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WMJ

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Dean Nita Ahuja, MD, MBA: Wisconsin's opportunity to become a beacon for the nation in advancing health

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COVER ART

Human Heart

Emily Kammerud

8x10, Poured Acrylic on Canvas-board, 2023

Artist Statement:

Powerhouse of the human body, the heart pumps nearly 2000 gallons of blood throughout the body each day providing oxygen and the nutrients the body needs to function.

See page 502 for information about the artist.

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The mission of *WMJ* is to provide an opportunity to publish original research, case reports, review articles, and essays about current medical and public health issues. *WMJ* is published through a partnership between the Medical College of Wisconsin and the University of Wisconsin School of Medicine and Public Health.

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Vimkunya – Hope Against Chikungunya: Science, Safety, and Access

To the Editor:

Chikungunya virus (CHIKV) is a mosquito-borne alphavirus that originated over 500 years ago in Africa and was later introduced to Asia. It is contracted from the bite of a female mosquito of the *Aedes* species, particularly *Aedes aegypti* and *Aedes albopictus*,[1] and is endemic in regions of Africa, Asia, and the Americas. Vertical transmission – the transmission of a disease from a pregnant individual to the fetus – is rare. While 3% to 28% of the cases are asymptomatic,[1] symptoms are typically characterized by sudden fever associated with joint pain, headache, and skin rash. Among the infected, a significant proportion may experience severe muscle pain and long-lasting joint pain that can persist in the chronic phase of the disease.[2]

Until the development of Vimkunya, a chikungunya virus virus-like particle (VLP) vaccine, patients who contracted CHIKV were treated primarily with anti0inflammatory medications aimed at symptom relief.[1] However, the development of Vimkunya – the second vaccine approved by the US Food and Drug Administration (FD) for CHIKV – offers a preventive intervention through induction of a seroprotective antibody response.[3]

Vimkunya is a novel adjuvanted recombinant vaccine containing CHIKV virus-like particles adsorbed onto aluminum hydroxide. The virus-like particles consist of envelope proteins E1 and E2 and CHIKV capsid protein (C), which are derived from the CHIKV Senegal strain 37997.[3] The vaccine triggers the production of neutralizing antibodies as early as 22 days after vaccination, with immunity sustained up to 183 days, offering robust protection against CHIKV disease.[3] Approved on February 14, 2025, under the FDA's accelerated approval pathway, the vaccine is indicated for individuals aged 12 years and older and is administered as a single 0.8-mL intramuscular dose.[4]

Prior to approval, 2 pivotal clinical trials evaluated the vaccine's immunogenicity: one registered as NCT05072080, enrolling 3258 individuals aged 12 to 64, and registered as NCT05349617, enrolling 413 participants aged 65 years and older in the United States. Because these trials were conducted outside endemic regions, they assessed immunogenicity rather than clinical efficacy, using neutralizing antibody titers as the primary endpoint. High geometric mean titers and seroresponse rates demonstrated a strong immune response in both studies.[4] The FDA's accelerated approval was based on these antibody levels, and the indication will remain valid until August 31, 2030, unless confirmatory trials demonstrate additional clinical benefit – such as improved immune response and tolerability.[4]

In the NCT05072080 trial, a single dose of Vimkunya induced a robust immune response, with 97.8% of participants achieving protective antibody levels within 24 days.[5] Although true clinical efficacy could not be measured in a non-endemic setting, this high seroconversion rate suggests the vaccine is likely to reduce infection risk once deployed in endemic areas. The vaccine was generally well tolerated, with common side effects including headache, fatigue, muscle and joint pain, and fever – most of which were mild to moderate and resolved within a few days. Importantly, no severe adverse events were reported, reinforcing Vimkunya's favorable safety profile and acceptable risk-benefit ratio.[3,6] As a recently approved CHIKV vaccine, Vimkunya represents a critical advancement in combating this debilitating mosquito-borne disease.

Vimkunya is particularly important for people living in regions where mosquito-borne diseases are common, including parts of Asia, Africa, and Latin America. While CHIKV is not currently causing widespread hospital strain in these regions, populations remain at high risk of infection. This is supported by recent Centers for Disease Control and Prevention surveillance data, which document the continued presence and geographic spread of CHIKV.[7] However, making the vaccine widely accessible remains a challenge due to the high costs and limited supply in low- and middle-income countries. Future studies should examine the duration of immunity and evaluate whether it could be incorporated into routine vaccination programs. Although this vaccine represents a major step forward in addressing mosquito-borne diseases, expanded funding and global distribution support are essential to ensure equitable access and to help control future outbreaks.

—Muhammad Affan Abid, MBBS; Ashmat Naqvi, MBBS; Muhammad Taha Kamal, MBBS; Muhammad Ali Kamal, MBBS

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WMJ

CALL FOR PAPERS & REVIEWERS

Since 1903, the *Wisconsin Medical Journal*—*WMJ* (ISSN 2379-3961)—has served as a forum for professional communication and continuing education for physicians and other health professionals. This tradition continues today, but with a broader focus that extends across the country and even around the world.

Published six times per year through a partnership between the Medical College of Wisconsin and the University of Wisconsin School of Medicine and Public Health, *WMJ* is a peer-reviewed, indexed scientific journal available electronically—free, full text online and through PubMed.

WMJ invites original research, case reports, review articles, brief reports, essays and letters to the editor about current medical and public health issues.

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Fahad Aziz, MD, FASN

A Season of Gratitude: Honoring the Community That Sustains Us

Fahad Aziz, MD, FASN, *WMJ* Editor-in-Chief

"Gratitude is not only the greatest of virtues, but the parent of all the others." — *Cicero*

Every year, the holiday season gives us a chance to pause. To breathe. To remember what truly matters. In the middle of our deadlines, clinics, call schedules, meetings, and the steady flow of manuscripts, this time of year gently nudges us to look up from the day-to-day work and acknowledge the people who make all this possible. Gratitude has a way of settling us. It reminds us why we do this work in the first place.

For the *Wisconsin Medical Journal* (*WMJ*), this moment of reflection carries special meaning. The past several years have brought tremendous change – more than any of us could have imagined when we first began this journey. Our submissions have grown by more than 100%, and the reach of the journal has expanded far beyond the Wisconsin's borders. That kind of growth doesn't happen on its own. It happens because people believe in the mission of this journal and choose to invest their time, their work, and their trust.

Together, we have produced special issues that captured important moments and needs in our community—from lessons learned from the COVID-19 pandemic to maternal and child health. And now we are preparing for an issue on medical education, a topic that feels especially timely and meaningful for Wisconsin's medical community.

> During this holiday season, my hope is that each of us can find a quiet moment – somewhere between the deadlines, the patients, the travel, and the celebrations – to truly feel the warmth of gratitude.

When I look at these milestones, I see more than numbers or completed projects. I see the collaboration, conversations, and collective effort behind them. The growth of *WMJ* reflects something deeper: a shared belief that scholarship matters, that local voices deserve a platform, and that through this work we can improve the health of the people we serve.

WMJ's progress has been possible because of the steady support of our academic institutions. We remain deeply grateful to both the University of Wisconsin School of Medicine and Public Health and the Medical College of Wisconsin. This partnership began with the visionary leadership of Dean Robert Golden, MD, Dean Joseph Kerschner, MD, and MCW President John Raymond, MD, who understood that a statewide journal thrives only when the medical schools stand behind it. Today, that torch is carried forward by Dean Nita Ahuja, MD (UW School of Medicine and Public Health) and Dean Deborah Costakos, MD (MCW), whose guidance, encouragement, and belief in the journal's mission have allowed *WMJ* to continue growing. Their support is not just organizational—it is personal, steady, and deeply appreciated.

Our Publishing Board remains one of our greatest strengths. Jonathan Temte, MD, PhD, Elizabeth Petty, MD, and Robyn Perrin, PhD, from the School of Medicine and Public Health; Asriani Chiu, MD, Andrew Petroll, MD, MS, and Sara Wilkins, MA, MPA, from MCW; and Abdul Khan, MD, representing the Medical Society of Wisconsin, have been the quiet architects behind our policies, processes, and strategic direction. They bring wisdom, steadiness, and a profound commitment to elevating the journal. Their influence is woven into every issue we publish.

We are fortunate as well to be guided by an exceptional Editorial Board—leaders from our medical schools and health systems across

• • •

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Wisconsin. In a world where information moves quickly and attention is scarce, their expertise helps ensure that *WMJ* remains relevant, rigorous, and resilient.

The journal is also stronger because of our partnership with the team at Ebling Library. From indexing to confirming each manuscript's references prior to publication and providing guidance on myriad issues in the world of academic publishing, their contributions are immeasurable.

This past year has marked transitions that speak to the strength of our editorial community. Robert Treat, PhD, our former deputy editor, provided six years of service that helped modernize our processes and strengthen the journal's foundation. Now, Sanjay Bhandari, MD, and Shanthi Narla, MD, our newly appointed deputy editors, bring a renewed energy and vision that is already expanding what *WMJ* can be.

Our current editorial fellows – Victoria Ronin, MD, Raul Rodriguez, MD, Apurva Popat, MD, and Jiajie Yan, PhD – represent the promise of the future. Their curiosity, creativity, and commitment have brought a fresh vibrancy to *WMJ*. They are learning from us, but we are also learning from them.

To our authors – you are the heart and soul of this journal. Every manuscript you send represents hours of effort, reflection, and the courage to share your work with the world. You turn observations from clinics, labs, classrooms, and communities into knowledge that can change practice and improve lives. You are the storytellers of science, the ones who give meaning to data and help us better understand the world around us.

We know you have many choices about where to submit your work, and it is never a small decision. When you choose *WMJ*, you place your trust in us – trust that your research will be handled with care, evaluated with fairness, and shared with the audiences who need it most. For that trust, we are profoundly grateful. Your discoveries, your questions, and your insights are what bring these pages to life. You give this journal its purpose.

And to our reviewers: your generosity is the steady heartbeat that keeps this journal strong. Much of what you do is invisible to the broader community, but we see it – the late-night reviews, the thoughtful comments, the careful attention to accuracy and clarity. You give not because you must, but because you care deeply about the quality of scholarship in our state. You believe in lifting others up, in strengthening their work, and in upholding the standards that make *WMJ* worthy of the trust our readers place in it.

Your dedication ensures that each article is clearer, stronger, and more meaningful than when it first arrived. You shape the integrity of this journal in ways that can't be quantified but are felt in every issue we publish. For your time, your expertise, and your unwavering commitment, we are truly thankful.

Finally, no expression of gratitude would be complete without recognizing Kendi Neff-Parvin, our remarkable managing editor. So much of what she does happens quietly, without spotlight or recognition, yet every issue of this journal carries her fingerprints. Her calm leadership, her ability to navigate challenges with grace, and her unwavering dedication – even on the days when deadlines collide and the unexpected happens – are what keep *WMJ* moving forward. She is the person who holds the threads together, who makes sure the work gets done, and who cares deeply about the quality and integrity of every page we publish. The truth is simple: this journal is possible because of her, and I am profoundly grateful for all she brings to *WMJ*.

And to our readers across Wisconsin and beyond – we are deeply grateful for you. Everything we do, every issue we assemble, every article we refine, is ultimately for the people who open these pages with curiosity and purpose. You are the reason this journal exists. Whether you read *WMJ* to stay informed, to challenge your thinking, to learn from colleagues across the state, or simply to stay connected to Wisconsin's medical community, your engagement gives this work meaning. Your continued interest reminds us that the impact of this journal extends further than we ever imagined. We know how busy your days are – patients to see, notes to finish, families to care for, research to pursue – and yet you still make time to read, to reflect, and to grow. Your trust in the journal sustains us; your feedback sharpens us; and your presence reminds us that our efforts matter. When we think about why we do this work, we think of you – our readers who carry the knowledge forward into clinics, classrooms, laboratories, and communities. For all of that, we are sincerely and profoundly thankful.

During this holiday season, my hope is that each of us can find a quiet moment – somewhere between the deadlines, the patients, the travel, and the celebrations – to truly feel the warmth of gratitude. We move fast in medicine; we rarely stop long enough to take in the good that surrounds us. But when I look at this journal, at the people who pour their time and heart into it, I am reminded that *WMJ* is far more than pages and publications. It is a community. A family of clinicians, scientists, educators, and learners who share a belief that knowledge – honestly created and generously shared – can make a difference.

Thank you for being part of that family, for lifting this journal forward, and for reminding us of what is possible when people choose to work together with purpose.

Wishing you peace, joy, and a season filled with gratitude – and the grace to pause long enough to feel it.

Navigating the Haze: Delivering Patient-Wanted Care Amidst the Uncertainty of Medical Cannabis

Michael Chen, MD

The air was crisp, the clouds reflecting a fiery glow from the rising sun as the chairlift carried me up the silent mountain. At the summit, I assessed the empty slope below. As a ski racer, I started training at dawn, long before the lifts opened to the public. Each of my thousands of runs a season was a lesson in rapid assessment and adaptation. Some days, a dense fog would settle on the mountain, obscuring the path and demanding absolute trust in my preparation and instincts. This is the art of navigating uncertainty, a skill I learned on the slopes that I now apply daily in family medicine – a field defined by incomplete information and the profound responsibility of guiding others.

This uncertainty is certainly palpable when it comes to medical cannabis. I served on Utah's Medical Cannabis Compassionate Use Board, where I witnessed this landscape up close. The Compassionate Use Board was created to navigate the uncertainty around medical cannabis and operates on a case-by-case basis, reviewing petitions for patients whose conditions are not explicitly listed by law but who may still benefit from its use. This process, guided by seven clinicians from different specialties, acknowledges that rigid guidelines are insufficient when evidence is limited and that a deliberate, individualized approach is necessary. This work has highlighted the central tension physicians face: patient-reported benefits often coexist with a lack of definitive clinical trial data.

This seeming contradiction poses a fundamental challenge to our daily clinical practice. In an age where patients often arrive with their own information from varied and sometimes unreliable online sources, it is no longer enough to be "patient centered." As Dr Singh points out in his narrative, we must strive for a "patient-wanted" approach.[1] And when evidence is hazy – as it is with medical cannabis – our ability to build this relationship is paramount.

First, we must practice with intellectual humility and embrace the **patient as an expert**. This approach echoes Sir William Osler's timeless advice: "Listen to your patient, he is telling you the diagnosis." In the context of medical cannabis, the "diagnosis" is not just a disease label but a deeper understanding of the patient's suffering and what might alleviate it. My experience has shown that many patients turn to medical cannabis after exhausting conventional treatments, and they possess a deep, experiential knowledge of their condition that sometimes has not been "heard" by their clinicians. Truly listening to and valuing this expertise transforms the clinical encounter from a top-down directive into a mutual exchange, building the trust required to be a "patient-wanted" physician.

Second, this humility leads directly to **shared decision-making.** The goal is not to provide a simple "yes" or "no" but to facilitate a collaborative conversation. This involves transparently discussing the limits of our knowledge. The clinician's role is to discuss potential benefits – such as improved quality of life – alongside the known risks, lack of evidence, and practical barriers, such as cost and legal issues. Trust is built through this collaborative process. Eliciting the patient's goals and co-creating a plan that integrates both the evidence and the patient's expertise is central to patient-wanted care.

Third, **harm reduction** can be a primary goal. Given that patients may seek out cannabis regardless of our approval, our role is to help them do it as safely as possible. An open, nonjudgmental dialogue about harm reduction encourages honest disclosure from our patients, which is essential for comprehensive and safe care. Patients often value our professional guidance, and our ability to provide it makes us "patient-wanted" clinicians.

Medical cannabis serves as a powerful and timely case study for a timeless challenge in medicine. By embracing humility, shared decision-making, and harm reduction, we do more than just manage a difficult clinical scenario. We become the kind of compassionate and effective physicians that patients genuinely want and trust – especially when the path forward is hazy.

• • •

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Reclaiming Names, Establishing Identity: A Personal Journey in Medicine

Ankit Choudhury, BA; Sagar S. Matharu, BS

We are both Indian American medical students with culturally distinct names – Ankit and Sagar. Through our experiences, we hope to spotlight the profound impact one's name has in shaping perceptions in medicine.

Ankit grew up in the Midwest, and his name was rarely pronounced as his parents intended. To ease interactions, he introduced himself as "Ann-kit," instead of the correct, "Ahn-kith." This alteration minimized discomfort--both his and others'. However, when he entered college and was exposed to a more diverse and culturally aware community, he gained the confidence to embrace a pronunciation closer to its true form: "Ahn-kit." It's a little closer, but not quite correct, and he was still hesitant to share the authentic pronunciation of his name except with those who shared his cultural heritage.

Similar to Ankit, Sagar tends to introduce himself this way: "Sagar, but it's like Soccer with a G." While it may be tongue-in-cheek, it serves as a preemptive strike against inevitable mispronunciations, as in this example:

"Where are you from, 'Cigar'? the patient asks, head tilted in curiosity.

• • •

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"Maryland," responds Sagar with a practiced smile.

"Oh." The patient hesitates, slightly nodding his head, "Where are you really from?"

A bit taken aback – even though he has heard this before – Sagar replies, "Oh right, my family is from India," trying to maintain a stiffened smile.

Moments like these are not new for us. Our names, unfamiliar to many, often function as a signal, prompting assumptions about our background before we have the chance to define ourselves. Names carry immense significance: they are the quintessential marker of who you are. For us, introducing ourselves has always been a lifelong balancing act. These subtle, yet impactful, moments of identity negotiation have shaped our interpersonal dynamics and professional experiences, highlighting how deeply ingrained perceptions influence interactions in medicine.

In medical school, we often find ourselves weighing the desire for proper pronunciation of our names against the fear of bringing too much attention to ourselves. Introducing ourselves in clinical or academic settings involves an unspoken calculation: is it worth the time and discomfort to ensure a proper pronunciation of our names? Or does correcting someone detract from the task at hand?

Names can also serve as bridges, connecting us to others in profound ways. Before medical school, Ankit worked as a medical assistant at a gastroenterology clinic in Missouri. One patient, noticing his nametag, asked, "Are you Indian?" Their shared heritage led to a warm conversation about a familiar cultural experience. Such moments of bonding, while brief, bridge a gap of understanding that allows the patient to feel seen and heard in a way that extends beyond the standard provider-patient relationship.

Ankit previously worked with a physician who was an immigrant from India and who often tailored care to reflect cultural nuances. For instance, he encouraged providing modified colonoscopy prep instructions to include dietary swaps familiar to Indian cultures, ensuring adherence without disrupting cultural norms. This is a poignant reminder that diversity in medicine enriches care by fostering authentic empathy alongside cultural competency.

Diversity is a systemic necessity, enriching health care by reflecting the communities it serves. When patients see their identities mirrored in their providers, it fosters trust and improves care[1-3] Embracing our identities as Indian Americans has become a source of strength, informing our interactions with patients.

Diversity in medical education is not just an abstract ideal; it is a practical necessity. A diverse learning environment enriches the educational experience, equipping future physicians to provide culturally sensitive care. Yet, the system often overlooks the nuances of identity. While medical education celebrates diversity on paper, it rarely addresses the practical challenges that come with it. How do

Table. Strategies for Integrating Diversity and Cultural Competency in Medical Education

Setting	Strategy	Description	Source
Classroom	Inclusive curriculum design	Incorporate case studies and materials that reflect diverse populations, ensuring representation of various cultural identities and to foster an environment of belonging.	Luke[4]
Classroom	Diversity-focused student subgroups	Support the implementation of student subgroups focused on diversity and inclusion, providing platforms for underrepresented students to share experiences and advocate for inclusive practices. Participation in these groups are important to students and enhance a supportive learning environment.	Ludwig et al[6]
Classroom	Diversity awareness training with visual reflection tools	Utilize visual reflection tools to encourage self-awareness, exploration of personal biases and reflexivity in managing patient diversity. These tools create a safe space for discussing identity, bias, and communicationchallenges.	Ang et al[7]
Clinical	Cultural competence OSCEs	Develop OSCE stations that emphasize cross-cultural communication skills, allowing students to practice and be evaluated on their ability to navigate culturally sensitive scenarios. This hands-on approach enhances readiness for real-world diverse patient interactions.	Green et al[9]
Classroom and clinical	Implicit bias recognition	Implement a framework that aids medical students in recognizing and addressing implicit biases in clinical scenarios, ensuring fair and equitable treatment of all patients.	Chao et al[5]
Classroom and clinical	Cultural competence model	Apply models such as the Purnell Model for Cultural Competence to guide healthcare practitioners in understanding how cultural factors influence health behaviors, treatment adherence, and communication styles.	Purnell[10]
Institutional	Mentorship programs with diverse faculty	Establish mentorship initiatives connecting students underrepresented in medicine with faculty from diverse backgrounds. Such relationships provide guidance, support, and role modeling, aiding professional development and reinforcing the value of diversity within medicine.	Bonifacino et al[8]

we foster inclusivity when names are mispronounced, cultural differences are misunderstood, or identities are reduced to stereotypes?

Fostering inclusivity in medicine starts with integrating diverse realities into medical curriculum. Case studies reflecting cultural nuances and open dialogues about identities, bias, and health beliefs cultivate understanding and cultural humility.[4] Workshops on implicit bias and structured discussions about identity in clinical practice equip future physicians with empathy and sensitivity.[5-7]

Beyond the classroom, medical institutions can support mentorship programs that connect underrepresented students with role models who share their backgrounds.[8] Representation matters not only for the aspiring physician, but also for the patients we serve. A diverse physician workforce allows the diverse patient population to feel seen, understood, and represented during their most vulnerable moments. *(The Table provides an overview of several evidence-based strategies.)*

Identity in medicine weaves into a larger tapestry, bridging gaps in understanding and building trust with communities. This trust is vital in addressing health disparities, fostering patient compliance, and ensuring equitable care. The richness of diversity is a strength, not just for individuals navigating the complexities of medical education but for the entire health care system striving to deliver compassionate and culturally sensitive care.

The patient's question, "Where are you really from?" isn't just about our origin; it is a reminder of how names often carry more than just phonetic weight. Reclaiming our names has been an act of reclaiming our identities, a refusal to let them be diminished or overlooked.

Names are more than identifiers. They are a bridge to understanding, offering opportunities to connect with others in ways that transcend language. In medicine, where connection and trust are paramount, acknowledging the importance of a name is not just politeness – it enhances the quality of care. When institutions create spaces where every name is valued, they send a powerful message: every identity matters.

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Association of Frailty Score and Surgical Site Infection After Open Lower Extremity Revascularization

Andrew Edsall, MD; Andrew J. Borgert, PhD; Alec Fitzsimmons, MPH; Irina Shakhnovich, MD

ABSTRACT

Introduction: Surgical site infection (SSI) after lower extremity procedures is a persistent source of significant morbidity for vascular surgery patients. Frailty scores capture risk factors for postoperative outcomes associated with SSI. This study aimed to retrospectively evaluate the association between SSI and a validated measure of frailty, the Vascular Quality Initiative-Risk Analysis Index (VQI-RAI).

