concordance with the existing literature.5 While hospitalized trauma patients with ADHD have higher ISS compared to non-ADHD, there was no statistically significant difference in ISS between ADHD+ patients or ADHD Only. Patients with ADHD Only had higher ISS than non-ADHD patients, and ADHD+ patients had the highest ISS overall. This suggests that ADHD with or without other psychiatric comorbidity is associated with worsening injury severity in adult trauma patients. Additionally, trauma patients with ADHD had longer hospitalizations than those without ADHD, and the presence of an additional psychiatric comorbidity increased the hospital length of stay to a greater extent.

CONCLUSION

Hospitalized trauma patients with ADHD have more psychiatric comorbidities and worse outcomes than non-ADHD patients. Patients with ADHD with or without additional psychiatric comorbidities are at risk for worse outcomes in trauma care compared to non-ADHD patients, despite similar GCS and ISS. Patients with ADHD+ in trauma have the greatest risk for worse outcomes in trauma and may require greater attention and resources.

Patients with ADHD with or without additional psychiatric comorbidities are at risk for worse outcomes in trauma care compared to non-ADHD patients, despite similar GCS and ISS.

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The Link Between COVID-19 and Glomerulonephritis: A Systematic Review

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Since its first reported case of human infection in China in December 2019, severe acute respiratory coronavirus 2 (SARS-CoV-2) has spread throughout nearly every major country in the world.[1] Although COVID-19, the disease caused by SARS-CoV-2, is most often characterized as a respiratory pathology, kidney involvement during SARS-CoV-2 infection and immunization is also extensively reported. Among patients hospitalized with COVID-19, reported incidence of protein and blood in the urine is upwards of 43.9% and 26.7%, respectively.[2] Glomerulonephritis, inflammation of glomeruli within the kidney's nephrons, is one of the renal complications associated with COVID-19. However, the precise nature of this association has yet to be fully understood. This study is a systematic review of the current literature with the goal of ascertaining which forms of glomerulonephritis are most commonly associated with SARS-CoV-2 as well as the underlying mechanisms driving such kidney injury.

METHODS

Relevant literature included clinical studies, case reports, and case series, which the two authors independently screened by title, abstract, and full text. Literature searches were primarily performed via PubMed and Google Scholar, and search results were reviewed and agreed upon by the two authors. Non-English articles were not evaluated in the searches. Data were collected on each article, including comorbidities, clinical features, laboratory tests and serology, kidney pathology, disease course, and complications. The number of cases in which glomerulonephritis had a temporal association with SARS-CoV-2 were tallied. Each patient case was broadly categorized by whether the glomerulonephritis followed infection versus immunization of SARS-CoV-2, and whether the patient presentation was acute versus a relapsed flare of underlying glomerulonephritis.

RESULTS

Nine forms of glomerulonephritis were assessed for their potential relationship with COVID disease and vaccination. These included both glomerulopathies driven by immune complex deposition and those driven by cytokine-mediated damage. Focal segmental glomerulosclerosis (FSGS), particularly the collapsing morphology, was found to have the greatest overall number of reported associations with COVID-19, whereas membranoproliferative glomerulonephritis (MPGN) was found to have the fewest number of associated cases (Figure 1).