Methods: A retrospective review was performed of patients who underwent open lower extremity revascularization at a single independent academic medical center from January 1, 2007, through December 31, 2019. Frailty score was calculated using VQI-RAI, a composite score based on patient demographic and clinical variables. VQI-RAI scores were compared between patients who developed SSI and those who did not. SSI outcomes were compared between patients defined as frail (VQI-RAI ≥ 35) and not frail (VQI-RAI < 35).

Results: The study population comprised 1130 patients. The overall SSI rate was 8.1%. The median VQI-RAI score was 29 for patients with SSI and 28 for patients without SSI ($P = 0.4$). No significant association was observed between VQI-RAI and SSI or between patients defined as frail and not frail. Of the individual components of the VQI-RAI score, only body mass index was significantly associated with SSI ($P < .0001$).

Conclusions: VQI-RAI frailty score was not associated with risk of SSI in our study population; however, body mass index was significantly associated with SSI. Obesity poses a high risk of SSI, whereas frailty alone may not be associated with an increased risk of SSI.

INTRODUCTION

Surgical site infection (SSI) poses a persistent challenge for vascular surgeons performing lower extremity procedures. The incidence of SSI after open lower extremity vascular surgery ranges from 5% to 32%.[1-2] Preoperative risk factors include diabetes, hypertension, smoking, dialysis, tissue loss, and obesity.[2-3] Strategies to address modifiable risk factors for SSI—such as antibiotic prophylaxis, preoperative showers, iodine-impregnated drapes, and negative pressure therapy—have been widely implemented.[1] Nevertheless, SSI rates remain elevated for lower extremity vascular surgeries relative to other procedures across surgical specialties.[4] These infections are associated with prolonged hospitalization, increased morbidity and mortality, and higher health care costs.[4]

Surgical frailty is a state of decreased physiologic reserve that predisposes patients to excess morbidity and mortality after surgery.[5,6] Frailty has been associated with longer hospitalization, higher 30-day readmission rates, and increased perioperative complications.[7,8] Historically, surgical frailty was assessed indirectly using metrics such as age and American Society of Anesthesiologists (ASA) physical status or subjectively using the "eyeball test" employed preoperatively by experienced surgeons.[7] More objective approaches have emerged, including using validated frailty models.[7] Two primary paradigms have been described: the phenotypic model, which focuses on physical manifestations such as sarcopenia, and the deficit accumulation model,[6] which assigns frailty based on current and past diagnoses.[9-10]

One widely employed frailty metric is the Risk Analysis Index (RAI) which, along with its vascular surgery–specific derivative Vascular Quality Initiative (VQI)-RAI, captures deficit accumulation across multiple domains.[8] VQI-RAI has been associated with outcomes related to abdominal aortic aneurysm repair.[11]

Although frailty has been linked to SSI in some circumstances, evidence is limited regarding its role in lower extremity SSI.[12] Therefore, we aimed to evaluate the utility of VQI-RAI in pre-

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dicting SSI among patients undergoing open lower extremity procedures.

METHODS

Institutional Review Board approval was obtained for this study. A retrospective review was conducted of electronic health records for all patients undergoing an open lower extremity procedure at a single independent academic medical center from January 1, 2007, through December 31, 2019. During the study period, vascular surgery services were provided predominantly by a team of 3 fellowship-trained vascular surgeons, with a small number of procedures performed by 2 general surgeons experienced in vascular surgical care. Percutaneous procedures (eg, endovascular aneurysm repair performed with percutaneous access and no open arterial exposure) were excluded from the analysis. The prespecified primary outcome was the incidence of SSI. Secondary outcomes were unplanned return to the operating room due to SSI and death within 30 days of surgery.

Preoperative frailty was evaluated using the VQI-RAI, a metric derived from the RAI, which uses American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) variables to predict postoperative morbidity and mortality.[5] Since its inception, the RAI has been cross-walked to Vascular Quality Initiative (VQI) variables to create the VQI-RAI.[8] The VQI-RAI is a composite score based on age, sex, body mass index (BMI), renal disease, congestive heart failure (CHF), dyspnea, living status, and functional status. For this study, frailty was defined as a VQI-RAI score ≥ 35, consistent with previous applications of the VQI-RAI.[11] The Wilcoxon rank sum test was used to compare the VQI-RAI scores between patients who developed SSI and those who did not. Chi-square and Fisher exact tests were used to compare SSI outcomes between patients defined as frail and not frail. Statistical significance was set at $P \leq .05$. All statistical analyses were performed using the SAS software, version 9.4 (SAS Institute Inc, Cary, North Carolina).

RESULTS

From January 1, 2007, through December 31, 2019, 1506 open lower extremity vascular surgery procedures were performed; 376 were excluded because of incomplete data. The remaining 1130 procedures were included in the analysis. Baseline study population demographics and clinical characteristics are shown in Table 1. The median age was 72 years. Women comprised 27.4% of the study population, and men comprised 72.6%. Participants with self-reported current smoking status accounted for 24.5% of the study population, 51.9% were former smokers, and 11.2% were never smokers. The median VQI-RAI score was 28 (range, 10-56). Fourteen percent of patients met criteria for frailty (VQI-RAI ≥ 35). Thirty-two percent of patients with VQI-RAI ≥ 35 had gangrene or ischemic ulcerations at the time of operation, compared with 15% of patients with VQI-RAI <35 ($P < .0001$) (Table 2). Hybrid procedures involving open arterial exposure for delivery of an arterial stent were the most common and accounted for 47.6% of the total. Femoral endarterectomy and lower extremity bypass accounted for 21.7% and 21% of procedures, respectively (Table 3).

Table 1. Baseline Patient Characteristics

Characteristic	Median (Range)[a]
Age	72 (29–99)
Body mass index (kg/m^2)	28.5 (12.6–58.7)
Sex, n (%)	
Female	310 (27.4)
Male	820 (72.6)
Preoperative creatinine (mg/dL)	0.97 (0.33–9.62}
VQI-RAI	28 (10–56)

Abbreviation: VQI-RAI, Vascular Quality Initiative-Risk Analysis Index.
[a]Data presented are median and range, unless otherwise specified.

Table 2. Preoperative Ulceration/Gangrene and Incidence of Surgical Site Infection by VQI-RAI Score

	Not Frail (VQI-RAI < 35) (n = 977)	Frail (VQI-RAI ≥ 35) (n = 153)
Preoperative ulceration/gangrene, n (%)		
Yes	147 (15.0)	49 (32.0)
No	830 (85.0)	104 (68.0)
Surgical site infection, n (%)		
Yes	75 (7.7)	16 (10.5)
No	902 (92.3)	137 (89.5)

Abbreviation: VQI-RAI, Vascular Quality Initiative-Risk Analysis Index.

Table 3. Number of Patients by Type of Vascular Surgery Procedure

Primary Procedure	No. of Patients (%)[a]
Hybrid – Open exposure for delivery of endovascular stent (aorta, iliac, femoral, popliteal)	537 (47.6)
Femoral endarterectomy	245 (21.7)
Lower extremity bypass, non-vein graft	137 (12.1)
Lower extremity bypass, vein graft	101 (8.9)
Lower extremity embolectomy	53 (4.7)
Other (groin exposure during open aortic surgery)	57 (5.0)

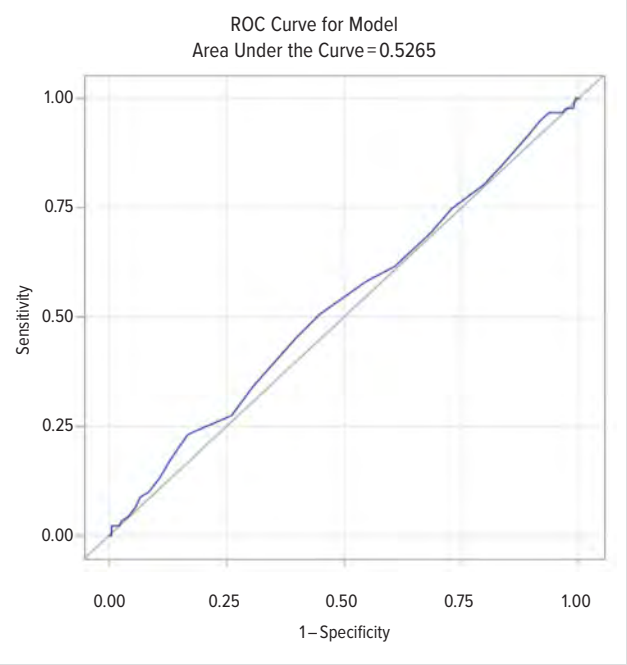
[a]Total does not equal 100% due to rounding.

Primary Outcome

Ninety-one of the 1130 patients (8.1%) developed at least 1 SSI. Among SSIs, 76.3% were classified as Superficial Incisional SSI, 17.2% as Deep Incisional SSI, and 6.5% as Organ/Space SSI. The incidence of SSI among frail patients was 10.5% compared with 7.7% among non-frail patients ($P = .31$) (Table 2). The median VQI-RAI score among patients who experienced SSI was 29, compared with a median of 28 for those who did not experience SSI ($P = .4$). The receiver operating characteristic (ROC) area under the curve for VQI-RAI association with SSI was 0.53 (Figure).

Associations between SSI and each individual component of

Figure. VQI-RAI Association With Surgical Site Infection



Abbreviation: VQI-RAI, Vascular Quality Initiative-Risk Analysis Index; ROC, receiver operating characteristic.

Table 4. Individual VQI-RAI Component Association With Surgical Site Infection

VQI-RAI Component	No SSI (n = 1039) n (%)[a]	SSI (n = 91) n (%)[a]	*P* value
Age, mean (SD)	70.9 (10.7)	70.3 (10.1)	.66
BMI (kg/m^2), mean (SD)	28.7 (5.9)	31.3 (6.2)	< .0001
Preop creatinine (mg/dL), mean (SD)	1.2 (0.9)	1.4 (1.3)	.36
Sex			
Female	281 (27.0)	29 (31.9)	.32
Male	758 (73.0)	62 (68.1)	
Requiring dialysis			
No	1002 (96.4)	86 (94.5)	.38
Yes	37 (3.6)	5 (5.5)	
Dyspnea			
No	223 (24.5)	19 (20.9)	.9
Yes	816 (78.5)	72 (79.1)	
Congestive heart failure within 30 days			
No	1029 (99.0)	89 (97.8)	.25
Yes	10 (1.0)	2 (2.2)	
Functional status			
Independent	955 (91.9)	80 (87.9)	.23
Partially dependent	78 (7.5)	11 (12.1)	
Totally dependent	6 (0.6)	0 (0.0)	
Transfer status			
Acute care hospital	14 (1.3)	1 (1.1)	.88
Directly from home	950 (91.4)	82 (90.1)	
Chronic care facility	22 (2.1)	2 (2.2)	
Other	52 (5.0)	6 (6.6)	
VA acute care hospital	1 (0.1)	0 (0.0)	

[a]Data presented are n (%) unless specified otherwise.
Abbreviations: VQI-RAI, Vascular Quality Initiative-Risk Analysis Index; preop, preoperative.

the VQI-RAI frailty score were independently assessed (Table 4). Of these, a statistically significant association was observed only between SSI and BMI, with a mean BMI of 31.3 kg/m^2 among patients with SSI compared with 28.7 kg/m^2 among those without SSI ($P < .0001$).

Secondary Outcomes

A total of 53 patients (4.7%) died within 30 days of surgery. These patients had a median VQI-RAI score of 29, compared with 28 for those who did not die within 30 days of surgery ($P = .03$). Thirty-six patients (3.2%) experienced SSI and unplanned return to the operating room; their median VQI-RAI score was 26, compared with a median score of 28 for those who did not have SSI and unplanned return to the OR ($P = .12$).

DISCUSSION

Our results should be interpreted within the context of the SSI and frailty score literature. The overall incidence of SSI observed in our study aligns with published estimates of SSI for lower extremity procedures.[1-2] Similarly, our finding of a significant association between BMI and SSI is consistent with previous work using the VQI database.[13] Finally, our finding that patients who died within 30 days of surgery had significantly higher frailty scores than those who did not die is consistent with extensive studies of frailty in both vascular and general surgery populations.[5,7]

Study population demographics (median age, 72 years; 27.4% female), as well as the median VQI-RAI score of 28 and overall frailty rate of 14%, are generally similar to those reported for patients undergoing open lower extremity vascular procedures nationally in studies using VQI data.[12] Similarly, the self-reported smoking prevalence of 24.5% mirrors the prevalence of smoking among patients with clinical peripheral artery disease (PAD).[14] While these findings support the comparability of our study population with the population of PAD patients more broadly, center-specific factors may limit such comparisons. In particular, our center is located in a urban area of the Upper Midwest with a population of fewer than 200 000 and serves a primarily rural referral region.[15] As such, regional trends in antibiotic resistance—particularly to gram-positive organisms—and associated infection-related outcomes may differ from other regions in the United States and abroad.[16] Moreover, the predominantly rural patient population served by our center may experience different outcomes than populations with a greater proportion of urban and suburban residents.[17]

The primary motivation for this study was to further elucidate causes of persistently high SSI rates among patients undergoing lower extremity revascularization. During the study period, interventions were implemented at our institution to reduce SSI rates, including patient education, preoperative scrub and normothermia protocols, and standardized protocols among all vascular surgeons. After reviewing operative cultures following SSI, antibiotic

prophylaxis coverage was broadened to include anaerobic flora. Postoperative dressings included silver-impregnated and incisional negative pressure dressings. In addition, muscle flaps were performed for selected high-risk patients, including those with reoperative groins and obesity. Despite these efforts, no significant decrease in SSI rates was observed.

Our study also found that frail patients were significantly more likely to have gangrene/ischemic ulceration present at the time of surgery, yet they were no more likely to experience SSI than nonfrail patients. This suggests that frail patients have a higher incidence of tissue ischemia at presentation, and that spread of preexisting infection may be effectively mitigated through current infection control measures.

In finding no significant association between frailty score and SSI, our results diverge from earlier published work. In contrast, 1 prior VQI-based study demonstrated a significant association between frailty score and SSI after infra-inguinal bypass.[12] That study also found a significant association between frailty and unplanned return to the operating room attributable to SSI.[12] However, differences in study design may limit comparability. First, our study included a large proportion of hybrid procedures and femoral endarterectomies, in addition to lower extremity bypass procedures. Moreover, we did not differentiate between patients who experienced an unplanned return to the operating room with SSI and those who underwent re-operation for SSI, as opposed to another indication, such as proximal amputation.

The limitations of our study relate primarily to our single-center, nonrandomized sample. All patients underwent open procedures, which may have produced a study population significantly different from the general vascular surgery population. Open procedures – particularly open arterial exposures for endovascular access – may have been selected over percutaneous approaches based on preoperative surgeon assessment of each patient's morbidity and mortality risk. Patients with higher frailty scores may have undergone percutaneous procedures and thus been excluded, potentially confounding the relationship between frailty and SSA. Surgeon decision making may represent an additional confounder: when highly frail patients underwent open procedures, intra-operative choices – such as incision location and size – may have been influenced by awareness of frailty. However, this may not threaten external validity, as similar considerations likely apply to procedure selection in the broader vascular surgery population. Our results may therefore provide pragmatic insights into patients who undergo open revascularization procedures.

CONCLUSIONS

Frailty, as measured by VQI-RAI score, was not significantly associated with SSI in patients undergoing open lower extremity revascularization. VQI-RAI score was significantly associated with death within 30 days of surgery. Given prior evidence supporting VQI-RAI as a robust measure of surgical frailty, these findings do not necessarily indicate a need for a more sensitive frailty model; rather, investigation of specific pathophysiologic drivers of SSI – such as BMI – may be a more fruitful approach to estimating SSI risk preoperatively. Such work will undoubtedly be challenged by the non-modifiability of risk factors, such as BMI, in the context of urgent or emergent procedures. However, better understanding of the mechanisms underlying these associations may help inform strategies to mitigate, if not eliminate, their impact.

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Area Socioeconomic Status and Early Onset Rectal Cancer in a Comprehensive Cancer Center: Evidence from Wisconsin

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ABSTRACT

Introduction: The incidence of early-onset rectal cancer has increased over the past 3 decades and the causes are unknown. Neighborhood socioeconomic status, a measure of social and economic characteristics in a given area, may be associated with early-onset rectal cancer through environments that affect diet, exercise, and health care utilization. We investigated the association between neighborhood-level socioeconomic status and age at rectal cancer diagnosis in Wisconsin.

Methods: We utilized data on 172 rectal cancer patients from the Carbone Cancer Center rectal cancer registry. We measured neighborhood socioeconomic status using the Area Deprivation Index, derived from 17 census measures of education, employment, income, and housing, standardized at the state and national levels. Linear and logistic regression models were employed to estimate the association between the Area Deprivation Index and age at diagnosis.

Results: Of the 172 cases of rectal cancer, 47 (27%) were considered early-onset (<50 years). Null associations were observed between the Area Deprivation Index and age at diagnosis using the national- and state-standardized index. Moreover, estimates using the nationally standardized index suggested lower odds of early-onset rectal cancer in lower socioeconomic status neighborhoods ($OR_{Q5} = 0.11$, 95% CI, 0.01–1.89).

Conclusions: This study initiates research investigating the association between area-level socioeconomic status and early-onset rectal cancer. While we find no association between the Area Deprivation Index and early-onset rectal cancer, we posit these findings are due to the characteristics of our sample. Future studies are needed to comprehensively explore associations between social factors and early rectal cancer outcomes.

INTRODUCTION

Despite the decline in overall rectal cancer incidence in recent decades, the incidence of early-onset rectal cancer (EORC) has increased annually by 2% to 3% since the mid-1990s.[1] Defined as onset before age 50, EORC prompted recent screening guideline changes: the American Cancer Society and US Preventive Services Task Force now recommend screening beginning at age 45.[2,3] Causes of the increase are unclear; hypotheses include increases in sedentary lifestyle, changes in diet quality, and obesity.[4-6]

Evidence supports an association between neighborhood socioeconomic status (SES) and rectal cancer outcomes, including higher risk of rectal cancer incidence, mortality, and late-stage diagnosis in lower SES areas.[7-11] Neighborhood SES is a relative measure of a given area's social and economic status, via composite indices of census data at the neighborhood level.[12] The environment in which one resides may influence rectal cancer risk by affecting access to health care and screening.[13-15] Other area-level contextual factors such as spaces for physical activity, nutritious food options, and environmental stressors like crime, may influence EORC indirectly through associations with obesity and inflammation.[6,16-20] Previous studies have found that the prevalence of EORC varies geographically,[4,5] but no studies have examined the association between area-level SES and EORC directly.

We evaluated this association using the publicly available and validated Area Deprivation Index (ADI), with the newly established University of Wisconsin (UW) Carbone Cancer Center

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Rectal Cancer Registry. The ADI is compiled using 17 census measures of education, employment, income, and housing at the census-block group level and is free to download from the University of Wisconsin Center for Health Disparities Research in the School of Medicine and Public Health.[12] We hypothesized an inverse association between area SES and EORC, where lower SES areas would experience higher rates of EORC.

METHODS

Data

Data were obtained from the UW Carbone Cancer Center Rectal Cancer Registry. The Carbone Cancer Center is a National Cancer Institute (NCI)-designated comprehensive cancer center in Madison, Wisconsin, serving patients from across the state and Midwest. The registry includes 181 adult patients age 18 and older enrolled between 2018 and 2024 who were seen at UW Health with a histologic diagnosis of rectal adenocarcinoma or squamous cell carcinoma of the rectum or anal canal, defined by the International Classification of Diseases for Oncology, Third Edition (ICD-O-3) code C20.9. Patients with squamous cell carcinoma were excluded. All participants provided written consent to participate in the study.

Demographic variables, including sex, race, ethnicity, education, insurance status, alcohol use, tobacco use, and date of diagnosis, were abstracted from electronic health records and stored in REDCap, hosted by the UW-School of Medicine and Public Health.

This study was deemed minimal risk and granted exemption by the UW-Madison Health Sciences Institutional Review Board (IRB-2018-0149). All study procedures conformed to the tenets of the Declaration of Helsinki.

Table 1. Descriptive Statistics of the Carbone Cancer Center Rectal Cancer Registry, 2018–2024

Variable	Full Sample (N = 172)	Early-Onset (EORC)		Mid-Onset	Late-Onset
		<45 Years (N = 28)	45–49 Years (N = 19)	50–64 Years (N = 68)	≥65 Years (N = 57)
Age at diagnosis (years)	57 (19)	40 (4)	48 (2)	56 (9)	73 (11)
Sex					
Male	111 (65%)	18 (64%)	12 (63%)	47 (69%)	34 (60%)
Female	61 (35%)	10 (36%)	7 (37%)	21 (31%)	23 (40%)
Race/ethnicity					
Non-Hispanic White	163 (95%)	27 (96%)	19 (100%)	62 (91%)	55 (96%)
Non-Hispanic Black	1 (1%)	0 (0%)	0 (0%)	1 (1%)	0 (0%)
Asian	3 (2%)	0 (0%)	0 (0%)	3 (4%)	0 (0%)
Hispanic	3 (2%)	1 (4%)	0 (0%)	1 (1%)	1 (2%)
Missing	2 (1%)	0 (0%)	0 (0%)	1 (1%)	1 (2%)
Alcohol use					
Missing	22 (13%)	5 (18%)	3 (16%)	7 (10%)	7 (12%)
No	40 (23%)	3 (11%)	5 (26%)	14 (21%)	18 (32%)
Yes	110 (64%)	20 (71%)	11 (58%)	47 (69%)	32 (56%)
Tobacco use					
No	96 (56%)	18 (64%)	12 (63%)	37 (54%)	29 (51%)
Yes	76 (44%)	10 (36%)	7 (37%)	31 (46%)	28 (49%)
Insurance status[a]					
Private	131 (76%)	28 (100%)	17 (89%)	54 (79%)	32 (56%)
Medicaid	10 (6%)	0 (0%)	2 (11%)	7 (10%)	1 (2%)
Medicare	23 (13%)	0 (0%)	0 (0%)	2 (3%)	21 (37%)
Missing	8 (5%)	0 (0%)	0 (0%)	5 (7%)	3 (5%)
Bowel disease[b]					
No	167 (97%)	28 (100%)	18 (95%)	68 (100%)	53 (93%)
Yes	5 (3%)	0 (0%)	1 (5%)	0 (0%)	4 (7%)
ADI state quintile					
Q1 (highest SES)	53 (31%)	11 (39%)	5 (26%)	17 (25%)	20 (35%)
Q2	36 (21%)	4 (14%)	9 (47%)	14 (21%)	9 (16%)
Q3	38 (22%)	4 (14%)	2 (11%)	18 (26%)	14 (25%)
Q4	26 (15%)	7 (25%)	2 (11%)	11 (16%)	6 (11%)
Q5 (lowest SES)	19 (11%)	2 (7%)	1 (5%)	8 (12%)	8 (14%)
ADI national quintile					
Q1 (highest SES)	9 (5%)	3 (11%)	1 (5%)	3 (4%)	2 (4%)
Q2	45 (26%)	8 (29%)	5 (26%)	14 (21%)	18 (32%)
Q3	54 (31%)	5 (18%)	10 (53%)	24 (35%)	15 (26%)
Q4	48 (28%)	11 (39%)	3 (16%)	21 (31%)	13 (23%)
Q5 (lowest SES)	16 (9%)	1 (4%)	0 (0%)	6 (9%)	9 (16%)

Abbreviations: ADI, area deprivation index; SES, socioeconomic status.

Data presented as N (%) for categorical variables and median (interquartile range) for continuous variables.

[a]If participants are dually insured by Medicare and private insurance or Medicaid, they are included in the private insurance or Medicaid groups.

[b]Bowel disease includes Crohn's disease and ulcerative colitis.

Analytical Cohort

Of 181 registry patients, we excluded those with missing data on age (n=1) and ADI (n=8), of whom only 1 was younger than age 50. For the single participant missing data on tobacco use, the sex-specific mode was used for imputation. Missing data on alcohol use (n=22) and insurance status (n=8) were treated as separate categories within the respective variable. The final analytic cohort consisted of 172 participants.

Exposure Measurement

Participant addresses were geocoded, and census block-level Federal Information Processing Standards (FIPS) codes were linked to the publicly available ADI.[12] The ADI was derived from 17 census variables in education, income, employment, and housing domains using 2022 American Community Survey

5-year estimates (2018-2022). Scores reflect relative socioeconomic disadvantage at the census block group level and are standardized state and national levels. The ADI has been scientifically validated in hundreds of studies predicting health outcomes such as obesity,[21] cancer,[22] and COVID-19.[23] Our analyses included both national- and state-standardized ADI measures, represented in quintiles (1 = highest SES, 5 = lowest SES).

Health insurance coverage was included as a secondary exposure, categorized as private insurance, Medicaid, Medicare, or missing. Those with dual Medicare and private insurance or Medicaid coverage were categorized as private insurance or Medicaid to capture socioeconomic differences. A subset of participants was missing insurance data because they were deceased at the time of data extraction. Private insurance was defined as employer-sponsored or individually purchased coverage.

Table 2. The Association Between ADI and Early Rectal Cancer Diagnosis, N = 172

ADI (State Quintiles)	EORC < 50 Years (N = 47)	Mid to Late Onset ≥ 50 Years (N = 125)	EORC vs Mid to Late Onset OR[a] (95% CI)	EORC vs Mid to Late Onset OR[b] (95% CI)
Q1 (highest SES)	16	37	1 (ref)	1 (ref)
Q2	13	23	1.31 (0.53–3.21)	1.86 (0.68–5.10)
Q3	6	32	0.43 (0.15–1.24)	0.58 (0.19–1.78)
Q4	9	17	1.22 (0.45–3.32)	1.30 (0.41–4.14)
Q5 (lowest SES)	3	16	0.43 (0.11–1.70)	0.38 (0.09–1.67)
ADI (National Quintiles)	**EORC <50 years (N = 47)**	**Mid to Late Onset > 50 Years (N = 125)**	**EORC vs Mid to Late Onset OR[a] (95% CI)**	**EORC vs Mid to Late Onset OR[b] (95% CI)**
Q1 (highest SES)	4	5	1 (ref)	1 (ref)
Q2	13	32	0.51 (0.12–2.20)	0.48 (0.10–2.36)
Q3	15	39	0.48 (0.11–2.04)	0.57 (0.11–2.76)
Q4	14	34	0.52 (0.12–2.20)	0.57 (0.11–2.85)
Q5 (lowest SES)	1	15	0.08 (0.01–0.93)	0.06 (0.0–0.73)

Abbreviations: ADI, area deprivation index, EORC, early onset rectal cancer, OR, odds ratio; Q, quintile; SES, socioeconomic status.

[a]OR unadjusted for any covariates.

[b]OR adjusted for sex, alcohol, tobacco, and insurance type, and bowel disease.

Outcome Measurement

Age of diagnosis of rectal cancer was included as a continuous and categorical variable (< 45, 45–49, 50–64, ≥ 65). EORC was defined as diagnosis before age 50. Mid-onset (50-64 years) and late-onset (≥ 65 years) categories were combined because of sample size limitations.

Statistical Analysis

Demographic and behavioral characteristics were tabulated by age at diagnosis. We used logistic regression models to assess the association between ADI quintiles and EORC, adjusting for sex (male, female), insurance status (public, private, both), tobacco use (yes, no), alcohol use (yes, no, missing), and bowel disease (yes, no). Those with missing insurance status were excluded from logistic regression models as quasi-separation of values occurred. Additionally, linear regression models examined associations between ADI quintiles and age of diagnosis, adjusting for the same covariates (sex, insurance status, tobacco use, alcohol use, and bowel disease). Secondary analyses evaluated the association between insurance type and age at diagnosis using linear regression, adjusted for sex, tobacco use, and alcohol use.

RESULTS

This study included 172 cases of rectal cancer from the UW Carbone Cancer Center Rectal Cancer Registry; 47 (27%) cases were classified as EORC (Table 1). Overall, 65% of the cohort was male, 95% identified as non-Hispanic White, 64% reported alcohol use, 44% reported tobacco use, 95% had private, public, or combined health insurance coverage, and 3% reported a history of bowel disease. A greater proportion of EORC cases were insured by private insurance (96%) compared to those diagnosed at ages 50 to 64 (79%) or 65 years and older (0%) (Table 1).

The distribution of participants varied across neighborhood SES quintiles standardized at the state and national levels. Participants were more likely to live in the highest neighborhood SES quintile compared with neighborhoods across Wisconsin (31% in Q1), and in mid-tier SES quintiles (quintiles 2-4) compared with neighborhoods across the United States (31% in quintile 3) (Table 1, Supplemental Table 1).

Generally, we did not observe an association between neighborhood SES and EORC using either state- or nationally standardized ADI measures. In models that utilized the state-standardized ADI, the direction of the association was inconsistent: estimates for quintile 2 and quintile 4 suggested higher odds of EORC, whereas quintile 3 suggested lower odds; all confidence intervals passed unity (Table 2). In models that used the nationally standardized ADI measure, participants in the lowest SES neighborhoods (quintile 5) had the lowest odds of EORC (OR, 0.08; 95% CI, 0.01–0.93); however, confidence intervals for all other quintiles passed unity (Table 2). Among participants with private insurance only, associations between ADI and EORC were also null (Supplemental Table 2).

Similarly, linear regression models did not identify a clear association between ADI quintile and the age at rectal cancer diagnosis. In state-standardized models, the direction of association was unclear, with mean age increasing in quintile 5 and decreasing in all other quintiles; only the estimate for quintile 4 reached statistical significance (quintile 4: mean age, 78.52 years; standard error [SE], 2.99) (Table 3). In nationally standardized models, lower SES appeared to correspond with older age at diagnosis (quin-

tile 1: mean age, 74.3 years; standard error [SE], 8.61; quintile 5: mean age, 86.12 years, SE, 4.94; $P = .02$), but statistical significance was not established for quintiles 2-4 (Table 3).

Individual-level insurance type varied greatly by age group. Most participants younger than age 65 had private insurance (86%), whereas those 65 years and older primarily had public insurance (39%) or a combination of public and private coverage (56%), reflecting Medicare eligibility at age 65 (Table 1). To isolate associations between insurance type and diagnosis age, we analyzed participants younger than 65 years and found that insurance type was associated with age at diagnosis: participants with public insurance were, on average, 9.71 years older at diagnosis than those with private insurance (SE, 2.48; $P < .001$), and those with both public and private insurance were 11.50 years older than those with private insurance only (SE, 2.93; $P < .001$) (Supplemental Table 3).

Table 3. The Association Between ADI and Age of Rectal Cancer Diagnosis, N = 172

ADI (State Quintiles)	Age Estimate[a]	Standard Error (95%)	*P* value
Q1 (highest SES)	84.80 (ref)	7.74	—
Q2	-4.07	2.58	.11
Q3	-1.62	2.54	.52
Q4	-6.28	2.99	.04
Q5 (lowest SES)	1.13	3.29	.73
ADI (National Quintiles)	**Age Estimate[a]**	**Standard Error (95%)**	***P* value**
Q1 (highest SES)	74.3 (ref)	8.61	—
Q2	7.72	4.24	.07
Q3	3.59	4.22	.40
Q4	1.68	4.24	.69
Q5 (lowest SES)	11.82	4.94	.02

Abbreviations: ADI, area deprivation index; SES, socioeconomic status, std err, standard error.
[a]Estimates adjusted for sex, alcohol, tobacco, insurance type, and bowel disease.

DISCUSSION

This study suggests that area-level SES may not be associated with early-onset rectal cancer in this cohort from a comprehensive cancer center in Wisconsin, contrary to the hypothesis that lower SES may be linked to a higher incidence of EORC. Prior literature indicates that low neighborhood-level SES is associated with increased rectal cancer incidence and late-stage diagnosis.[11,13,22,24-26] Additionally, other studies have reported associations between low SES and limited access to healthy fresh food options and outdoor physical activity areas, which may contribute to a heightened risk of rectal cancer.[27,28]

We hypothesize that our findings may reflect sample characteristics. The majority of the 172 participants in our study self-identified as non-Hispanic White, a population diagnosed with EORC at a lower rate than African American and Hispanic populations.[29] Additionally, most participants had health insurance, which has previously been established as a strong predictor of screening and diagnostic testing completion.[30,31] Finally, the incidence of EORC may be lower at NCI-designated comprehensive cancer centers such as Carbone, since these centers have goals to address inequities in cancer detection and treatment, in addition to providing guideline-concordant care.[32]

Despite null associations between ADI and EORC, we found that individual-level insurance type was associated with age at diagnosis among participants younger than 65 years. Those with public insurance were diagnosed at older ages compared with those with private insurance, suggesting that lack of private coverage may delay screening and diagnostic evaluation. Future research should further investigate the role of insurance coverage in early detection of rectal cancer.

Strengths

This study is, to our knowledge, the first to investigate the association between area-level SES and EORC. Investigating potential risk factors for EORC is critical for researchers, clinicians, and policymakers seeking to address the rising incidence among younger adults. Use of the ADI strengthens this study because it is a validated, publicly available, neighborhood-level measure of SES. Its granularity captures variation that broader measures may miss, and its composite nature reflects multiple dimensions of SES more accurately than single indicators such as median household income. Finally, ADI's widespread use also facilitates comparability across studies.

Limitations

Our findings do not come without limitations. The Carbone Cancer Center rectal cancer registry is relatively new (initiated in 2018) and continues to grow, limiting sample size and stratification. Additionally, participants included in this study were highly homogeneous in terms of race (95% non-Hispanic White) and having insurance coverage, which may limit the generalizability of our findings. Finally, individual-level SES measures such as income and education were unavailable in electronic health records, restricting adjustment for these factors.

CONCLUSIONS

This study initiates research on the association between area-level SES and EORC. Although no association was observed between ADI and EORC, insurance type was linked to age at diagnosis, underscoring the importance of individual-level socioeconomic factors. Future studies should examine associations between social factors in diverse populations and early rectal cancer outcomes.

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Barometric Pressure Drops and Premature Rupture of Membranes

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ABSTRACT

Introduction: Many patients and health care providers believe that barometric pressure drops increase the incidence of premature rupture of membranes (PROM). To test this, we studied high risk women living near a weather station.

Methods: This cohort chart review study investigated 189 PROMs, diagnosed between 24 and 42 weeks gestation, at Wheaton Franciscan-St Joseph Campus, Milwaukee, Wisconsin. National Oceanic and Atmospheric Administration (NOAA) data from the 24 hours preceding each PROM occurrence were analyzed. The sample provided 91% power to detect a two-fold increase in the PROM rate.

Results: The PROM rate, 9.5%, within the 24 hours following a NOAA-defined substantial pressure drop, was similar to that predicted using the percentage of the total study period time within 24 hours after a substantial pressure drop, 10.8%, (P=.64). The findings for within 3, 6, and 12 hours after a substantial pressure drop were similar.

Conclusions: The incidence of PROM does not increase following substantial atmospheric pressure drops.

INTRODUCTION

Certain beliefs are widely held among obstetrical patients and health care providers working on labor and delivery units. One of the most common—and perhaps strongest—is that a drop in barometric pressure, often associated with the onset of stormy weather, quickly leads to an increase in the number of women presenting with premature rupture of membranes (PROM). A small number of studies, many conducted 30 to 40 years ago, reported a statistically significant association between a declining barometric pressure and an increased incidence of PROM.[1,2] As climate change intensifies and severe weather intensifies, if stormy weather increases the incidence of PROM, labor and delivery units may need to increase staffing to prepare for a patient influx during severe weather forecasts.

We studied a geographically concentrated, inner-city population near a United States National Oceanic and Atmospheric Administration (NOAA) weather station to reexamine the potential relationship between PROM and a drop in barometric pressure.

METHODS

This retrospective chart review study was conducted at Wheaton Franciscan-St Joseph Campus (WF-SJ) in Milwaukee, Wisconsin, a safety-net hospital that serves an economically disadvantaged population. Data were collected initially for a resident research project; the manuscript was completed later, after climate change was widely recognized and severe weather became more common, highlighting the importance of this investigation.

This study was approved with waiver of consent by both the Wheaton Franciscan Health Care and the Medical College of Wisconsin Institutional Review Boards. Women aged 18 years and older with gestational ages between 24 and 42 weeks who presented with PROM during July 5, 2005, through November 24, 2006, were included, except those who presented during August 3, 2005 through September 9, 2005, for whom data were unavailable.

PROM was defined as ruptured chorioamniotic membranes

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without contractions, based on patient report and tocodynameter evaluation. Rupture was diagnosed clinically by obvious pooling with a positive nitrazine test and/or ferning of the vaginal fluid. Patients with known polyhydramnios or uterine anomalies were excluded. The time of PROM reported by the patient was recorded.

Hourly barometric pressure data from Milwaukee's General Mitchell International Airport weather station, starting 24 hours before the study period, were obtained from the NOAA National Climatic Data Center. The weather station is 8.8 miles from WF-SJ. NOAA designated episodes of pressure falling rapidly (PFR), which are defined as a decrease of at least 0.06 inches of mercury per hour and a total change of 0.02 inches or more of mercury at the time of the observation.[3] For each PROM occurrence, barometric pressure readings for the preceding 24 hours were analyzed to determine whether a PFR episode had occurred. The start of the PFR episode was the time immediately before the required pressure drop began (eg, if pressure was stable before 1 PM and > 0.06 inches of mercury lower at 2 PM, the PFR began at 1 PM).

Table 1. Descriptive Statistics

Characteristic	PROM Within 24 Hours of Rapidly Falling Pressure Event (n = 18)	PROM Without Corresponding Rapidly Falling Pressure Event (n = 171)	Test Statistic
Maternal age (years)	22.2 **26.0** 28.5 (25.8 ±) 5.0[a]	21.0 **26.0** 310.0 (26.9 ± 6.4)	F = 0.22, *P* = .64[b]
Maternal weight[c] (lb)	164 **178** 201 (186 ± 48)	153 **181** 210 (186 ± 46)	F = 0.03, *P* = .87[b]
Gravida	1.2 **3.0** 5.0 (4.2 ± 5.5)[d]	1.0 **2.0** 3.5 (2.7 ± 2.3)	F = 0.17, *P* = .17[b]
Race			
Black	8 (44%)[e]	85 (50%)	$\chi_2^2 = 0.23$, *P* = .89[f]
White	7 (39%)	63 (37%)	
Other	3 (17%)	23 (13%)	
Gestational age (days)	226 **242** 267 (244 ± 25)	228 **251** 271 (246 ± 29)	F = 0.24, *P* = .62[b]
Infant sex: female	7 (39%)	78 (46%)	$\chi_1^2 = 0.3$, *P* = .58[f]
Infant weight (g)	1831 **2600** 3078 (2482 ± 956)	2038 **2687** 3208 (2573 ± 836)	F = 0.14, *P* = .71[b]
Apgar score			
1 min	7.25 **8.00** 8.00 (7.78 ± 0.88)	7.00 **8.00** 8.00 (7.30 ± 1.74)	F = 0.67, *P* = .41[b]
5 min	9.00 **9.00** 9.00 (8.72 ± 0.75)	9.00 **9.00** 9.00 (8.65 ± 0.98)	F = 0.29, *P* = .59[b]
Twins	2 (11%)	12 (7%)	$\chi_1^2 = 0.4$, *P* = .53[f]

Abbreviations: PROM, premature rupture of membranes; lb, pounds.

[a]X**Y**Z: X = lower quartile, **Y** = median, Z = upper quartile for continuous variables; (m ± s) = mean ± 1 SD.

[b]Wilcoxon rank sum test.

[c]Data available for only 178 subjects. For all other characteristics, data were available for all 189 subjects.

[d]Mean and standard deviation were driven by 1 subject reporting gravida of 25.

[e]Numbers after percents are frequencies.

[f]Pearson chi-square test.

The primary analysis compared the proportion of PROM occurrences within 24 hours after a PFR (P_1) with the proportion of the total study period within 24 hours after a PFR (P_0). Using the Bayes theorem, the odds ratio, $[P_1/(1-P_1)]/[P_0/(1-P_0)]$ equals the relative risk of PROM within 24 hours after a PFR compared with no PFR within the preceding 24 hours. For the binomial test, at a 5% significance level, the sample size of 189 PROM cases provided 91% power to detect a twofold increase in risk.

The study population lived very close to both the hospital and the weather station: 80.9% within 10 miles of the hospital and 77.3% within 15 miles of the weather station. Strobe reporting guidelines for cohort studies were followed.

RESULTS

During the study period, 189 PROM cases occurred. The mean gestational age was 245.7 days (35 weeks), the median was 250 days (35 weeks), and the range was 168 to 290 days (24-41 weeks). The PROM rate among labor and delivery admissions was 3.3%.

Table 1 summarizes patient and infant demographics. For twin gestations, data from the first-born infants were used. No significant differences were observed between women experiencing PROM within 24 hours after a PFR and those without a corresponding PFR. Overall, 83 PFR episodes occurred, averaging 1.24 PFRs per week. Because episodes were unevenly spaced, 10.8% of the study time fell within 24 hours after a PFR and 1.9% within 3 hours after a PFR.

Table 2. Portion of the PROM Events and the Total Study Time Within the Specified Interval Following a Rapidly Falling Pressure

	≤ 3 hours	≤ 6 hours	≤ 12 hours	≤ 24 hours
PROM events	1.1%	1.6%	4.8%	9.5%
Total study time	1.9%	3.4%	6.1%	10.8%

Abbreviation: PROM, premature rupture of membranes.

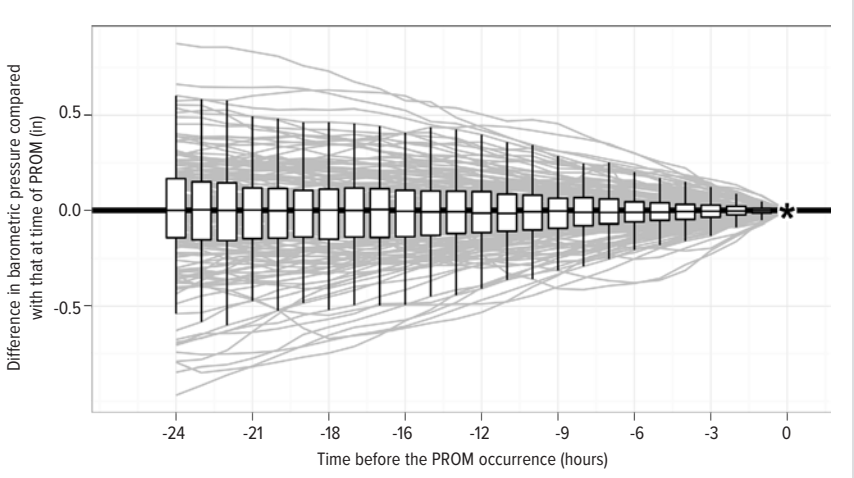
The Figure illustrates the barometric pressures during the 24 hours preceding PROM occurrences. Pressure differences were symmetrically distributed around the line labeled 0.0, indicating the pressure at PROM onset. This suggests that the barometric pressure before PROM was as likely to rise as fall.

Table 2 shows the proportion of PROM occurrences preceded by a PFR event. In the primary analysis, based on 24-hour periods after such a pressure drop, fewer PROM cases occurred than predicted by the percentage of study time within 24 hours after a PFR. That is, the observed proportion was 9.5% (95% CI, 5.7%–14.6%), consistent with the expected 10.8% (binomial test, *P* = .64). The odds ratio comparing observed and expected proportions yielded a relative risk of 0.87 (95% CI, 0.50–1.41) for PROM within 24 hours after a PFR versus periods greater than 24 hours after the latest PFR. Findings for other intervals—within

3, 6, and 12 hours following a PFR—were similar, with relative risk estimates of 0.56, 0.46, and 0.77, respectively.

Analysis of the rate of PROM across time intervals revealed similar findings. The overall rate was 0.4 PROMs/day; during periods within 24 hours after a pressure drop, the rate was 0.35 PROMs/day. During periods within 24 hours after a sudden pressure rise, the rate was also 0.35/day.

Figure. Barometric Pressures in the 24 Hours Preceding Premature Rupture of Membranes Occurrences



A difference of zero corresponds to a barometric pressure equal to that at the time of the premature rupture of membranes (PROM) occurrence. For each hour, a box plot contains the middle 50% of the values. The horizontal bar within each box indicates the median.

*Indicates the time of the PROM occurrences.

DISCUSSION

No increased incidence of PROM was observed within the 24-, 12-, 6-, or 3-hour periods after a PFR; in fact, fewer PROMs occurred than expected.

Strengths of this study include the relatively high latitude and relatively flat topography of Southeastern Wisconsin, the highly geographically concentrated patient population, and use of the accepted meteorological definition of a substantial pressure change. Latitude is important because frontal passages in midlatitudes occur regularly, typically every 3 to 5 days. Both cold fronts and warm fronts produce noteworthy pressure fall/rise couplets, with cold fronts generally associated with the most pronounced pressure changes and significant weather impacts, including precipitation. Because of the relatively high latitude of Milwaukee, it is exposed to more of these cold fronts than lower latitudes within the United States. The relatively flat topography is advantageous because frontal passage characteristics are often more sharply delineated in flat versus complex terrains, where significant surface topographical features, such as mountains and valleys, can disrupt frontal movement. The absence of such features increases the likelihood that our patient population experienced the weather conditions recorded at the weather station.