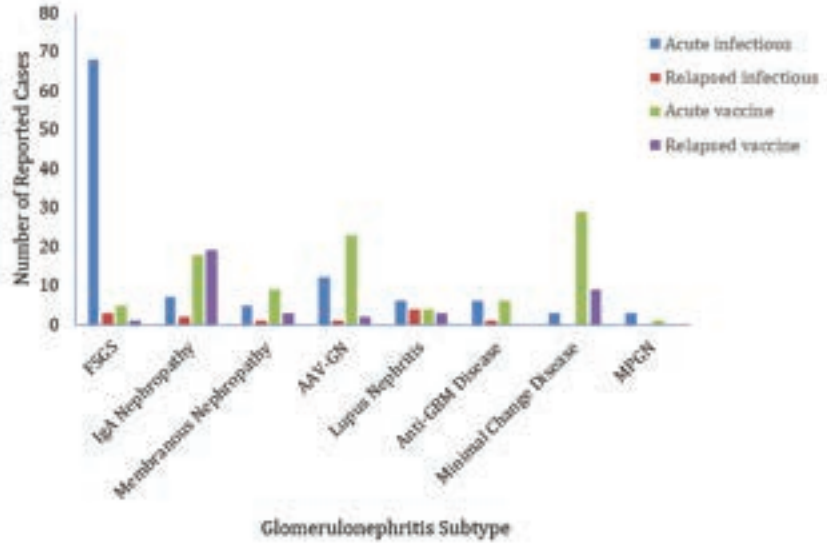

FIGURE 1: Mean reported cases of nephropathies associated with COVID-19. FSGS = Focal segmental glomerulosclerosis, AAV-GN = Autoimmune-associated vasculitis with glomerulonephritis, Anti-GBM Disease = Anti-glomerular basement membrane disease, MPGN = membranoproliferative glomerulonephritis.

DISCUSSION

Overall, the literature indicates that a cytokine storm, which may or may not be accompanied by immune complex deposition, is the most consistently prevalent mechanism underlying tissue inflammation in COVID-associated

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glomerulonephritis. Specifically, SARS-CoV-2 infection or immunization likely induces a robust CD4+ T cell upregulation, with a prominence of Th1 subtype.[3] The cytokine storm that ensues involves NF-kB and STAT3 activation, resulting in an IL-6 amplifier feedback loop that is further enhanced by interactions with the renin-angiotensin-aldosterone system (RAAS) and complement pathways.[4,5] Upregulated pathways involving these inflammatory mediators likely contribute to glomerular inflammation and damage, both via direct cytotoxicity and stimulation of polyclonal immunoglobulin. Thus, continued attention toward these cytokine pathways may prove fruitful in furthering our understanding of COVID-19 pathophysiology and treatment.

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Utilization of Provider Education with Electronic Medical Record and Web-Based Tools to Improve Diet and Activity Counseling in Primary Care, a Clinical Quality Improvement Initiative for the Management of Diet Related Chronic Disease

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Pediatric obesity has rapidly grown in prevalence in the United States, reaching 19.7% in recent reports.1 Despite obesity being recognized as a disease, it is often treated as a personal responsibility rather than a clinical diagnosis with specific management guidelines.[1]

OBJECTIVES

Our study aimed to improve clinician counseling and coding for physical activity and nutrition by at least 20% using electronic health records and web based tools.

DESIGN/METHODS

A 2019 needs assessment of primary care pediatricians in Washington, DC showed disparities between recommendations on pediatric obesity management and realities of clinical practice.1 Our team then employed a multidisciplinary quality improvement initiative to align management practices with existing guidelines, which involved automating nutrition and physical activity counseling International Classification of Diseases (ICD) codes in electronic health record (EHR) templates, holding monthly educational sessions for providers on counseling and coding, and monthly coaching sessions on management of obesity. A monthly Plan-Do-Study-Act cycle was used to assess effectiveness of interventions. This quality improvement (QI) study involved 12-month baseline data collection at two academic community health centers in Washington, DC, then data collection for 12 months during the QI period and 6 months after.

RESULTS

After educational intervention, specifically on coding of nutrition and physical activity ICD documentation, both sites improved documentation to incorporate correct codes within 15% of charts. However, after implementation of EHR automation in March of 2022, providers were able to improve and sustain documentation of physical activity and nutrition counseling coding to 75% of all charts reviewed.

CONCLUSIONS

These observed improvements support that while educational sessions and resources are beneficial tools for changing provider behaviors, EHR automation serves as a more effective management approach to optimize billing and coding behaviors for improved management of diet-related chronic diseases. These findings support the automation of systems as a sustainable way to transform provider behaviors to improve quality of care.

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