Another strength of this study is proximity: the study group lived very close to the hospital, which was near the weather station. At Milwaukee's latitude, the most significant prefrontal pressure falls and postfrontal pressure rises routinely occur within approximately 50 km (31 miles).[4] Most patients, (>77%) lived within half this distance of the weather station, again increasing the likelihood they experienced the recorded conditions. Finally, use of NOAA's definition of PFR enabled evaluation of meteorologically significant pressure drops on PROM incidence.

Weaknesses of this study include limitations inherent to chart review studies and the decision to combine preterm and term PROM cases, which likely have different etiologies. However, if barometric pressure changes exert stress on the membranes, predisposed membranes—regardless of the etiology—should be more likely to rupture. Additionally, this study focused on a high-risk population, limiting generalizability to lower-risk populations.

Our findings contradict some previous studies, possibly due to more rigorous study design. Steinman and Kleinerl[1] reported lower mean barometric pressure at PROM compared with a reference standard calculated from readings at noon over 6 days in June 1975. Their study included 32 PROM cases and 227 controls without PROM. Polansky et al[2] found a significant increase in PROM within 3 hours after any pressure drop among term patients at the University of Iowa Hospitals. Their 109 PROM subjects lived within 100 miles of the weather station at the Cedar Rapids (Iowa) Municipal Airport. One hundred nine women experiencing the spontaneous onset of labor, matched for age, served as their control group. Because their patient population was less concentrated, it is more likely that they experienced weather conditions different from those recorded at the weather station. Finally, Akutagawa et al[5] studied 547 Tokyo women who experienced PROM at an average gestational age of 39 weeks, 5 days. They divided this population into 2 groups: those delivering while the barometric pressure was above the mean and those delivering while the barometric pressure was below the mean. They found a significant increase in PROM occurrence at lower absolute barometric pressures but did not assess pressure changes or geographic proximity to the weather station.

Two studies agree with our findings. Marks et al[6] found that PROM occurred randomly among women >36 weeks gestation who gave birth at the University Hospital of Jacksonville, Florida, with no clustering of ruptures around barometric pressure or lunar phase. Trap et al[7] studied 254 PROM cases that occurred in Denmark and found no relationship between PROM frequency and the absolute barometric pressure or pressure changes up to 9 hours before rupture. They also reported that the average changes

in barometric height in the 4 time periods investigated within the 9 hours preceding PROM did not significantly differ from zero, and there was no association between the time of the year and PROM frequency. Neither study included a control population, evaluated defined pressure drops, or commented on the geographic distribution of their population with respect to the weather station.

Another study examined barometric pressure changes and the onset of labor among term deliveries at the Medical Center of Central Massachusetts-Memorial Hospital.[8] They reported a significant deficit in spontaneous labor onset after continuous 3-hour pressure decreases but did not use NOAA's PFR definition and included a less concentrated population, living within a 50-mile radius of their hospital.

Previous investigators[2] hypothesized that sudden barometric pressure changes create a gradient across chorioamniotic membranes, making rupture of membranes more likely. This explanation is not biologically plausible. The amniotic sac can be modeled as a balloon: a drop in atmospheric pressure decreases pressure on the abdomen, reducing pressure on the cervix and, theoretically, making rupture less likely. The vagina is a potential space: when there is nothing inside the vagina, the walls collapse together; it is closed to barometric pressure changes. So, at most, a drop in atmospheric pressure should decrease overall pressure on the ballon. Based on anatomy, atmospheric pressure drops should decrease the PROM risk, consistent with our finding that PFR episodes were not associated with increased PROM risk and the trend toward lower-than-expected risk after PFR episodes.

CONCLUSIONS

Episodes of rapidly falling barometric pressure were not associated with increased PROM incidence in this geographically concentrated, high-risk population. These findings suggest that labor and delivery units do not need to increase staffing in anticipation of severe weather. Further research in diverse populations may clarify whether these results are generalizable.

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Characteristics and Predictors of Pediatric and Adult Patients with Inherited Retinal Degenerations: Tertiary Care Ophthalmology Clinic Data

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ABSTRACT

Introduction: Inherited retinal degenerations (IRDs) are genetically driven disorders affecting retinal photoreceptors, the retinal pigment epithelium, bipolar cells, and other retinal structures. This study aimed to compare characteristics of pediatric versus adult patients at the time of initial presentation to a tertiary care IRD clinic.

Methods: A retrospective chart review of 527 patients diagnosed with IRDs was conducted. Data collected included age at presentation, diagnosis, ocular and systemic characteristics, demographics, distance from home to the clinic, and type of referring provider.

Results: High hyperopia, high myopia, high astigmatism, congenital syndactyly, and developmental delay were more common among pediatric patients. Adult patients more frequently presented with reduced central vision, peripheral vision loss, color vision deficits, nyctalopia, flashes/floaters, cataracts, and family history of cataracts. Compared to a control population, adult IRD patients had higher rates of cardiac conditions, lower prevalence of obesity, and similar rates of diabetes. No significant differences were found in type of referring provider or proximity to the clinic.

Discussion: Distinct clinical and familial characteristics were associated with age at presentation. Pediatric patients often exhibited refractive and developmental features, while adults presented with progressive vision symptoms. Despite assumptions, geographic proximity did not significantly influence age at presentation, suggesting other barriers to care.

Conclusions: This study identifies characteristics associated with pediatric and adult presentation in patients with IRDs. Better understanding of these patterns may improve early recognition, clinician education, and timely treatment.

INTRODUCTION

Inherited retinal diseases (IRDs) represent a diverse group of genetically heterogeneous disorders characterized by dysfunction of multiple retinal structures, including photoreceptors, the retinal pigment epithelium, and associated neural layers. These disorders present with a spectrum of clinical symptoms ranging from early-onset visual impairment to progressive vision loss in adulthood. While refractive errors such as myopia and hyperopia are commonly associated, other symptoms including nyctalopia, photophobia, and developmental delays—are equally critical in pediatric presentations. To date, more than 280 genes have been implicated in IRD pathogenesis, each associated with distinct clinical phenotypes.[1] Given the diversity of IRD presentations, early identification and diagnosis are challenging.

IRDs present with a wide range of symptoms and are frequently associated with refractive errors, particularly myopia.[2] Early-onset high myopia has been linked consistently with IRDs, including retinitis pigmentosa (RP) caused by mutations in *RPGR* and *RP1*,[3-6] congenital stationary night blindness,[7] and cone dystrophy and cone-rod dystrophy.[8] High hyperopia also has been associated with IRDs, including RP[4,9] and other dystrophies.[2]

Gene-based therapies represent a promising area of research for treatment of IRDs with known monogenic variants. In 2017, voretigene neparvovec-rzyl became the first gene therapy approved by the US Food and Drug Administration for the treatment of *RPE65*-mediated IRD.[10] This landmark achieve-

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ment spurred significant international investment in research for other IRD gene therapeutics. Despite these advancements, a recent analysis of IRD knowledge identified the natural history and environmental factors as areas requiring continued research.[11] Significant knowledge gaps remain in understanding patient factors that contribute to early or delayed presentation at tertiary care centers. Further exploration of these factors is essential to ensure timely access to gene therapy and other treatments or resources.

The primary objective of this study was to compare the characteristics of patients who present for the first time to the IRD clinic in adulthood versus childhood. We hypothesized that poor visual acuity and family history would be the most predictive factors for early recognition of IRDs and that proximity to a tertiary care center would be associated with a younger age at referral compared to patients living farther away.

METHODS

Patient Inclusion

After Institutional Review Board approval (protocol number 2020-1207), we conducted a retrospective cohort study of patients of all ages diagnosed with an IRD at a single tertiary ophthalmology referral center—the Inherited Retinal Degeneration Clinic at the University of Wisconsin Department of Ophthalmology and Visual Sciences—from January 1, 1990, to January 1, 2020. All patients who presented to the clinic with IRDs who consented to participate were included in an IRB-approved REDCap database hosted at the University of Wisconsin-Madison. Inclusion criteria were a confirmed clinical or molecular diagnosis of IRD following referral. Final diagnoses were determined based on clinical examination, imaging, functional testing, and genetic testing when available. Diagnoses were cross-validated through referral notes and follow-up assessments. Exclusion criteria included patients whose initial clinic visit was not with one of the study's IRD ophthalmologists, those who did not consent to database inclusion, and those not diagnosed with IRDs.

Data Collection

A manual chart review was conducted to collect demographic information, relevant personal and family medical history, IRD diagnosis, disease characteristics, and treatment data from a single patient encounter using a standardized interview template. Demographic variables included age, sex, race (White, Black, Asian, Hispanic, Native American, other), education (high school or less, bachelor's degree, graduate degree, not applicable [N/A]), driving status, employment status, and home address. Each patient's home address and the clinic address were used to estimate commute distance (<20, 20-80, >80 miles) using Google Maps (Google LLC, Mountain View, California).

IRD-information included ocular diagnosis, syndrome, variant gene name(s), left and right eye distance visual acuity, logarithm of the minimum angle of resolution (logMAR) scores for both eyes, and lens status (phakic – no cataract, phakic – cataract, pseudophakic) for both eyes. Referring provider type (ophthalmologist, optometrist, primary care physician, emergency department physician, other) and prior consultation with a low vision specialist were recorded. IRD signs and symptoms included high hyperopia, high myopia, high astigmatism, use of corrective lenses, central or peripheral vision loss, nyctalopia, photophobia, color vision deficits, flashes or floaters, ptosis, cataracts, nystagmus, retinal abnormalities, functional vision loss, strabismus, and amblyopia. High astigmatism was defined as >2.50 diopters; high refractive error was defined as >6.00 diopters.

Additional medical history included obesity, diabetes, cardiac conditions, hearing loss, developmental delay, intellectual disability, neurological conditions, abnormal dentition, prematurity, congenital renal malformations, polydactyly, and syndactyly. Family history variables included IRD diagnosis, nystagmus, high refractive error, nyctalopia, vision loss, color vision deficits, polydactyly, syndactyly, cataracts, strabismus, amblyopia, cardiac conditions, and neurological conditions. The Wisconsin Behavioral Risk Factor Surveillance System (BRFSS) from 2022 was used to serve as a control population for comparison.

Outcomes

The primary outcome was identification of characteristics predictive of age at presentation to the IRD clinic (adult vs pediatric). Secondary outcomes included differences in proximity to the tertiary care center, referring provider type, and diagnoses between pediatric and adult patients.

Statistical Analysis

Fisher exact tests were used to analyze all categorical covariates to determine significant associations between pediatric and adult clinical characteristics. For tables larger than 2x2, the Hommel post-hoc adjustment was applied to correct for multiple comparisons. Significant associations were further quantified by calculating odds ratios and corresponding 95% confidence intervals to provide a more detailed understanding of the relationship within the data.

RESULTS

Patient Characteristics

A total of 538 patients with IRDs were identified, of whom 11 were excluded. Data were collected on 527 patients, including 124 pediatric and 403 adult patients. Patient characteristics are detailed in Table 1.

Characteristics of Presentation to IRD Clinic During Childhood

Among the 124 pediatric patients, the following characteristics were observed: nystagmus (39%), high myopia (24%), high astigmatism (24%), high hyperopia (13%), strabismus (13%), and ptosis (5%) (Table 2). These characteristics differed significantly

from those of adult patients presenting to the clinic for the first time, with statistical significance noted for high hyperopia ($P < .001$), high myopia ($P = .004$), high astigmatism ($P < .001$), ptosis ($P = .022$), nystagmus ($P < .001$), and strabismus ($P = .001$) (Table 2).

Medical characteristics associated with pediatric presentation compared with adult presentation included syndactyly ($P = .041$), developmental delay ($P < .001$), and intellectual disability ($P < .001$) (Table 1). Having a family history of nystagmus ($P < .001$), high refractive error ($P = .002$), vision loss ($P < .001$), strabismus ($P = .002$), and amblyopia ($P = .045$) was also associated with pediatric presentation (Table 2).

Among these variables, the strongest associations with pediatric presentation were found for high hyperopia (odds ratio [OR], 49.34; 95% CI, 9.89-1195.80), congenital syndactyly (OR, 9.62; 95% CI, 1.10-227.57), high astigmatism (OR, 6.19; 95% CI, 3.31-11.86), and a history of developmental delay (OR, 6.11; 95% CI, 2.62-15.08) (Supplemental Table 1). Although these findings were statistically significant, their low prevalence limits their generalizability and underscores the need for further studies to validate these associations.

Table 1. Patient Characteristics

	Pediatric (<18 yo) n (%)	Adult (≥18 yo) n (%)	Total n (%)	*P* value	BRFSS Control[a] (≥18 yo) n (%)	BRFSS Control Adult[a] *P* value
N	124	403	527		11276	
Age, n; mean (SD)	9 (5)	49 (17)	39 (22)			
Sex						
Male	79 (64)	212 (53)	291	.04	5338	0.04
Female	45 (36)	190 (47)	235		5938	
NA[b]	1	1	1		0	
Race/ethnicity						
White	86 (84)	325 (93)	411	.30	9749	0.21
Black/African American	10 (10)	18 (5)	28		603	
Asian	3 (3)	6 (2)	9		144	
AI/AN	3 (3)	2 (<1)	5		134	
Other[b]	5	8	10		488	
Declined[b]	0	1	1		NA	
N/A[b]	13	43	63		NA	
Patient drives						
Yes	4 (5)	180 (49)	184	<.001		
No	76 (95)	190 (51)	266			
NA[b]	1	13	14			
Referring provider						
Ophthalmologist	51 (59)	181 (56)	232	.36		
Optometrist	13 (15)	71 (22)	84			
Primary care	22 (26)	72 (22)	94			
Emergency	0 (0)	0 (0)	0			
Other[b]	38	74	112			
Unknown[b]	0	5	5			
Medical characteristics at presentation						
Congenital						
Polydactyly	0 (0)	12 (3)	12 (2)	.078		
Syndactyly	3 (3)	1 (0)	4 (1)	.041		
Kidney malfunction	0 (0)	11 (3)	11 (2)	.076		
Prematurity	14 (12)	30 (8)	44 (9)	.187		
Developmental delay	15 (13)	9 (2)	24 (5)	<.001		
Intellectual disability	16 (14)	17 (4)	33 (6)	<.001		
Abnormal teeth	2 (0)	1 (0)	3 (1)	0.134		
Diabetes	1 (0)	41 (10)	42 (8)	<.001	1506 (10.3)	1
Obesity	9 (8)	77 (20)	86 (17)	.002	3782 (37.7)	<.001
Cardiac condition	7 (6)	100 (26)	107 (20)	<.001	698 (4.6)	<.001
Neurologic condition	19 (16)	75 (19)	94 (18)	.502		
Hearing loss	19 (16)	89 (23)	108 (21)	.125		

Abbreviations: AI/AN, American Indian/Alaska Native; yo, years old; BRFSS, Behavioral Risk Factor Surveillance System; NA, not applicable.

[a]Shows the BRFSS control data from 2022. Control data only included individuals over age 17, thus pediatric comparison was not feasible.

[b]All NA, other, declined, were removed for analyses.

Characteristics of Presentation to IRD Clinic During Adulthood

Among the 403 adult patients, the ocular characteristics most associated with adult presentation included reduced central vision ($P = .002$), peripheral vision loss ($P = .003$), color vision deficits ($P = .002$), nyctalopia ($P < .001$), flashes/floaters ($P < .001$), and cataracts ($P < .001$) compared to pediatric patients (Table 2). Diabetes, obesity, and heart disease were more common in adults than in pediatric patients ($P < .001$ for all) (Table 1).

Compared to BRFSS control population, obesity ($P < .001$) and cardiac condition ($P < .001$) were significantly more prevalent in the adult IRD population, while diabetes was not statistically significant ($P = 1.00$). Additionally, a family history of cataracts ($P = .022$) was associated with adult presentation (Table 2).

Proximity to Tertiary Care Center

A smaller proportion of pediatric patients lived less than 20 miles from the tertiary ophthalmology center (13.3%, 95% CI, 8.7-19.7) compared to those living 20 to 80 miles (28.0%, 95% CI 22.0-36.1) and more than 80 miles (28.6%, 95% CI 21.9-35.0) away (Figure 1). There was no significant difference in the proportion of pediatric patients between those living 20 to 80 miles and more than 80 miles from the center (Figure 1).

Referring Provider

There was no significant difference in referring provider type between pediatric and adult patients ($P = .36$) (Table 1). Ophthalmologists accounted for the highest number of referrals in both groups, followed by primary care physicians (Table 1). There was no significant difference in the proportion of pediatric patients referred by any specific clinician type (Supplemental Table 2).

Diagnosis

The most common IRDs among pediatric patients were Leber congenital amaurosis (LCA) and cone-rod dystrophy (Figure 2 and Supplemental Table 3). Other diagnoses, including choroideremia, RP, Stargardt disease, and vitelliform dystrophy, were present at lower proportions in pediatric patients (Figure 2 and Supplemental Table 3). Among adult patients, the most common IRD diagnoses were RP, followed by Stargardt disease (Figure 2).

DISCUSSION

This retrospective cohort study of 527 patients with IRDs identified characteristics most associated with pediatric versus adult presentation to a tertiary care center. Consistent with prior studies,[3-8] our findings confirmed a strong association between high myopia and IRDs, supporting our initial hypothesis. Notably, high hyperopia was significantly associated with pediatric presentation, a finding that is less frequently reported in the literature, although previous studies have noted this association.[2,4,9] Similarly, our results align with prior research demonstrating a strong association between astigmatism and IRD.[6]

Our finding that developmental delay is a predictor of pediatric IRD presentation is consistent with the understanding that children with poor vision may be at increased risk for developmental delays due to limited cues regarding the world around them.[12] Additionally, developmental delay has been reported in certain syndromic IRDs.[13,14] Anatomic variants such as polydactyly, brachydactyly, and syndactyly have also been described in patients with IRDs[15] which supports our finding that syndactyly was more commonly associated with pediatric presentation compared to adult presentation.

High proportions of pediatric and adult patients presented with reduced central vision (33%), color vision deficits (34%), nyctalopia (37%), and photophobia (53%), with no significant differences between the groups.

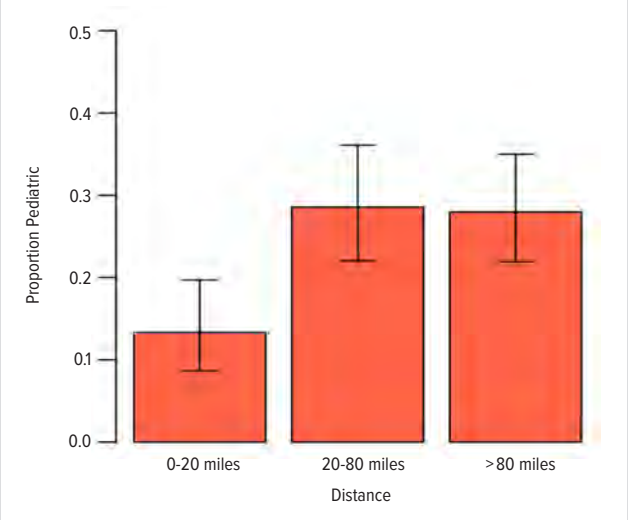
In adults, the characteristics most associated with IRD presentation included flashes/floaters, reduced central vision, peripheral vision loss, cataracts, diabetes, obesity, cardiac conditions, and a family history of cataracts. Previous research has linked syndromic IRDs with diabetes, obesity, and cardiac conditions.[16] In our study, cardiac conditions were more prevalent in the adult IRD population compared to the control group. Obesity was significantly less prevalent, and diabetes prevalence was similar between the IRD adult population and the control group.

Table 2. Patient Ocular Characteristics and Family History at Presentation

	Pediatric n (%)	Adult n (%)	Total N (%)	*P* value
Ocular characteristics				
High hyperopia	16 (13)	1 (0)	17 (3)	<.001
High myopia	29 (24)	47 (12)	76 (15)	.004
High astigmatism	29 (24)	18 (5)	47 (9)	<.001
Wears correction	81 (70)	299 (75)	380 (73)	.078
Reduced central vision	36 (33)	196 (50)	232 (46)	.002
Peripheral vision loss	27 (25)	158 (40)	185 (37)	.003
Color vision deficits	37 (34)	197 (50)	234 (47)	.002
Functional vision loss	0 (0)	0 (0)	0 (0)	1
Nyctalopia	41 (37)	256 (65)	297 (59)	<.001
Photophobia	63 (53)	240 (61)	303 (59)	.138
Flashes/floaters	21 (19)	257 (66)	278 (56)	<.001
Cataracts	7 (6)	212 (53)	219 (42)	<.001
Ptosis	6 (5)	5 (1)	11 (2)	.022
Nystagmus	47 (39)	43 (11)	90 (17)	<.001
Retinal abnormalities	117 (98)	394 (99)	511 (99)	.141
Both eyes affected	120 (99)	391 (99)	511 (99)	1
Strabismus	16 (13)	17 (4)	33 (6)	.001
Amblyopia	11 (9)	18 (5)	29 (5)	.077
Family history				
Diagnosed IRD	33 (27)	137 (35)	170 (33)	.151
Nystagmus	13 (11)	10 (3)	23 (5)	<.001
High refractive error	8 (7)	4 (1)	12 (2)	.002
Nyctalopia	16 (13)	35 (9)	51 (10)	.224
Vision loss	50 (75)	167 (43)	217 (42)	<.001
Color vision deficit	11 (9)	27 (7)	38 (7)	.432
Polydactyly/syndactyly	1 (0)	6 (2)	7 (1)	1
Cataract	20 (16)	105 (27)	125 (24)	.022
Strabismus	28 (24)	46 (12)	74 (14)	.002
Amblyopia	17 (15)	31 (8)	48 (9)	.045
Cardiac condition	9 (8)	46 (12)	55 (11)	.239
Neurological condition	15 (12)	63 (16)	77 (15)	.317

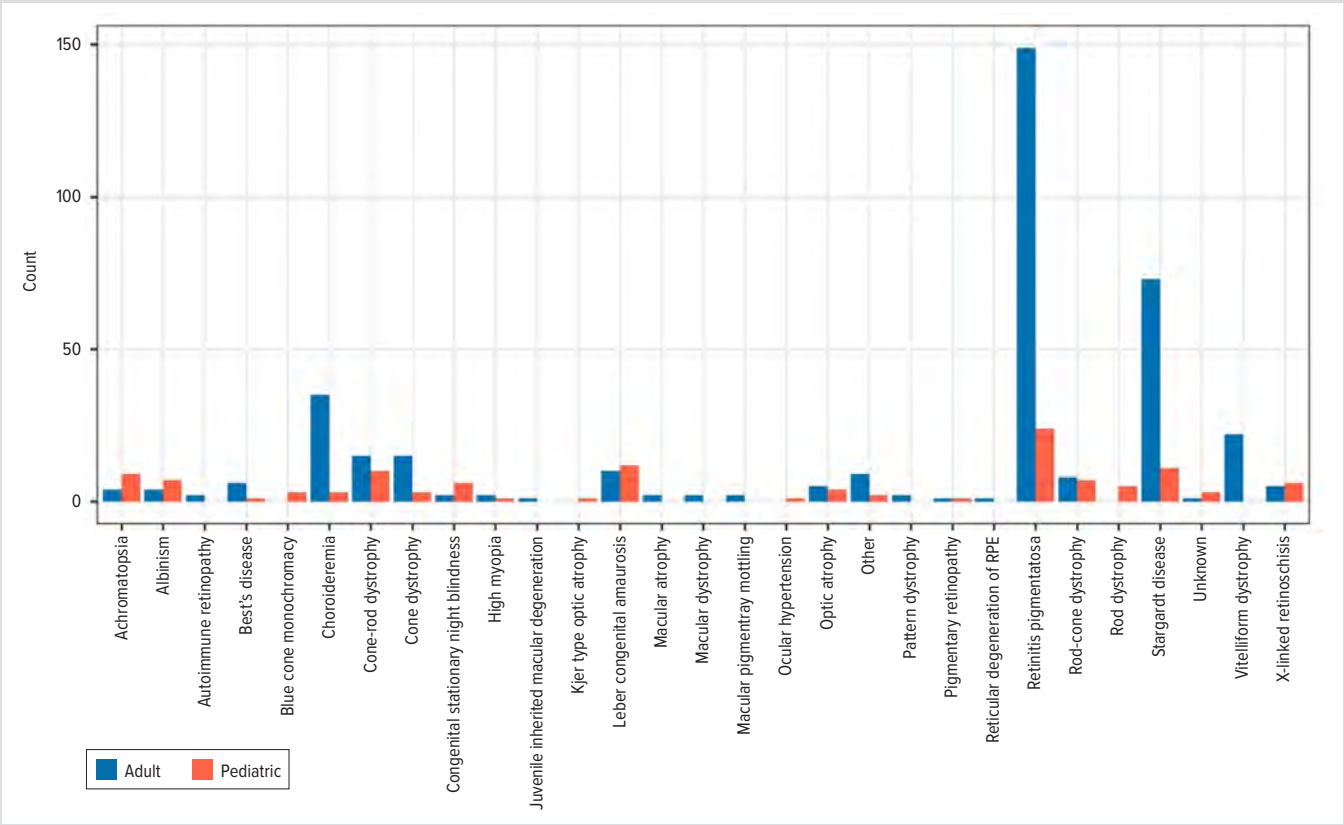
Abbreviation: IRD, Inherited retinal degenerations.
Pediatric: <18 years old; adult ≥18 years old.

Figure 1. Proportion of Pediatric IRD Patients by Distance From Tertiary Care Center



Error bars indicate 95% CIs. Distances are categorized as <20 miles, 20–80 miles, and >80 miles.

Figure 2. Counts of Pediatric and Adult IRD Patients by Ocular Diagnosis at Initial Presentation



In a large study of patients with RP, 170 individuals reported light flashes as a common problem,[17] which is consistent with our findings. The predictors of reduced central and peripheral vision align with previous literature describing patients with RP becoming legally blind by age 40 due to severely reduced visual fields and experiencing central visual loss by age 60.[18] Our finding that cataracts are associated with adult presentation is also supported by prior studies. Based on absolute counts, RP was the most common diagnosis, and RP has previously been linked to cataract development. In a study by Fishman et al, half of the sample of RP patients were found to have cataracts.[5] We also found that a family history of cataracts was associated with adult presentation, which may reflect both the genetic basis of IRDs and the higher prevalence of cataracts in the general adult population.

Compared to pediatric patients, adults presented with more medical comorbidities, including diabetes, obesity, and cardiac conditions. These differences may reflect the type of systemic diseases that typically present during childhood versus adulthood. It is also possible that adult patients were more likely to regularly receive health care, increasing the likelihood of comorbidity diagnosis. This study contributes to our understanding of predictors of pediatric versus adult presentation of IRDs.

Contrary to our hypothesis that closer proximity to a tertiary care center would result in more pediatric referrals, we found the opposite. A smaller proportion of pediatric patients lived less than 20 miles from the center compared to those living farther away. Pediatric patients were more likely to originate from 20 miles away or more. Access to a tertiary care center did not correlate with increased pediatric referrals, suggesting that other factors may influence this finding. Parents may be more willing to travel longer distances for their children, or transportation barriers may affect access. Another possibility is that comprehensive ophthalmologists may feel more comfortable managing adult IRD patients, while fewer may be equipped to care for pediatric patients. Additionally, the shortage of pediatric ophthalmologists and the challenges of examining children may contribute to this finding.

Regarding type of referring provider, no significant difference was found between pediatric and adult patients. Based on raw data, ophthalmologists accounted for the highest number of referrals, followed by primary care physicians. This may reflect the role of primary care physicians as initial points of contact and the specialized training of ophthalmologists in recognizing IRD signs. Given that non-eye care professionals comprised a substantial portion of referrals, it is important to educate clinicians on symptoms that warrant referral for IRD evaluation.

The diagnoses most prevalent in pediatric versus adult patients in this study reflect current knowledge regarding age of

onset of IRDs.[19,20] For example, we found a higher proportion of pediatric patients diagnosed with LCA, and a greater number of vitelliform maculopathy diagnoses in adults. The larger number of RP diagnoses in adults is consistent with RP being the most common IRD, with an estimated prevalence of 1 in 4000 individuals.[21] Our sample reflects these prevalence patterns across age groups.

Limitations of this study include its single-site design and the absence of a pediatric control population for comparison. Despite these limitations, the study included a large sample size of 527 patients with extensive data points, which is notable given the low prevalence of IRDs in the population. Another consideration is that the majority of the patients were White, likely reflecting the local demographics of the tertiary care center, which limited our abilility to examine racial disparities.

CONCLUSIONS

We identified characteristics associated with pediatric and adult presentation in patients with IRDs, thereby addressing current knowledge gaps. Recognizing these characteristics is essential to initiate treatment early and reduce vision loss. A better understanding of these characteristics may facilitate earlier recognition, improve education for clinicians most likely to encounter IRDs, and support timely treatment.

Proximity to a tertiary care center was not the primary factor influencing age at presentation. Further research is needed to explore barriers faced by patients living farther from specialty centers and to develop outreach strategies that promote early recognition and referral. Additionally, exploration of genetic patterns across different regions and communities remains an important area for future study.

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Conditions Conducive to the Screening Auditory Brainstem Response Test: A Pilot Study

Gretchen Sackmann, AuD; Marc Drake, MD; Cecille Sulman, MD

ABSTRACT

Introduction: Early screening and identification of hearing loss is important to optimize hearing and speech outcomes. However, much is unknown regarding the youngest age and under what circumstances a premature infant may undergo an automated auditory brainstem response (AABR) screening in the neonatal intensive care unit (NICU) population. This study aimed to identify environmental factors conducive to AABR screening in the NICU population.

Methods: Premature infants in a tertiary, freestanding, 70-bed children's hospital level IV NICU were screened using Natus ALGO 3i AABR technology under the following circumstances: isolette crib, ventilation with RAM Cannula continuous positive airway pressure (CPAP), bubble CPAP, high-flow nasal cannula, nasal cannula, neurally adjusted ventilatory assist, tracheostomy tube, and room air.

Results: Forty infants were enrolled in the pilot study. Of these, 29 (73%) were successfully screened, 4 (10%) screenings were unsuccessful, and 7 (18%) were inconclusive. A successful screening was defined as an AABR with good electrode impedance that ran to completion, regardless of test results. The youngest successful screen occurred at 33 weeks and 5 days. Screening success rates were highest in patients on room air (100%) and nasal cannula (100%), followed by high-flow nasal cannula (84%) and RAM CPAP (75%). Lower success rates were observed with bubble CPAP (17%), and isolette (50%). Screening was inconclusive for all invasively ventilated patients.

Conclusions: AABR screening is possible in the NICU under various circumstances, including assisted breathing. However, invasive ventilation interferes with accurate screening. Screening may be possible at younger gestational ages than previously recognized. Early detection supports improved outcomes and adherence to Joint Committee on Infant Hearing 1-3-6 guidelines.

INTRODUCTION

Hearing loss is one of the most common congenital conditions, affecting approximately 1.7 infants per 1000.[1] Among infants discharged from the neonatal intensive care unit (NICU), the incidence increases to 2 to 4 per 100.[2] Universal newborn hearing screening, first established in 1990, aims to diagnose hearing loss early and initiate timely intervention.[2] The Joint Committee on Infant Hearing (JCIH) recommends screening in all infants by 1 month of age.[2,3] Those who do not pass the initial screening should have subsequent testing by 3 months of age and, when applicable, intervention and amplification by 6 months of age—known as the 1-3-6 guidelines.

Newborn hearing screening is typically performed using automated auditory brainstem response (AABR) testing, auditory brainstem response (ABR) testing, and/or otoacoustic emissions (OAE). AABR is a technique in which sounds are transmitted to the ear and resulting waveforms from the auditory pathway are recorded. As the test relies on delivering noise to elicit a waveform response, ambient noise may affect successful testing. Ideally, screening occurs in quiet environments and when the infant is very relaxed or asleep.

Several different types of nasal cannula continuous positive airway pressure (CPAP) exist, each with differing mechanisms that lead to very different ambient noise conditions for testing.[4] In bubble CPAP, a water column is used as a resistor to generate CPAP. High flow nasal cannula alters the flow rate of sup-

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plemental air to generate positive end-expiratory pressure. The RAM Cannula delivery system is created using more flexible and softer material than conventional nasal prongs and is designed to decrease airflow resistance.[5] In neurally adjusted ventilatory assist (NAVA) ventilation, a special nasogastric tube is used to detect electrical activity of the diaphragm and generate appropriate breaths.[4]

NICUs and birthing hospitals typically delay screening until the infant reaches at least 37 weeks gestational age, is in room air, and placed in an open crib – frequently the day before or day of discharge. Infants who spend more than 5 days in the NICU may be at increased risk for hearing loss, and those discharged after a failed hearing screening are at a higher risk of being lost to follow-up.

It was hypothesized that screening opportunities may be missed while an infant is hospitalized in the NICU. And given the limited literature on ideal screening conditions in this population, this study aimed to identify environmental and patient factors associated with successful ABR screening in the NICU.

METHODS

Over the course of 3 months beginning in August 2020, environmental conditions and basic patient factors were recorded during newborn hearing screening in a 70-bed, level IV NICU. All infants are required to undergo screening, and the 40 included in this study were deemed healthy enough to receive screening by their medical care team. Gestational ages of tested infants ranged from 28 weeks through 45 weeks, with a mean weight of 890 g to 3885 g.

AABR testing was conducted using the Natus ALGO 3i device. Each test ran for at least 10 minutes when applicable, with up to 3 same-day attempts before classifying the test as successful, unsuccessful, or inconclusive. A successful screening was defined as an AABR with good electrode impedance that ran to completion, regardless of the result. A unsuccessful screening included instances when too much artifact (eg, ambient or patient noise) prevented test completion. Screening was deemed inconclusive when electrodes could not be placed in order to achieve low impedance, likely due to factors such as small head size or other interfering medical devices on the patient. Attempts to reduce ambient noise levels included quieting monitors and testing when no other staff or family members were present.

Standard demographic data noted during the screening included age, sex, and weight in grams. Test conditions included isolette crib, open crib, continuous positive airway pressure (CPAP), bubble CPAP, high-flow nasal cannula, nasal cannula, room air, NAVA ventilation, and tracheostomy ventilation.

Standard descriptive statistics and Fishers exact tests were used to study the sample population. The study was deemed exempt by the Institutional Review Board.

Table. Screening Results by Type of Ventilatory Support and Environment

	Screening Result			
Condition	**Inconclusive**	**Successful**	**Unsuccessful**	**Total**
Bubble CPAP	2	1	3	6
Isolette	0	1	2	3
Open	2	0	1	3
Ventilator (intubated)	2	0	0	2
Isolette	1	0	0	1
Open	1	0	0	1
High flow nasal cannula	3	16	0	19
Isolette	1	2	0	3
Open	2	14	0	16
Nasal cannula	0	4	0	4
Isolette	0	0	0	0
Open	0	4	0	4
Room air	0	4	0	4
Isolette	0	0	0	0
Open	0	4	0	4
RAM Cannula	0	3	1	4
Isolette	0	1	0	1
Open	0	2	1	3
Ventilator (tracheostomy)	1	0	0	1
Isolette	0	0	0	0
Open	1	0	0	1
Total	8	28	4	40

Abbreviation: CPAP, continuous positive airway pressure.

Individuals with open crib were more likely to have a successful result compared to the isolette (Fisher exact = 0.02). Method of ventilation was related to test success (nasal cannula, high flow nasal cannula, and room air are best; bubble CPAP worst), Fischer exact = 0.001.

RESULTS

Forty infants in the NICU were enrolled in this pilot study; 20 were female (50%). Of the cohort, 29 (73%) infants were screened successfully. The earliest gestational age at which a successful screen was performed was 33 weeks and 5 days. The mean gestational age of successfully screened infants was 33.68 weeks (SD, 4.67), compared with 28.17 weeks (SD, 5.51) in the unsuccessful group ($P = .005$). Mean weight in the successful group was 2314.9 g (SD, 790.2), compared with 2256.4 (SD, 1012.9 g) in the unsuccessful group ($P = .424$). However, successful screenings were obtained in infants weighing as little as 1800 g.

Of the 29 infants screened successfully, 16 (55%) were on high flow nasal cannula (HFNC), 4 (14%) were on nasal cannula, 3 (10%) were on RAM CPAP, and 1 (3%) was on bubble CPAP ($P = .03$). Screening was inconclusive for infants who were intubated or had a tracheostomy.

Three infants who were screened were ventilated. Ventilation method was related to screening success, with HFNC and room air yielding the best results, and bubble CPAP the worst (Fisher exact test = 0.0001). All 4 infants < 36 weeks gestation who were screened in room air were screened successfully. A summary of screening results by ventilatory condition is presented in the Table.

Of 8 screens attempted in the isolette crib, 4 were successful (50%). Infants in open cribs were more likely to be screened successfully than those in isolettes (Fisher exact test = 0.02).

DISCUSSION

Newborn hearing screening is a very important aspect of early pediatric care, though environmental and patient factors that affect screening success have not been well studied. Certain risk factors, such as prematurity, prolonged mechanical ventilation, low birth weight, and NICU stays longer than 5 days increase the likelihood of hearing loss. Identifying environmental conditions that support successful screening may enable earlier intervention.[6]

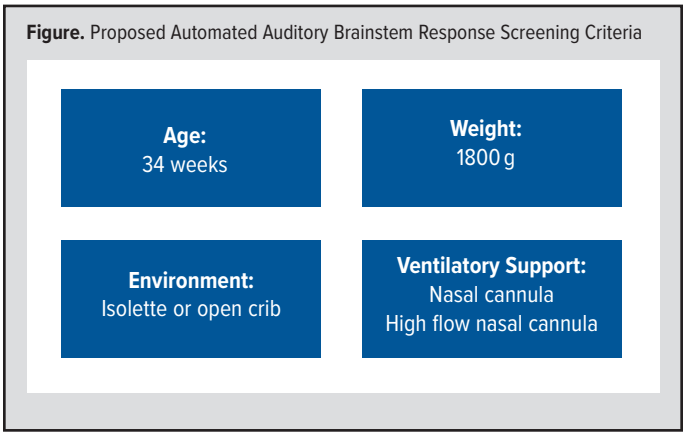
In this study, we found that successful screening can be performed in infants with a variety of methods of supplemental oxygenation delivery, especially for those using a nasal cannula and HFNC. It is important to note that there were no differences noted regarding gender. A proposed screening algorithm for infants is included in the Figure.

A variety of factors contributed to the inconclusive results. Often, inability to adequately apply the forehead and/or the neck electrodes due to the ventilation system in place led to poor electrode impedance. Ventilated infants consistently produced high artifact levels, preventing test completion. In one of these infants, the machine defaulted in a non-physiological noise interference message. Using a volume control ventilator, the ALGO machine noise was low, but infant noise was high; thus, the screening was inconclusive. Testing of infants on HFNC in an open crib was deemed inconclusive after the machine failed to run 3 times. This infant was 39 weeks gestation and approximately 3000 g, but the flow rate > 5 liters of HFNC was a higher flow rate of supplemental air than other neonates in the study. Attempts were made to eliminate all other sources of noise during the screening, but the higher flow of oxygen likely was responsible for the failed AABR. The ALGO equipment also would not run for an infant in an isolette and on a ventilator, likely due to the noise from the ventilator. Testing was most successful when an infant was quiet and asleep, though screening was possible if the infant was awake but quiet. Level of infant arousal was generally unrelated to successful screening, with both sleeping and quiet but awake infants yielding inconclusive results.

Limitations

There are limitations to this study. It was performed at a single institution NICU with a relatively small sample size. Infants with low or very low birth weight did not have enough skin surface area to adequately place electrodes as intended by the equipment manufacturer. Presence of syndromes was not controlled for and may have affected screening results. Future areas of study include expanding the sample size and confirming screening ABR findings with confirmatory ABR in the form of a diagnostic ABR.

Figure. Proposed Automated Auditory Brainstem Response Screening Criteria



CONCLUSIONS

Newborn AABR screening can be successfully performed in NICU infants receiving supplemental oxygen and in various crib configurations. Screening is feasible at younger gestational ages than typically practiced, with successful tests obtained in infants as early as 33 weeks and weighing ≥1800 g. High-flow nasal cannula and nasal cannula support screening success, while invasive ventilation remains a barrier.

Early detection of hearing loss improves outcomes and supports adherence to JCIH 1-3-6 guidelines. Earlier screening in the NICU may reduce loss to follow-up and facilitate timely intervention for affected infants.

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US Medical Schools Provide Limited Information and Coverage for Fertility Treatment and Preservation

Micaela Stevenson Wyszewianski, MD; Eliyah Stevenson, BS; Sarah Okeke, BS

ABSTRACT

Introduction: Female physicians experience high rates of infertility and report barriers to accessing treatment, including lack of health insurance coverage and limited knowledge of available benefits. Given the extended duration of training, medical school may be an optimal time for fertility preservation or treatment. However, whether medical schools provide information or coverage for these services in unclear. This study aimed to assess (1) whether US medical school websites provide information on health insurance coverage for fertility preservation and treatment and (2) whether medical schools offer health insurance coverage for these services.

Methods: Accredited allopathic and osteopathic medical school websites were reviewed for information on fertility coverage available. Summary-of-benefits documents were examined for coverage of in vitro fertilization (IVF), intrauterine insemination (IUI), elective oocyte cryopreservation, fertility medications, and infertility evaluation. Chi-squared tests assessed differences by school type, funding source, and geographic region.

Results: Of 108 medical school websites reviewed, 48.2% provided information on elective fertility preservation and 52.7% on IVF coverage. Osteopathic schools more frequently provided information on IVF coverage (48.71% vs 24.51%; $P = .006$) and fertility preservation coverage (43.58% vs 22.58%; $P = .014$). Only 8.33% of schools offered coverage for IVF or elective fertility preservation. Publicly funded schools more often offered coverage for IUI (23.3% vs 3.57%; $P = .027$), fertility medications (23.33 % vs 0%; $P = .005$), and infertility evaluation (31.03% vs 3.57%; $P = .006$). Schools in the Northeast most frequently offered coverage for these services.

Conclusions: US medical schools provide limited information and health insurance coverage for fertility preservation and treatment. Publicly funded and Northeastern schools more frequently offer coverage, which may influence prospective students' decisions.

INTRODUCTION

Infertility is a common diagnosis, with approximately 14% of female patients experiencing infertility in the United States.[1] Infertility among female physicians is even more common than in the general population, with rates as high as 33% depending on physician subspeciality.[2,3] This high rate of infertility frequently has been attributed to female physicians' decision to delay childbearing compared with nonphysicians, which is often required to complete training and achieve promotions in their respective fields.[4-5]

Given this high rate of infertility among female physicians, access to fertility treatment and fertility preservation is often warranted. This is supported by calls from the American Medical Women's Association for access to fertility services for all female physicians.[6]

Prior studies have called for increased access to infertility treatment for physicians;[6] however, given that many physicians report that they may have accessed fertility preservation earlier had they known that infertility might be an issue in the future,[3] earlier access to oocyte preservation and potentially fertility treatment is warranted. Many medical schools in the United States require enrolled students to hold active health insurance coverage during training and provide plans through the institution that can be purchased by medical students.[7] Many medical students also express interest in fertility preservation while in medical school but perceive high financial barriers and limited access to health insurance coverage for these services.[8-10] Although medical students may perceive that

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they are unable to access fertility services for financial and insurance reasons, it remains unknown how frequently medical schools provide any information regarding fertility preservation or infertility coverage for medical students through offered health plans. Additionally, it remains unknown how frequently the plans used across the country by various osteopathic and allopathic medical schools provide coverage for infertility and fertility preservation.

Given that medical school may be the most optimal time to undergo fertility preservation or initiate fertility treatment depending on the patient's age and other reproductive factors or goals, many students may be interested in seeking infertility treatment or fertility preservation during this time. However, in the absence of knowing what is covered by medical school health plans, students are unable to use this information to make decisions about purchasing or enrolling in health insurance plans or enrolling at different medical schools based on services they may or may not provide.

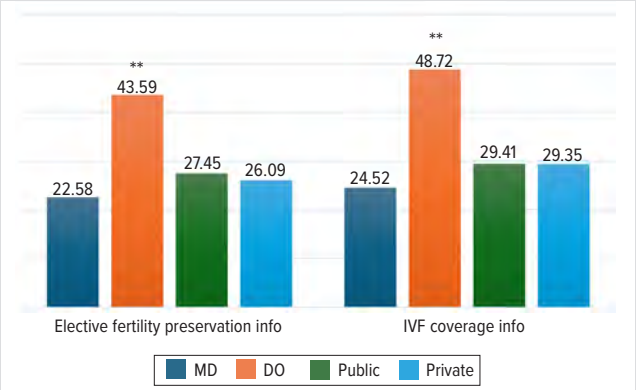
The primary objective of this study was to assess how frequently medical schools provide prospective and current medical students with information regarding coverage for infertility and fertility preservation. The secondary objective was to assess the frequency with which medical schools provide coverage for infertility and fertility preservation through health plans made available to medical students. We hypothesized that, considering the knowledge that medical students regularly report limited knowledge about fertility and fertility preservation, medical school websites would likely provide limited information. Additionally, we hypothesized that there would be limited, if any, coverage offered by health insurance plans that are offered to medical students for fertility preservation or treatment.

METHODS

No institutional review board approval was required because this study contained no human or animal subjects. A complete list of accredited allopathic and osteopathic medical schools was obtained through the Association of American Medical Colleges and American Osteopathic Association websites. Medical school websites were identified and accessed independently by 2 authors from December 17, 2024, through December 31, 2024. Authors were allotted 2.5 minutes to access the website and assess whether any health insurance information sponsored by the medical school was listed by searching "health insurance" in the respective search bars. If a health plan was found and benefits could be accessed, these were assessed by reading the benefits plans to determine whether they contained any information regarding coverage for infertility services or fertility preservation.

For medical schools that were found to have a health plan sponsored by the institution whose benefits could be reviewed, 2 authors then independently assessed health plans and determined whether coverage was provided for in vitro fertilization (IVF), intrauterine insemination (IUI), elective oocyte cryopreservation, medications used for ovulation induction or ovarian hyperstimulation, and fertility evaluation. No time limit was placed on assessment of the summary of benefits. There was 100% concordance between what information was available on each website and what was present in summary of benefits documents.

Figure 1. Differences in Information Provided on Elective Fertility Preservation and In vitro Fertility



Abbreviation: IVF, in vitro fertilization.
**$P < .05$.

Analyses were performed in R version 4.4.2 (R Core Team; R Foundation for Statistical Computing, Vienna, Austria) to assess whether medical schools in different regions of the country were more likely to provide information using chi-squared analyses. Additionally, differences were assessed using chi-squared analyses for likelihood of providing any information based on the presence of state-based insurance mandates for fertility coverage, whether the school was an osteopathic or allopathic medical school, and whether the schools were publicly or privately funded.

Medical schools that had previously been identified as providing information regarding coverage of infertility and fertility preservation were then analyzed using chi-squared analyses to assess regional differences in whether coverage was provided for IUI, IVF, fertility preservation through oocyte cryopreservation, fertility medications, IUIs, and evaluation for infertility. Additionally, we examined differences in provision of these services based on whether the school was an osteopathic or allopathic medical school, regional location of the medical school, and whether the schools were publicly or privately funded.

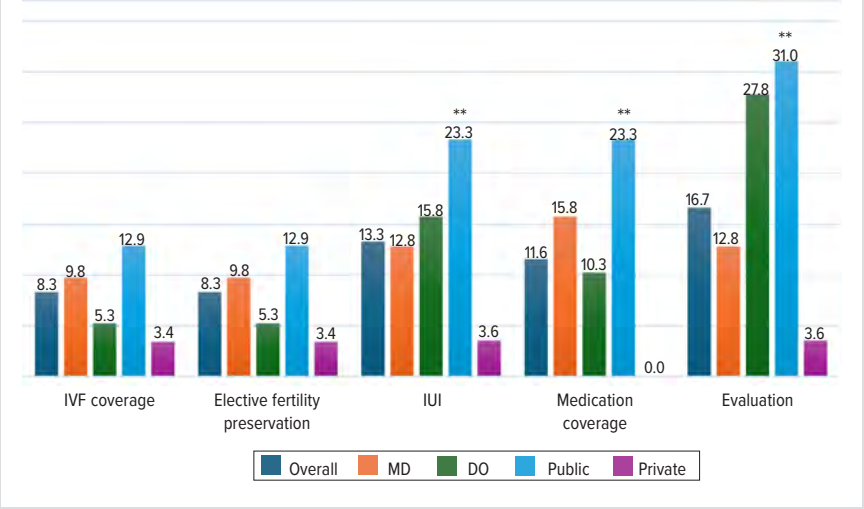
RESULTS

A total of 108 medical school websites were reviewed. Overall, 48.2% of medical schools provided information on elective fertility preservation, and 52.7% provide information on elective IVF coverage. Osteopathic medical schools more frequently provided information on IVF coverage (48.72% vs 24.52%; $P = .006$) (Figure 1) and fertility preservation coverage (43.59% vs 22.58%; $P = .014$) (Figure 1). There were no differences in information provided based on geographic region. Additionally, there were

no differences in whether states provided information based on the presence of state mandates for fertility treatment (25% vs 27.47%; $P = 1$).

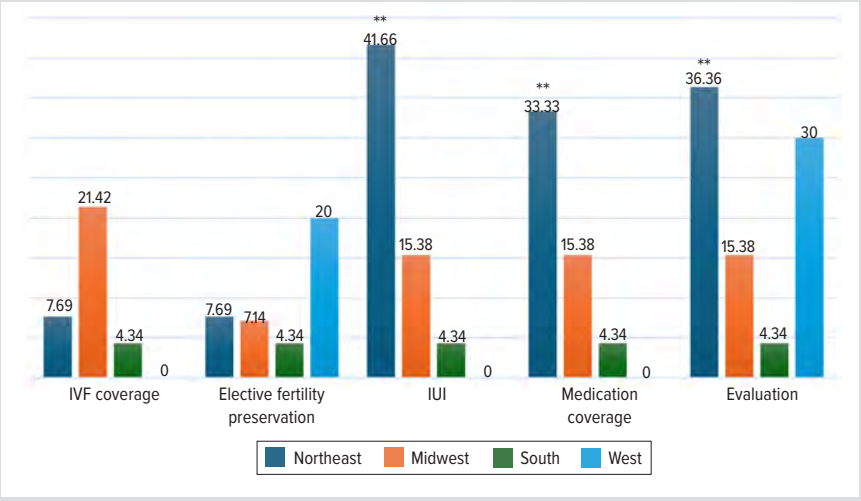
Sixty medical schools contained explanation-of-benefits pages that could be assessed for possible coverage for infertility services and fertility preservation. Only 8.33% of medical schools offered coverage for IVF or elective fertility preservation (Figure 2). There were no differences in coverage for IVF or elective fertility preservation based on public versus private funding or by allopathic versus osteopathic school (Figure 2). Publicly funded medical schools more frequently offered coverage for IUI (23.3% vs 3.57%, $P = .027$) (Figure 2), fertility medications (23.33 % vs 0%, $P = .005$) (Figure 2), and fertility evaluation (31.03% vs 3.57%, $P = .006$) (Figure 2). Medical schools in the Northeast most frequently offered coverage for IUI (41.66%), fertility medications (33.33%), and fertility evaluation (36.36%) and were more likely than other regions to offer coverage for these services (Figure 3). However, there were no regional differences in coverage for IVF or fertility preservation ($P = .021$ and $P = .531$, respectively) (Figure 3).

Figure 2. Differences in Coverage for Fertility Preservation and Treatment Based on MD vs DO Program vs Private Funding Status



Abbreviations: IVF, in vitro fertilization; IUI, intrauterine insemination.
**$P < .05$.

Figure 3. Regional Differences in Coverage for Infertility Services



Abbreviations: IVF, in vitro fertilization; IUI, intrauterine insemination.
**$P < .05$.

DISCUSSION

This study demonstrates that almost half of all medical schools frequently provide no information to medical students for fertility preservation and fertility treatment. Additionally, schools that do provide information on fertility preservation and treatment frequently do not provide coverage for these services. Osteopathic medical schools more frequently provided information on fertility treatment and fertility preservation. However, among schools that did provide information, health insurance coverage was extremely limited, with the majority of MD, DO, public, and private schools providing no coverage for fertility preservation or treatment. Public medical schools and those in the Northeast were more likely to provide coverage for IUIs, infertility medication, and infertility evaluation, as documented by summary-of-benefits pages provided by medical schools. These findings are similar to prior studies demonstrating that graduate students have limited access to fertility coverage through graduate health insurance plans,[11,12] thereby adding to the available knowledge regarding fertility treatment coverage for students pursuing higher education.

This study significantly adds to the literature by documenting what health insurance coverage is available to a significant population of patients at risk for infertility. As indicated by our study, prospective medical students hoping to use infertility services during medical school who will not have alternative health insurance coverage may seek to attend medical schools that are publicly funded and located in the Northeast. However, given the very limited fertility preservation coverage offered by medical schools, students may have limited access to elective oocyte preservation regardless of where they attend medical school. Additionally, given that prior studies have shown that only 25% of health insurance

plans offer coverage for infertility[13] and that insurance coverage for fertility services increases access to these services,[14,15] this study demonstrates that, compared to the general population, medical students may be an extremely underserved population at risk for infertility who need further attention.

Strengths of this study include that we assessed 100% of active websites for all accredited medical schools in the United States. Additionally, a significant but not excessive amount of time was spent on each website attempting to adequately gather information, simulating the time students may spend assessing available information. Another strength is that more than one author assessed each website and verified what benefits were available. Given that there was 100% concordance between authors examining each website, these conclusions are likely sound. This strengthens our claims that if the information was absent, it was after 2 different authors had looked for it.

Limitations of this study include that this is based solely on health plan information available on or associated with medical student websites. It is possible that additional information regarding student health plans is available at the time of an interview, enrollment, or upon direct request to the school. Additionally, these findings are based on information available in the summary of benefits on the website without logging in and assessing the plans in detail after enrollment. This information may be outdated, as it relies upon regular updates and therefore may not be reflect current coverage. However, given that this information is what a prospective or enrolled medical student would have access to when deciding to enroll in the plan, the authors believe this is an adequate representation of the knowledge used to make decisions regarding health plan purchase. Additionally, only 2 medical schools provided information with explanation-of-benefits plans that could only be accessed after providing login information. Therefore, we likely have a complete assessment of publicly available information. While all explanation-of-benefits plans were reviewed, it is possible that additional coverage is available to medical students that may not have been captured in summary of benefits documents.

Future studies should assess why medical schools provide limited information and coverage on fertility preservation and treatment. Additionally, efforts should be made to improve access to information for these services for medical students and assess whether these efforts improve student uptake of fertility services.

CONCLUSIONS

American medical schools provide limited information regarding health insurance coverage for fertility preservation and treatment. Osteopathic medical schools more frequently provide information about coverage for these services. Additionally, American medical schools generally provide limited coverage for fertility preservation and treatment. Publicly funded schools and those in the Northeast more often offer coverage for these services. Prospective students hoping to utilize fertility preservation or treatment may prefer to consider publicly funded medical schools and those in the Northeast United States.

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Violence Against Emergency Department Health Care Workers and the Effect of Wisconsin Act 209

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ABSTRACT

Background: Health care settings are not immune to workplace violence, and emergency department workers are especially susceptible. In 2021, Wisconsin Act 209 made it a felony to "intentionally cause bodily harm or threaten to cause bodily harm to a person who works in a health care facility." We conducted a study of emergency department workers to assess their experiences with violence and the perceived effects of Act 209.

Methods: We developed a survey for health care workers (nurses, physicians, and advanced practice providers) who were currently practicing in a Wisconsin emergency department. The reporting timeframe was March 23, 2022, through June 30, 2023.

Results: A total of 194 Wisconsin emergency department workers responded; 70.6% reported experiencing bodily harm, threats of bodily harm, or both. The median number of bodily harm incidents was 2, and 51.4% did not report these incidents. The median number of threats reported was 4, and 66.7% did not report them. Nurses experienced more threats of bodily harm than physicians. Overall, 40.2% of respondents were unaware of Act 209, and 67.6% indicated that abuse toward health care workers occurred at the same rate after its enactment as before. The most frequent barrier to reporting was "Person has a medical condition that might complicate application of the law."

Discussion: Most workers reported experiencing bodily harm or threats, and most did not report these incidents. Beyond clinical factors and time constraints, limited law enforcement bandwidth and perceptions of law enforcement as obstructive were the next most cited barriers. Only 1.2% of respondents reported feeling "definitely safer" after Act 209.

Conclusions: Violence against health care workers has become an expected consequence of working in the field. Legislative action is one tool to attempt to curb this trend. Further efforts to identify strategies that ensure the safety and wellness of health care workers should be a priority.

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BACKGROUND

The Joint Commission defines workplace violence as "an act or threat occurring at the workplace that can include any of the following: verbal, nonverbal, written, or physical aggression; threatening, intimidating, harassing, or humiliating words or actions; bullying; sabotage; sexual harassment; physical assaults; or other behaviors of concern involving staff, licensed practitioners, patients, or visitors."[1] Health care settings are not immune to workplace violence. The Bureau of Labor Statistics reported that in 2013, 27 out of 100 fatalities in health care and social service settings were due to assaults and violent acts.[2] The Occupational Safety and Health Administration reported that between 2011 and 2013, 70% to 74% of reported workplace assaults occurred in health care and social service settings compared with other settings.[2] Additionally, health care workers are nearly 4 times more likely to require time away from work because of injury due to violence compared with other types of injury.[2]

Several studies have shown that emergency department (ED) workers are especially susceptible to violence. For example, emergency nurses reported a 100% incidence of verbal assault and 82.1% incidence of physical assault in the previous year.[3] A 2009 study found that 78% of emergency medicine physicians experienced at least one workplace violence incidence in the previous 12 months, and 21% reported more than one incident; violence was experienced similarly among male and female physicians. Verbal threats were the most com-

mon type of workplace violence reported by physicians (75%), followed by physical assaults (21%).[4]

Recently, health care violence has become increasingly concerning. The Wisconsin Hospital Association reported increased verbal and physical acts of aggression directed at hospital staff since the COVID-19 pandemic.[5] In 2018, the Joint Commission published a Sentinel Event Alert regarding physical and verbal violence against health care workers that detailed the prevalence of the issue, contributing factors, and suggested actions. The Joint Commission recommended that health care workers remain alert and prepared to act when encountering violence and that organizations address the growing problem beyond simply increasing security; they offered seven actions to help. The most pertinent action included a recommendation to "clearly define workplace violence and put systems into place across the organization that enable staff to report workplace violence instances, including verbal abuse."[6]

The actions listed by the Joint Commission have often served as the foundation for legislation to mitigate workplace violence. A federal bill called Safety from Violence for Healthcare Employees (SAVE) Act (HR 2584/S 2768) has been introduced to the US House of Representatives and Senate.[7] Additionally, many states have implemented legislation at the state level to protect health care workers.[8]

Wisconsin Act 209 (2021 Assembly Bill 960) was enacted on March 23, 2022, and created Wisconsin Statute 940.204, which made it a Class H felony (punishable by up to 6 years' imprisonment and/or a fine not to exceed $10 000) to "intentionally cause bodily harm or threaten to cause bodily harm to a person who works in a health care facility or to a family member of a person who works in a health care facility" when the "actor knows or should have known that the victim works or formerly worked in a health care facility or is a family member of the person who…worked in a health care facility" and there is "no consent by the person harmed or threatened."[9,10] The act also created model language that health care facilities could post at their entrances alerting the public to the penalties under this statute.[11] "Health care facility" was defined to include a "hospital" as well as nine other care settings.[9]

We conducted a study of health care workers in Wisconsin EDs to assess the effect of Act 209 and reports of workplace violence. To our knowledge, no prior study has evaluated the impact of legislation on workplace violence in health care.

METHODS

The project was reviewed and approved by the institutional review board (IRB) at the Medical College of Wisconsin.

An anonymous, online survey was created in Qualtrics (Seattle, Washington) for distribution to registered nurses (RN), physicians (MD/DOs, including residents and attending physicians), and advanced practice providers (APP), including both physician assistants and nurse practitioners, who were currently practicing in a Wisconsin ED. Survey respondents were required to attest that they were currently employed in an ED in Wisconsin at the time they completed the survey. The survey was open from August 28, 2023, until November 1, 2023.

Table 1. Participant Demographic Information

Variable	N (%) or Median [IQR]
Credential	
MD/DO	96 (49.5)
RN	71 (36.6)
Advanced practice provider (NP/PA)	27 (13.9)
Years of practice	9.0 [4.0-14.0]
Age	36.0 [29.0-43.0]
Age group	
21-30	56 (29.3)
31-40	71 (37.2)
41+	64 (33.5)
Gender	
Female	127 (65.8)
Male	66 (34.2)
County of primary clinical practice	
Milwaukee	108 (55.7)
Dane	30 (15.5)
Waukesha	15 (7.7)
Other[a]	41 (21.1)

Abbreviations: MD, medical doctor; DO, doctor of osteopathic medicine; RN, registered nurse; NP, nurse practioner; PA, physician assistant.
[a]Other counties include Brown, Calumet, Dunn, Eau Claire, Fond du Lac, Jefferson, Marathon, Ozaukee, Portage, Racine, Rock, Sauk, Washington, Winnebago, and Wood.

We collaborated with multiple Wisconsin emergency medicine (EM)-based organizations to distribute the survey via the following established listservs: the Wisconsin Emergency Nurses Association, the Wisconsin Chapter of the American College of Emergency Physicians, and the Wisconsin Academy of Physician Assistants. The survey was also distributed to colleagues at several EM physician groups and EDs within the state via the authors' connections. The survey included a statement that it could be forwarded to any contact of a recipient who met the inclusion criteria. The distribution rules were intended to allow the survey to reach as many clinicians as possible; because of these distribution rules, a response rate could not be reported.

The defined timeframe of reference for survey questions was March 23, 2022, through June 30, 2023, reflecting approximately 13 months after statute implementation.

The survey collected demographic information including gender, age, discipline (MD/DO, RN, or APP), years in practice, and county of primary ED employment. Remaining questions focused on respondents' knowledge on Wisconsin Act 209; experience of violence or threats; barriers to preventing violence or threats; and their subjective perception of safety (not safer, somewhat safer, definitely safer) in the ED. Branching logic was used to ask follow-up questions based on responses; for example, if a respondent reported being a victim of bodily harm during the study timeframe, they were directed to specific questions regarding that incident, whereas those who had not been victims skipped those

Table 2. Survey Responses Regarding Experiences of Bodily Harm and/or Threats of Bodily Harm in the Workplace and Reporting Them

		Discipline			Gender		Age		
	Overall n (%)	MD/DO n (%)	RN n (%)	APP n (%)	Male n (%)	Female n (%)	21–30 n (%)	31–40 n (%)	41+ n (%)
Participants who have experienced bodily harm or threats to cause bodily harm[a]									
Both	21 (11.4)	7 (7.4)	13 (20.3)	1 (3.8)	7 (10.8)	14 (11.9)	8 (14.5)	4 (5.8)	9 (15.5)
Bodily harm	14 (7.6)	7 (7.5)	6 (9.4)	1 (3.9)	5 (7.7)	9 (7.6)	5 (9.1)	6 (8.7)	3 (5.2)
Threats	95 (51.6)	45 (47.9)	35 (54.7)	15 (57.7)	30 (46.2)	64 (54.2)	25 (45.5)	36 (52.2)	33 (56.9)
Not sure	8 (4.3)	4 (4.3)	1 (1.6)	3 (11.5)	2 (3.1)	6 (5.1)	5 (9.1)	2 (2.9)	1 (1.7)
No	46 (25.0)	31 (33.0)	9 (14.1)	6 (23.1)	21 (32.3)	25 (21.2)	12 (21.8)	21 (30.4)	12 (20.7)
Incidents of bodily harm									
Incidents of bodily harm,median [IQR][b]	2 [1-3]	1 [1-2.25]	2 [1-2]	4.5 [4.25-4.75]	2 [2-3]	1 [1-2]	1.5 [1-4.75]	1 [1-2.75]	2 [1.25-2]
Incidents reported to employer/hospital or police[a]									
All	11 (31.4)	3 (21.4)	8 (42.1)	0 (0.0)	4 (33.3)	7 (30.4)	3 (23.1)	2 (20.0)	6 (50.0)
Some	6 (17.1)	1 (7.1)	4 (21.1)	1 (50.0)	3 (25.0)	3 (13.0)	3 (23.1)	1 (10.0)	2 (16.7)
None	18 (51.4)	10 (71.4)	7 (36.8)	1 (50.0)	5 (41.7)	13 (56.5)	7 (53.8)	7 (70.0)	4 (33.3)
Where incidents of bodily harm were reported									
Employer/hospital and police	8 (72.7)								
Police	2 (18.2)								
Employer/hospital	1 (9.1)								
Legal consequences for perpetrator of bodily harm									
Yes, all	3 (8.6)								
Yes, some	3 (8.6)								
No	29 (82.9)								
Threats to cause bodily harm									
No. of threats to cause bodily harm, median [IQR][b]	4 [2-7]	3 [2-5]	5 [3-10]	3 [2-5]	4 [2-7.75]	4 [2-7]	5 [2-10]	3 [2-5]	3 [2-7]
Incidents reported to employer/hospital or police[a]									
All	16 (14.2)	5 (9.8)	11 (23.4)	0 (0.0)	4 (11.1)	12 (15.8)	4 (12.5)	4 (10.3)	8 (19.5)
Some	22 (19.5)	3 (5.9)	16 (34.0)	3 (20.0)	6 (16.7)	16 (21.1)	7 (21.9)	9 (23.1)	6 (14.6)
None	75 (66.4)	43 (84.3)	20 (42.6)	12 (80.0)	26 (72.2)	48 (62.2)	21 (65.6)	26 (66.7)	27 (65.9)
Where threats to cause bodily harm were reported									
Employer/hospital and police	9 (28.1)								
Police	3 (9.4)								
Employer/hospital	20 (62.5)								
Legal consequences for perpetrator of threats to cause bodily harm									
Yes, all	1 (0.9)								
Yes, some	3 (2.7)								
No	108 (96.4)								
Considered leaving your current/previous position as a health care worker due to being a victim[a]									
Yes, and did leave	6 (4.9)	1 (1.8)	4 (7.7)	1 (6.7)	1 (2.5)	5 (6.2)	1 (2.8)	2 (4.7)	3 (7.1)
Yes, but have not left	69 (56.6)	28 (50.9)	33 (63.5)	8 (53.3)	23 (57.5)	45 (55.6)	26 (72.2)	21 (48.8)	22 (52.4)
No, have never considered leaving	47 (38.5)	26 (47.3)	15 (28.8)	6 (40.0)	16 (40.0)	31 (38.3)	9 (25.0)	20 (46.5)	17 (40.5)
Considered leaving your current/previous position as a health care worker due to concern of becoming a victim[a]									
Yes, and did leave	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Yes, but didn't leave	14 (28.0)	6 (18.2)	6 (66.7)	2 (25.0)	4 (18.2)	10 (35.7)	3 (23.1)	7 (30.4)	4 (30.8)
No, have never considered leaving	36 (72.0)	27 (81.8)	3 (33.3)	6 (75.0)	18 (81.8)	18 (64.3)	10 (76.9)	16 (69.6)	9 (69.2)
Reporting incidents and/or threats of bodily harm									
Aware of primary practice site's reporting policies and procedures for violence in the workplace[a]									
Yes	91 (52.6)	39 (44.3)	40 (64.5)	12 (52.2)	34 (54.8)	56 (50.9)	24 (49.0)	32 (47.8)	34 (61.8)
No	82 (47.4)	49 (55.7)	22 (35.5)	11 (47.8)	28 (45.2)	54 (49.1)	25 (51.0)	35 (52.2)	21 (38.2)

[a]Analyzed using chi-square test or Fisher exact test.

[b]Analyzed using Kruskal-Wallis test or Mann-Whitney U test.

Table 3. Survey Responses Regarding Act 209 and Its Impact

	Discipline				Gender		Age		
	Overall n (%)	MD/DO n (%)	RN n (%)	APP n (%)	Male n (%)	Female n (%)	21-30 n (%)	31-40 n (%)	41+ n (%)
Heard of Act 209[a]									
Yes, and completely understand it	30 (15.5)	11 (11.5)	15 (21.1)	4 (14.8)	11 (16.7)	19 (15.0)	5 (8.9)	9 (12.7)	14 (21.9)
Yes, but do not completely understand it	86 (44.3)	43 (44.8)	33 (46.5)	10 (37.0)	26 (39.4)	59 (46.5)	16 (28.6)	38 (53.5)	31 (48.4)
No	78 (40.2)	42 (43.7)	23 (32.4)	13 (48.1)	29 (43.9)	49 (38.6)	35 (62.5)	24 (33.8)	19 (29.7)
Frequency of verbal and/or physical abuse towards health care workers[a]									
More frequently	51 (29.5)	14 (15.9)	31 (50.0)	6 (26.1)	14 (22.6)	36 (32.7)	15 (30.6)	14 (20.9)	20 (36.4)
At the same rate	117 (67.6)	70 (79.5)	31 (50.0)	16 (69.6)	45 (72.6)	72 (65.5)	32 (65.3)	53 (79.1)	32 (58.2)
Less frequently	5 (2.9)	4 (4.5)	0 (0.0)	1 (4.3)	3 (4.8)	2 (1.8)	2 (4.1)	0 (0.0)	3 (5.5)
Improved personal safety since Act 209 enacted									
Yes, definitely safer	2 (1.2)	2 (2.3)	0 (0.0)	0 (0.0)	2 (3.2)	0 (0.0)	1 (2.0)	0 (0.0)	1 (1.8)
Yes, somewhat safer	29 (16.8)	19 (21.6)	8 (12.9)	2 (8.7)	10 (16.1)	19 (17.3)	8 (16.3)	11 (16.4)	9 (16.4)
No, not safer	142 (82.1)	67 (76.1)	54 (87.1)	21 (91.3)	50 (80.6)	91 (82.7)	40 (81.6)	56 (83.6)	45 (81.8)
Changes/additions at primary clinical practice site reporting/documentation policies or education on workplace violence?									
Reporting/documentation policies and education	22 (12.7)								
Reporting/documentation policies	9 (5.2)								
Education	26 (15.0)								
None	116 (67.1)								
Aware of signage about Act 209 being posted in health care facility for the public to view									
Yes	45 (26.0)								
No	128 (74.0)								

[a]Analyzed using chi-square test or Fisher exact test.

questions. The study team and local subject matter experts vetted the questions. A final qualitative question asked respondents about additional measures or changes they believed would promote safety in their ED.

Data were analyzed utilizing R (R Core Team, version 4.3.1). Frequencies and descriptive statistics were calculated; categorical variables were analyzed using Fisher exact test or chi-square test, and continuous variables using Kruskal-Wallis test or Mann-Whitney U test.

Data on initial charges under §940.204(2) (Bodily Harm or Threat to Employee of Healthcare Facility or Family) and § 940.204(3) (Bodily Harm or Threat to Healthcare Provider or Family) were obtained through a public records request from the Wisconsin Office of the Director of the State Courts via a Wisconsin representative. When analyzing data by county of primary clinical practice, only counties with 10 or more respondents were individually identified to ensure confidentiality per IRB restrictions.

RESULTS

A total of 194 Wisconsin ED staff responded to the survey (Table 1). Almost half were physicians (49.5%), and the sample had a median of 9 years in practice. Respondents' median age was 36 years, and about two-thirds were women (65.8%). When asked about the county of primary clinical practice, more than half (55.7%) reported Milwaukee County.

Experiences of Bodily Harm and/or Threats of Bodily Harm in the Workplace

Experiencing bodily harm and/or threats of bodily harm was common, with 70.6% indicating they had experienced bodily harm, threats of bodily harm, or both (Table 2) during the defined timeframe (March 23, 2022–June 30, 2023). There was a statistically significant difference by discipline: a greater proportion of nurses (84.4%) reported experiencing bodily harm and/or threats compared with physicians (62.8%) or APPs (65.4%) ($P = .02$). There was no relationship with gender ($P = .26$) or age ($P = .28$).

For bodily harm, the median number of incidents reported was 2 (IQR, 1-3; range 1-20). There was no statistically significant difference in median incidents by discipline ($P = .10$), gender ($P = .09$), or age ($P = .81$). When asked how many incidents were reported to an employer and/or law enforcement, more than half (n = 18; 51.4%) said they reported none; there was no significant difference by discipline ($P = .18$), gender ($P = .18$), or age ($P = .45$). Of those who did report instances of bodily harm, most (n = 8; 72.7%) reported to both their employer and law enforcement. However, most respondents who experienced bodily harm (n = 29; 82.9%) were unaware of any legal consequences for the perpetrator, although most did not report the incident.

For threats of bodily harm, the median number of incidents reported was 4.0 (IQR, 2.0-7.0; range, 1-120). There was a statistically significant difference by discipline ($P = .01$) but not gender ($P = .97$) or age ($P = .38$). Nurses (median, 5.0; IQR, 3-10) reported more threats than physicians (median, 3; IQR, 2-5). Similar to bodily harm, most respondents (66.4%) did not report threats to their employer or law enforcement. A greater percentage of nurses (n = 11; 23.4%) reported all incidents compared with] physicians (n = 5; 9.8%) or APPs (n = 0;

Table 4. Survey Responses Regarding Barriers to Reporting and Enforcement

	Barrier based on experience with incident, n (%)[a]	Barrier based understanding of Act 209, n (%)[b]
Clinical		
Person has a medical condition (to include psychiatric) that might complicate application of the law	95 (77.2)	34 (69.4)
Logistical		
I am unaware of infrastructure in place for reporting	41 (33.3)	21 (42.9)
Hospital personnel are unaware of infrastructure in place for reporting	31 (25.2)	19 (38.8)
Hospital personnel are obstructive or resistant to reporting	26 (21.1)	4 (8.2)
Legal		
Law enforcement are obstructive or resistant to reporting	41 (33.3)	10 (20.4)
Law enforcement bandwidth to respond and/or report incident	51 (41.5)	0 (0.00)
External legal counsel (i.e. district attorney) are obstructive or resistant to reporting	22 (17.9)	6 (12.2)
External legal counsel (i.e. district attorney) bandwidth to investigate or prosecute	28 (22.8)	6 (12.2)
Professional		
Conflict with your professional and moral obligation as a health care worker	33 (26.8)	10 (20.4)
Lack of desire to report the incident	40 (32.5)	18 (36.7)
Lack of time to report the incident	69 (56.1)	31 (63.3)

[a]This item was presented only to participants who said they had experienced bodily harm and/or threats to bodily harm (n = 130). Seven participants did not respond to items regarding barriers, leaving 123 participants who responded to these items.

[b]This item was presented only to participants who said they had not experienced bodily harm or threats to bodily harm, or those who said they were not sure (n = 54). Five participants did not respond to this item, resulting in n = 49.

0.0%) ($P < .01$); there was no difference by gender ($P = .69$) or age ($P = .72$). Most who reported threats (62.5%) reported to their employer only, and almost all (96.4%) were unaware of legal consequences to the perpetrator.

Of those who had experienced bodily harm and/or threats of bodily harm, more than half (56.6%) said they had considered leaving their position; this did not differ by discipline ($P = .22$), gender ($P = .80$), or age ($P = .24$). About one-quarter (28%) of respondents who had not experienced harm or threats said they had considered leaving due to concerns about becoming a victim. A greater proportion of nurses (66.7%) said they had considered leaving compared with physicians (18.2%) or APPs (25.0%) ($P = .02$). There was no significant difference by gender ($P = .22$) or age ($P = .39$).

Act 209 and Its Impact

When asked about their awareness and understanding of Act 209 prior to reading this study's informational materials, 15.5% of respondents stated they had heard of it and completely understood it, 44.3% had heard of it but did not completely understand it, and 40.2% were unaware of Act 209. Awareness and understanding of Act 209 did not differ by discipline ($P = .32$) or gender ($P = .63$) (Table 3). There was a statistically significant difference by age group ($P = .001$): a greater percentage of respondents ages 21 to 30 (62.5%) were unaware of Act 209 compared with those aged 31 to 40 (33.8%) or 41 and older (29.7%).

About two-thirds of respondents (n = 117; 67.6%) indicated that verbal and/or physical abuse toward health care workers occurred at about the same rate since enactment of Act 209 as before. There was a significant difference between nurses and physicians: 50.0% of nurses said abuse was happening more frequently compared with 15.9% of physicians. Conversely, 79.6% of physicians said abuse was happening at the same rate versus 50.0% of nurses ($P < .01$). There was no significant difference by gender ($P = .22$) or age ($P = .06$).

Respondents did not perceive a difference in their safety since Act 209 was enacted: 82.1% indicated that they did not feel safer and there was no significant difference by discipline ($P = .29$), gender ($P = .29$), or age ($P = .89$). Most respondents (67.1%) said there had been no change to reporting or documentation policies or education about workplace violence at their primary clinical site since enactment. When asked if they were aware that their system had posted the model language recommended in Act 209; almost three-quarters of respondents (74.0%) said they did not know of any language posted in public view at their site.

Reporting and Barriers to Reporting and Enforcement

More than half (52.6%) of respondents said they were aware of their primary practice site's reporting policies and procedures for workplace violence and were confident they could report an incident per policy. There was no significant difference by discipline ($P = .05$), gender ($P = .74$), or age ($P = .25$) (Table 2).

Respondents who had experienced harm and/or threats were asked to select and rank perceived barriers to reporting and enforcement of Act 209 (Table 4). The most frequently selected barriers were (1) "Person has a medical condition (to include psychiatric) that might complicate application of the law" (77.2% selected as a barrier); (2) "Lack of time to report the incident" (56.1%); and (3) "Law enforcement bandwidth to respond and/or report incident" (41.5%). Respondents who were not victims also were asked to indicate perceived barriers. The most frequently selected were (1) "Person has a medical condition (to include psy-

chiatric) that might complicate application of the law" (69.4% selected as a barrier); (2) "Lack of time to report the incident" (63.3%); and (3) "I am unaware of infrastructure in place for reporting" (42.9%).

Charges Under Act 209

When asked to estimate how many people had been charged (formal accusation of criminal activity) in the county of their primary clinical practice under Act 209 from March 23, 2022, through February 28, 2023, respondents from Milwaukee County estimated a median of 5 (IQR, 2-20; range, 0-500), respondents from Dane County estimated a median of 3.5 (IQR, 0.75-10.5; range, 0-65), and respondents from Waukesha County estimated a median of 4 (IQR, 1-10; range, 0-100). Based on an open records request, 15 people were charged in Milwaukee County, 12 in Dane County, and two in Waukesha County during this time period. When asked about the number of charges in the state of Wisconsin, the median response was 20 (IQR, 5-100; range, 0-1500); there were actually 131 charges.

Respondents' Recommendations for Improvement

A final qualitative question asked respondents about additional measures or changes they believed would promote safety in their ED. Thematic analysis showed that most felt the greatest opportunity was in execution of the statute rather than the statute itself. Barriers listed in the previous section were similarly cited as opportunities for improvement. Additional unique comments included increasing the severity of felony charges, enhancing mental health resources in the community, specifically addressing sexual assault within the statute, and improving collaboration with law enforcement and the entire justice system.

DISCUSSION

Violence against health care workers is an ongoing issue in the United States, and ED staff are often recipients of threatening and dangerous behavior. The percentage of Wisconsin survey respondents who reported being victims of threats or actual bodily harm (70.6%) is consistent with published literature. Additionally, our study supports previously published data demonstrating that nurses report experiencing a higher rate of violence than physicians and APPs.[4,13] Literature suggests that 70% to 80% of instances are not reported.[12,13] Our study substantiated that incidents are grossly underreported, with 51.4% of respondents not reporting any experienced instances of bodily harm and 66.4% not reporting any threats. Previous literature also has shown that health care team members who experience violence perceive a patient's clinical condition as precluding responsibility for their actions, which serves as a barrier to reporting; our study similarly found this to be the highest-ranked barrier.[14]

One notable finding was the degree to which law enforcement was perceived as a barrier to reporting violence. Beyond clinical factors and time constraints, law enforcement bandwidth and perceptions of law enforcement as obstructive or resistant to reporting were the next most cited barriers. Law enforcement in the ED has a long and complicated history, with varying degrees of trust and support from the health care teams—often related to clinical care disruptions, privacy concerns, and effects on patient trust. ED staff interactions with law enforcement have been described as a "dual loyalty" ethical framework, reflecting the idea that health care worker interactions with law enforcement can be influenced by both positive and negative perceptions of the criminal justice system and law enforcement presence in the ED.[15] It is unknown how these established relationships may introduce bias in reporting violence and in survey responses.[16] Given these perceptions, opportunities exist for enhanced collaboration and improved understanding between health care teams and local law enforcement when statutes such as Act 209 are enacted. The Wisconsin Department of Justice has posted model language per the statute to its website, but most health care workers did not recall seeing it posted at their hospital.[11]

Another unique aspect of this study was evaluating the effect of legislation criminalizing violence toward health care workers. Wisconsin Act 209 was lauded as a way to "send a strong message to the public that threats against workers are taken seriously and not tolerated in Wisconsin."[17] At a foundational level, the law struggles to maintain relevance amongst its intended protective population, as 40.2% of survey respondents were unaware of its existence. While well-intentioned, health care workers continued to report high levels of violence and minimal tangible changes to violence patterns in the post-Act study period. Only 1.2% of respondents reported feeling "definitely safer" after Act 209, while 82.1% did not feel safer. Almost all respondents (97.1%) indicated that violence was occurring at the same frequency or more frequently than before Act 209. Barriers to reporting, underreporting, and external factors—including law enforcement and the legal system—represent significant challenges to ensuring the safety of Wisconsin ED clinicians and staff. Violence against health care workers is far more complex than it appears: ethical, clinical, and legal quandaries intersect at the point of care.

Burnout among ED nurses and physicians far exceeds rates in other areas of health care, and respondents in this study reported understandably high rates of consideration of leaving their jobs.[18-20] For an already strained health care sector, addressing workplace violence is not only a matter of safety but also a requisite for sustaining a critically needed workforce.

Limitations

This study has several limitations. The survey required attestation that respondents were currently employed in a Wisconsin ED in one of the listed disciplines; however, we could not verify discipline or employment, nor confirm that respondents completed the survey only once. The survey was restricted to ED health

care workers—specifically nurses, physicians, and APPs—while Act 209 encompasses all health care settings and workers. Thus, these findings may not be representative of the broader health care workforce. Additionally, survey distribution methods relied on established listservs and word of mouth, likely skewing responses toward to large population centers in urban environments; rural areas were likely underrepresented. Respondents were disproportionately physicians despite nurses comprising a larger share of the ED workforce. Timeframes were based on publicly available data and statute enactment dates; recall bias likely influenced responses. These limitations are common in retrospective surveys. Additionally, the effect of the COVID-19 pandemic on workplace violence is unknown, though several studies have attributed increases in violence against health care workers to pandemic-related stress.[21,22]

CONCLUSIONS

Violence against health care workers has become an expected consequence of working in the field. Legislative action is one of the most recent tools to curb this trend, and as of 2024, nearly all 50 states have enacted or are considering laws to establish or increase criminal penalties for violence or threats against health care workers and/or to enable health care facilities to enhance worker protections. A federal law has also been introduced. Despite Wisconsin passing legislation in 2022, most ED health care workers in our study subjectively believe that workplace violence is unchanged or increasing. For an already struggling health care sector, addressing workplace violence is essential to sustaining a critically needed workforce.

Legislative action may be necessary, but implementation and effectiveness are limited by a lack of awareness among health care workers and substantial barriers to reporting and enforcement. With only a small proportion of respondents fully understanding the statute, efforts should focus on disseminating information about the law, as its true efficacy may not yet be realized. Further work to identify strategies that ensure the safety and wellness of health care workers should be a priority. This study adds to the available literature on the effect of legislative action but leaves many questions answered in solving this complex problem.

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Putting Out Fires: The Experiences of Wisconsin Rural Health Officers During the COVID-19 Pandemic

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ABSTRACT

Introduction: The COVID-19 pandemic created significant challenges for public health systems, which were exacerbated in rural settings due to chronic issues of resource allocation, underfunding, and politicization. Differences in attitudes about governmental roles have resulted in differences in acceptance of public health interventions, such as masking mandates and COVID-19 vaccinations. This study explored contemporaneously the pandemic's impact through the lens of Wisconsin rural health officers (RHOs).

Methods: We conducted semistructured key informant interviews with RHOs in 13 rural Wisconsin counties to explore the breadth and depth of their lived experiences during the COVID-19 pandemic. We applied directed content analysis to interview transcripts.

Results: RHOs identified numerous challenges faced during the pandemic, including lack of adequate resources and workforce capacity, inconsistent communication from state health officials, lack of support from their communities and local political leaders, misinformation and disinformation, strained personal relationships, and threats of physical violence. These challenges caused mental anguish and burnout among health officers and their colleagues. RHOs also identified successes, including strengthened partnerships with local health care organizations, school administrators, and businesses.

Conclusions: Health officers in rural Wisconsin faced significant challenges throughout the COVID-19 pandemic that impeded their ability to address COVID-19 and other health needs in their communities. Allocating resources such as increased funding for public health infrastructure, ensuring protections for public health employees, and supporting improved communication channels between state and local health departments could help RHOs mitigate effects of COVID-19 and successfully address the health of rural communities.

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INTRODUCTION

The COVID-19 pandemic has claimed the lives of more than 1.1 million people in the United States (US) since 2020[1] and highlighted myriad structural shortcomings of US public health and health care systems. While the COVID-19 virus has spread to rural and urban communities alike, rural communities experience disparate outcomes related to morbidity and mortality.[2] For example, as of October 2021, the cumulative mortality rate of COVID-19 in urban counties was 201 per 100 000 compared to 247 per 100 000 in rural counties, with the highest mortality rates in rural farming communities.[3]

In Wisconsin, where agriculture is a primary industry, nearly 1.5 million people live in a rural county.[4] As of January 2023, there were more than 15 900 deaths and 1.97 million COVID cases reported in Wisconsin.[5] Wisconsin's nonmetropolitan counties were disproportionately burdened with an additional 82 deaths per 100 000 compared to metropolitan counties. Similarly, counties designated as rural by the National Center for Health Statistics classification had an additional 98 deaths per 100 000 than large metro areas. In addition to the direct health consequences of the virus, Wisconsin has faced numerous challenges apparent throughout the US, including strains on the local economy, overburdened public health infrastructure, and increasing political divisiveness[6-8]—hardships that have disproportionately affected rural communities.[9]

People living in rural communities experience a range of persistent disparities in sociostructural determinants of health and

health care. Compared to those living in nonrural communities, populations residing in the rural US have higher poverty rates, poorer insurance coverage, fewer physicians, and limited access to public transportation and broadband internet.[10] In 2019, all 10 of the major causes of mortality were highest in rural areas, and the death rate was 20% higher than that of urban areas.[11] These factors made rural communities especially vulnerable to the challenges brought on by the pandemic.[2,9,12]

Health officers have a unique perspective that can enhance our understanding of this unprecedented public health crisis. Rural health departments are more likely to be underfunded and understaffed than health departments in urban areas.[13] Due to staff and funding constraints, rural health officers (RHOs) often assume multiple rules, such as local nurse, vaccine and testing coordinator, fiscal agent, and customer service representative. Existing evidence highlights the disparate impact of COVID-19 on rural areas,[11-13] but no studies to our knowledge have examined the unique experiences of and sought insight of RHOs during the pandemic. Such information could help inform how best to allocate resources to mitigate the effects of this and future pandemics.

The purpose of this study was to document the experiences of RHOs working on the frontline during the COVID-19 pandemic. RHOs have firsthand knowledge that is critical to understanding the successes and challenges unique to rural Wisconsin, as well as those commonly experienced across the country.

METHODS

Sampling

This study was undertaken through a partnership between the University of Wisconsin–Madison Department of Family Medicine and Community Health, the Wisconsin Office of Rural Health, and the University of Wisconsin–La Crosse Graduate Department of Public Health and Community Health Education. The UW-Madison Health Sciences Institutional Review Board categorized this work as quality improvement and deemed it exempt. To recruit participants, the lead author (SC) sent an email invitation to each health officer in all 32 Wisconsin counties that are designated as rural as defined by the Wisconsin Office of Rural Health (WORH).[14] The recruitment email included the purpose of the study, expectations of participants, and the semistructured interview guide. Participants were eligible if they had served in the health officer role in a rural county for at least 6 months.

Data Collection

The study team created an interview guide comprising 13 questions to explore RHOs' successes, challenges, and personal experiences during the COVID-19 pandemic (Box). SC obtained oral consent and conducted interviews via Zoom.

Data Analysis

Audio files were transcribed verbatim using Otter.ai software (Otter.ai, Inc,) and checked for accuracy by the interviewer. Clean transcripts were uploaded into NVivo (NVivo, Release 1.0; QSR International). Under the guidance of a researcher with expertise in mixed methods (SH), 2 coders (SC, HB) applied directed content analysis to transcripts by developing codes reflective of interview transcripts and RHOs' own words.[15] Together, the 3 analysts reviewed transcripts and developed a start list of deductive codes reflective of common successes, challenges, and personal experiences RHOs expressed. In an iterative process that included discussing the start list among the full study team and testing the start list across a subset of interviews, the team developed a near-final codebook for review across the full study team. SC and HB applied the final codebook to all transcripts. To promote coding reliability, coders both coded a subset of 4 (31%) of interviews. Discrepancies were resolved at weekly analyst check-in meetings. All authors participated in discussions about the analytic processes and emerging findings, thus ensuring continuing comprehensive review and commentary. The authors collaboratively selected illustrative quotes for inclusion in the manuscript and ensured that quotes originated from the range of participants. Due to the small sample size, the divisiveness of COVID-19 public health measures, the safety of health officers, and the potential for participants to be identified, identification numbers are not included in the manuscript.

Box. Interview Guide

1. How would you describe your role as a health officer in a rural setting?
2. Overall, what was the impact of the COVID-19 pandemic on your community?
3. Tell me about your experiences as a rural health officer during the COVID-19 pandemic (successes? challenges?)
4. How did your community respond to COVID-19 mitigation strategies?
5. Were there any policies (local, state, and/or federal) that enhanced your role during the pandemic?
6. Any policies (local, state, and/or federal) that hindered your role?
7. Thinking over the past 2.5 years, what are some of the best things about your position?
8. What are some of the worst?
9. What are your key lessons learned over the past 2.5 years?
10. What do you think should be the next steps for greater preparation regarding disease prevention and control in the future?
11. Are there any policies that you suggest could support your work in the future?
12. Have you been involved in any innovative community-based programs I should note?
13. Is there anything else that is of importance that we did not cover today?

RESULTS

During May and June 2022, 13 RHOs (41% of those invited) participated in semistructured interviews that lasted 30 to 60 minutes. At least 1 county from each of the Wisconsin Public Health Regions was represented (Figure), with the exception of the Southeastern Region, as there are no counties in that region designated as rural by WORH.[14] We grouped emergent themes

into 10 overarching categories: (1) professional partnerships, (2) public health workforce and capacity, (3) personal impact on RHOs, (4) politicization of COVID-19, (5) personal relationships, (6) misinformation and disinformation, (7) lack of capacity for other programs, (8) inconsistent communication, (9) unique rural considerations, (10) key insights and policy recommendations.

Figure. Representation of Rural Health Officer Participation Across Wisconsin Public Health Regions, Including the Number of Individual Health Officers From Each Region That Participated in Qualitative Interviews

No counties in the Southeastern Region are designated rural by the Wisconsin Office of Rural Health (Source: Wisconsin Department of Health Services[16])

Professional Partnerships

Many RHOs emphasized the strengthened partnerships they developed with other organizations and stakeholders in their communities as one of the few positive outcomes of the pandemic. Although many of these partnerships existed before the pandemic, RHOs said the pandemic provided opportunities to work more closely and align priorities—an outcome they suggested would positively influence future collaborations. They also described new partnerships that emerged among stakeholders who historically may not have focused on public health efforts and said this cooperation was imperative for successfully addressing COVID in their communities, as illustrated by these comments:

> *"The positive piece of COVID is within 4 months, I probably made the connections in the community that would have taken me 4 years to have developed. So there is positive that has come out. I work very closely with the schools. I meet with all the superintendents. We'll continue to meet with all the superintendents, they like that that's a connection piece. So we don't just have to talk about COVID. We talk about all other things that might be impacting them."*

> *"Our long-term-care facilities, we've established, we know each other's first names. When they have a turnover, I know that. Our schools, I have all the superintendents' cell phones, they have mine, we talk regularly. So it has strengthened a lot of our relationships, especially with entities and business too. … I think any time that you know people personally, now we can call each other when there's a situation and just talk through things. I think that's going to help in the future for everything related to public health."*

Public Health Workforce and Capacity

RHOs recalled working countless hours, week after week, month after month throughout the pandemic. Many noted that overtime was not compensated adequately, contributing to high turnover in their offices. RHOs also almost unanimously described insufficient workforce capacity related to staffing, basic financial resources, or both. Some said these factors were unique to rural areas and exacerbated by the pandemic, where staff sizes were already small and teams were working within thin margins when the pandemic began. Several RHOs explained that even prior to the pandemic, a single RHO often assumed multiple roles. When the pandemic emerged, they said they had little choice but to redirect their efforts nearly entirely to COVID-19 mitigation. Consequently, they said childhood immunizations and programs such as the Women, Infants, and Children supplemental nutrition program and childhood lead screening programs were necessarily neglected. Their comments included:

> *"We only have 6 staff here. So I am not only the supervisor, but a lot of time, I'm also a nurse. I also did a lot of the actual work as far as COVID went. I would take calls on questions, do testing, vaccines, in addition to kind of trying to work with community partners to set things up, like testing and vaccines, and just over-*

all manage the response. [I am] the fiscal agent too, just making sure our grants and everything are covering our hours."

"We got grants, so we had plenty of money, but finding any workers… for shots and testing…was hard because they were already overwhelmed at their job. So it's kind of the first time in history that I remember that we had more money than people. It's usually the other way around."

Personal Impact on Rural Health Officers

RHOs said that the pandemic and its sequelae took a significant toll on their mental health. Interviewees detailed mental anguish suffered while trying to keep their communities safe. One RHO observed that staff members who answered phone calls from community members and read the comments on their social media pages seemed to experience the most burnout. Another recalled leaving a county board meeting and not knowing whether they were going to return to work the next day because of how defeated they felt. They said:

"What happens when you're burned out and you are under high stress for 2 years is that it affects your brain. It affects your memory, …your ability to handle stress, …your efficiency. And I think that is what we're seeing, especially with the people that have been in COVID nonstop. It's difficult to remember, it's difficult to be motivated. My staff that didn't work in COVID, as much, you know, they were pulled in when we had huge surges, or they were pulled in when we were doing mass vaccination clinics. But it wasn't nonstop. They are not feeling the same. They don't have the same burnout. Myself. I am burned out."

"I had staff who had to come every single day. And when you're making dozens and dozens and dozens of calls related to contact tracing, at some point during that day, you're going to have an encounter with somebody who is verbally abusive, who is literally screaming at you, because you're the devil, and you're imposing things on them. I mean, it's verbally abusive. And so when you deal with that every single day, for months and months on end… My kids had to go to school. And, you know, they faced a lot of comments and backlash from their friends."

Politicization of COVID-19

Many of RHOs' efforts were further complicated by lack of support from their local county boards, law enforcement, and other community members. RHOs noted that these challenges were driven largely by politics. They described having to make difficult decisions about heeding guidance from state and national public health officials and responding to resistance from community members that ranged from simply refusing to follow masking orders to actively threatening RHOs with physical violence and death. Their comments included:

"My judge in our area didn't like all the stuff that we were doing. So he took on with the Tavern League to sue me in order to get to the state. So I tried to change an ordinance and I had 500 people showing up at my HHS (Health and Human Services) meeting. It was, you know, there were times when I wasn't feeling so safe."

"I wish we had an enforceable communicable disease ordinance…It would have been difficult, I will admit it, and part of not having an ordinance—it took the decision of whether or not to put a masking order in place out of my hands. So in a way, it was one less stress, because I know if I would have put a masking order in place, I would have been crucified."

"We're gonna have years of fallout from this with the polarization—not just public health, the country."

Personal Relationships

Most RHOs said that managing this divisiveness did not stop when they left their office for the day. They described having endured scrutiny from family and friends, in person and online. They said many of their personal relationships were damaged due to deeply held beliefs about the COVID-19 pandemic, as exemplified by these RHOs:

"Think about the personal implication. You go home and you get beat up on Facebook, and you're, again, this terrible person on Facebook. Or you try to have a conversation with extended family members. And, you know, these things get very personal and relationships get harmed, and they dissolve because of differing opinions and just not understanding. So those things have all contributed to the mental anguish."

"My little brother, for a while, actually called me the COVID Nazi. So as much as some of those relationships, you know, are really cool and really good, there is the complete opposite, where some relationships basically no longer exist. Because I'm just trying to do my job and people take it personally. Yeah, my little brother doesn't talk to me anymore."

Misinformation and Disinformation

Many RHOs said rampant misinformation and disinformation spreading in their communities—especially early in the pandemic—challenged their work to address COVID-19. They explained that lack of accurate public education, combined with rapidly changing guidance from state and national officials, led some community members to believe the public health department was deceiving them. These RHOs said:

"I think one [challenge] was just so much misinformation or disinformation out there. And some of that stemmed from, it's a pandemic, it's changing. We didn't know a lot. And then as we learned things, people took that as we were lying to them. Things would change so often, and that was hard to combat."

"You can put out as much information as you want. People don't read. They don't read good sources, they don't watch the news. …You can have a personal conversation and, you know, you might sway them to your side, but you just don't have enough time to do 45000 personal conversations."

Lack of Capacity for Other Programs

Because very few employees generally staff rural health departments, RHOs explained that nearly every person in their department had to work on pandemic response. All other public health programming was scaled back significantly or even stopped due to lack of capacity, as described by these RHOs:

> *"All other programming went on the back burner. Like with WIC, we're trying to get our families back in here. I know they can still do it virtually. But just even the first time we have a client maybe meet us, so they can form a bond, form some trust--trust us enough to be a resource. We are going to start doing more home visits…One of the biggest gaps we had is not being able to reach out to our community and to our children."*

> *"When the pandemic hit, everything else just kind of flew to the wayside, right. We had to focus on just communicable disease and trying to prevent that spread."*

Inconsistent Communication

RHOs explained that constantly evolving information and lack of concrete guidance from the state and national levels made it increasingly difficult for RHOs. Some recalled instances in which they received a phone call from a community member about a new vaccine or masking policy the governor announced on TV about which RHOs themselves had not received prior notice. They said they had to react quickly to implement new guidance, and their reputations were often harmed in the process. For example:

> *"That information flow, even bad information flow, whatever kind of information flow can happen so quickly. And I would have people that would call me up the minute the governor said something that we were not forewarned on, and they would call me up and say, 'Oh, okay, it says we can do this now. So it's happening tomorrow?' And I'd be like, 'I don't even know about it,' which always made us look stupid, much less."*

> *"The complexity of implementing any decision or guidance always had lots of lots of gray; it seemed like even with contact tracing, there was so much gray on quarantine periods and definitions. And we would ask for more clarity from [Department of Health Services], and it wouldn't come timely. So we had to just make a decision. And those things hindered operations a lot and created a lot of frustration. As I said, because we were forced to make a decision, we had to make a decision, we couldn't wait 3 days for [Department of Health Services] to weigh in. We had to give guidance."*

Unique Rural Considerations

RHOs also described challenges they perceived as unique to rural Wisconsin. For example, they recalled that the first COVID-19 cases were documented in urban counties Wisconsin and led to statewide masking and stay-at-home orders, despite no documented cases in the northern, rural counties. This led to mitigation strategy fatigue by the time COVID-19 was detected in rural areas. Furthermore, they said that rural areas are often more conservative and have significantly fewer staff and financial resources than urban health departments. One RHO said:

> *"I sometimes, looking back, question if the stay-at-home order actually did hinder us in the long run, because we cracked down so fast. And like in our little county, there wasn't any COVID here and probably wasn't any COVID here for a long time. So I think people got tired of it."*

Key Insights and Policy Recommendations

RHOs shared key insights about their experiences working on the frontlines of this unprecedented health crisis that they perceived would benefit other health officers, such as the need for RHOs to practice self-care to mitigate the burnout they could experience serving in this role and a need to direct resources to strengthen public health infrastructure in rural Wisconsin specifically. These RHOs said:

> *"Self-care. I think that is the biggest lesson that all of us learned is the burnout. It was bad. And I think the biggest lesson is self-care and your family comes first. You know, you can be replaced as an employee, but you need to take care of yourself, and you need to take care of your family."*

> *"It's super important to acknowledge how mentally exhausting it is and physically exhausting. And so I just think it's really important that we don't lose sight of that, because we've got a lot of work to do in public health infrastructure and building a public health infrastructure that's actually adequate. Because it's not—especially in the state of Wisconsin."*

RHOs collectively described several policy recommendations they perceived would improve the ability of RHOs and public health departments in general to respond to crises like pandemics and to address community health more broadly. For example, they suggested that establishing communication protocols between state and local health departments could facilitate more efficient implementation of guidelines and consequently may improve community members' perceptions of local public health entities. Some RHOs said that having the autonomy to enact local public health ordinances, such as mask mandates, would enable them to respond to their community's specific needs. They also emphasized a need to extend protections of health care workers from harassment to public health workers and to support a national health care system so community members could access care, regardless of their geographic location. These RHOs explained:

> *"The governor did come out with protection for health care workers, but it doesn't protect us. Public health was left out. So if you're a nurse, you're protected. But say if I wasn't a nurse, as a health officer, the law that protects health care workers from abuse or harassment wouldn't necessarily apply to me."*

> *"When I think about greater preparation regarding commu-*

nicable disease or pandemics, or whatever next new emerging infection, or really addressing any health issue in a community, it just cannot be overstated how much work needs to be done on the public health infrastructure, and I'm talking people. You cannot have a health department at a local level with such a small staff…There's no opportunity for true engagement in your community, because you are literally just putting out fires."

DISCUSSION

Across key informant interviews with 13 RHOs in Wisconsin, consistent themes emerged on experiences though the COVID-19 pandemic. The unique circumstances imposed by rurality–limited resources and capacity, need for multitasking, and differential time scales for illness burden–resulted in difficult, challenging, and protracted public health responses. The pandemic was devastating in terms of the emotional toll on RHOs and their staff and further resulted in significant effects on their mental health, strain on personal and professional relationships, increased workforce disruptions, and displaced duties. Some notable benefits were realized, however, in terms of new and strengthened partnerships and collaborative efforts. Important considerations pertaining to enhanced resources, workforce development, preparedness, protection, and embargoing of new communication arose through these interviews.

This study was the first to our knowledge to explore the experiences of RHOs during the COVID-19 pandemic using a rigorous qualitative methodology that resulted in theoretical saturation, the point at which no new data emerged. Prior to, during, and beyond the COVID-19 pandemic, health officers in rural Wisconsin have been positioned uniquely as members of their communities tasked with implementing lifesaving, yet often controversial, public health mitigation strategies in the midst of constantly evolving information. For this reason, these RHOs were able to provide an invaluable perspective on this unprecedented public health crisis. While their specific experiences varied from county to county, the overarching themes of being overworked, underresourced, and frequently undermined were consistent throughout each interview.

A recurring theme of a strained workforce was central throughout interviews. Combined effects of individuals leaving the workforce,[17] difficulty filling positions,[18] and inability to tend to other core public health measures have been noted elsewhere. This constant strain has been referred to as the "shadow epidemic" of mental health effects in public health workers[19] and was compounded in rural areas by pandemic-related staff attrition and limited budgets.

Our interviewees stressed the mental health consequences and burnout associated with caring for communities while being attacked for their efforts. Isolation, a common factor in rural health offices, has been related to anxiety, depression, posttraumatic stress disorder, and suicidal ideation in a recent survey of state and local public health workers.[20] Moreover, the severity of poor mental health has been associated with long work hours and amount of time committed to COVID-19 response efforts.[21] Especially in rural areas, isolation—from community and, sometimes, from family members—was often a consequence of the high politicization of COVID-19 mitigation efforts, such as masking and vaccination.[22] Our interviewees noted lack of support from elected officials and feeling that they were caught between two opposing forces. Accordingly, sentiments about the lack of statutory protections for public health workers were recorded–especially as workplace violence became more pronounced through the pandemic.[23]

The rapid spread of misinformation and disinformation,[24] noted by our interviewees, was amplified by the constantly shifting target of a newly emerged pathogen. Because federal and state public health recommendations evolved in response to emerging evidence, negativity expanded in social media and elsewhere, resulting in altered public perception.[25] Our interviewees also noted that new information or recommendations often were released at the state level prior to notification of county health officers, causing communication delays, inconsistency, public hesitancy, and/or suspicion. Similarly, others have noted that communication strategies need to consider wording, timing, and channel.[25] Finally, significant differences have been reported in disruptions of daily living among rural and urban areas in the upper Midwest.[26] Our respondents noted that differences in the timing of COVID-19 burden between Wisconsin urban centers and rural communities often resulted in a mismatch between statewide public health guidance and local conditions.

This study had several important limitations. First, it captured the impressions of a limited number of individuals in rural counties of 1 upper midwestern state. Although individuals came from multiple counties across all state public health regions, the generalizability may be constrained. Second, biases could be imposed by the study sampling frame. Participation was limited to those who were willing to be interviewed and who had been in their position for at least 6 months; we were not able to capture the impressions of the many health officers who left their positions. Further, this study captured impressions during a single time period across a very dynamic pandemic. Responses in June 2022 reflect only the sentiments of participants at that time. Lastly, the interviews were conducted virtually, a platform that could allow the researcher to miss out on some nonverbal cues.

This study also had numerous strengths. First, we used a robust methodology to capture and evaluate RHOs' qualitative responses. Moreover, the respondents tended to provide extensive content during interviews. We also attained a wide geographical sampling across Wisconsin with significant diversity in the counties and populations served. Our purposive sample consisted of just under half of the health officers in rural Wisconsin. The timing of these interviews, in Summer 2022, occurred as health officers were still

managing issues related to the pandemic, and the use of open-ended questions allowed for unconstrained responses and latitude. Additionally, the interviewer was a medical student with a Master of Public Health degree. Similarities in training and perspectives and lack of power differential supported open and honest interactions. Finally, we noted a very high degree of consistency among interviewees. The reported effects of the pandemic and other challenges in rural settings derived from this research could be more fully explored and potentially mitigated through prioritized efforts in rural areas, to include support from the newly established Centers for Disease Control and Prevention Office of Rural Health.[27]

CONCLUSIONS

The first 30 months of the COVID-19 pandemic exacted an enormous toll on RHOs in Wisconsin. Constraints unique to rural settings—inadequate finances and resources, limited personnel, routine multitasking, influences from political leanings, misinformation and disinformation, and indirect communication from state and federal sources—and differences in epidemiological features of this virus in concentrated versus dispersed populations, affected mental health and led to extensive burnout, altered personal relationships, and disruption of core public health duties. Through these trials, however, health offices created new and collaborative partnerships and—through their words and stories—provide key recommendations for enhanced communication, opportunities for greater coordinated collaboration, improved infrastructure, preparation, and statutory protections for public health workers.

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Evidence-Based Heart Failure Management: A Practical Guide for Hospitalists

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ABSTRACT

Heart failure is a growing global health concern, characterized by high morbidity, frequent hospitalizations, and significant mortality. The classification of heart failure based on left ventricular ejection fraction plays a critical role in diagnosis and management, encompassing heart failure with reduced ejection fraction (HFrEF), heart failure with preserved ejection fraction (HFpEF), heart failure with mildly reduced ejection fraction (HFmrEF), and heart failure with improved ejection fraction (HFimpEF). While advancements in therapy have transformed HFrEF management, challenges persist in optimizing treatment for HFmrEF and HFimpEF due to their heterogeneous nature. Emerging strategies emphasize the early and simultaneous initiation of key pharmacologic therapies across these subtypes to maximize clinical benefits. Individual approaches, guided by patient characteristics and evolving evidence, are essential for improving outcomes. This narrative review provides a comprehensive overview of current treatment strategies for the different classifications of HF, highlighting the role of rapid therapy initiation.

INTRODUCTION

Heart failure represents a significant public health burden. According to the 2019 American Heart Association (AHA) Heart Disease and Stroke Statistics report, an estimated 6.2 million Americans aged 20 and older were living with heart failure in 2016. Furthermore, its prevalence is expected to rise by 46% from 2012 to 2030, affecting more than 8 million adults aged 18 and older. This rising prevalence is attributed to aging populations, improved survival rates following myocardial infarction and other cardiovascular events, and the increasing incidence of risk factors such as hypertension, diabetes, and obesity.[1] These statistics highlight the urgent need for effective strategies to manage and prevent heart failure.

Heart failure is commonly classified based on the heart's ejection fraction (EF)—the percentage of blood ejected from the ventricle with each contraction—into heart failure with reduced EF (HFrEF, EF ≤ 40%), heart failure with preserved EF (HFpEF, EF ≥ 50%), and heart failure with mildly reduced EF (HFmrEF, EF 41%–49%) (Table 1). While HFmrEF lacks randomized controlled trials (RCTs) specific to its treatment, analyses from previous studies suggest these patients may benefit from therapies recommended for HFrEF.[2,3]

Additionally, a recently recognized category—heart failure with improved EF (HFimpEF)—accounts for patients whose EF improves with guideline-directed medical therapy (GDMT) but acknowledges that EF changes are not always unidirectional. EF may decline after initial improvement due to factors such as cardiotoxicity, disease progression, or withdrawal of treatment, and this decline is associated with worse outcomes. The AHA recommends the term HFimpEF for such patients, emphasizing the need for continued GDMT to maintain improved EF and prevent relapse, as EF trajectory is a critical prognostic factor in heart failure management.[2]

Purpose

Heart failure remains a leading cause of hospitalization and readmissions, placing hospitalists at the forefront of its management. This review provides a concise, evidence-based guide to help hospitalists implement early interventions, including decongestion strategies and disease-modifying therapies—particularly the "four pillars" of HFrEF treatment—to reduce morbidity, mortality, and rehospitalizations. Emphasizing practical strategies for optimizing

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care transitions, medication adherence, and cost considerations, this overview supports hospitalists in improving long-term outcomes for patients with heart failure.

PATHOPHYSIOLOGY AND CLASSIFICATION OF HEART FAILURE

HFrEF and HFpEF share many risk factors and comorbidities, yet their underlying pathophysiology reveals significant differences. HFrEF results primarily from impaired systolic function and cardiomyocyte loss, leading to increased left ventricular filling pressures, diastolic dysfunction, and pulmonary venous congestion. These changes often culminate in right heart failure with peripheral congestion, reduced cardiac output, and end-organ hypoperfusion. In HFrEF, systemic and cardiac inflammation is typically secondary to the causes of cardiomyocyte loss, while left ventricular stiffness may vary depending on the extent of fibrosis and titin isoform shifts.

HFpEF, on the other hand, is a multifactorial condition often observed in older females with clusters of noncardiac comorbidities, such as hypertension, type 2 diabetes, and pulmonary disease. The pathophysiology of HFpEF is less understood but is characterized by low-grade systemic and cardiac inflammation, endothelial dysfunction, and capillary dysfunction. These changes precede disease progression, contributing to microvascular inflammation, cardiomyocyte hypertrophy, and fibrosis. Left ventricular stiffness in HFpEF is driven by reduced calcium signaling, titin modifications favoring stiffer isoforms, and increased perivascular and interstitial fibrosis.[4] These mechanisms impair diastolic filling, elevate pulmonary venous pressures, and exacerbate congestion and afterload.

Both HFrEF and HFpEF involve fibrosis, although the type and distribution differ. HFrEF often features replacement fibrosis following myocardial infarction, while HFpEF involves perivascular fibrosis linked to metabolic risks and interstitial fibrosis driven by aging and hypertension.[4] Neurohormonal activation—particularly of the renin-angiotensin-aldosterone system (RAAS)—exacerbates fluid retention and vasoconstriction in both conditions, contributing to intravascular congestion.[5] Additionally, endothelin-1, a potent vasoconstrictor, amplifies vascular smooth muscle contraction and afterload.

The natriuretic peptide system, including atrial natriuretic peptide and brain natriuretic peptide, counterbalances neurohormonal activation by promoting vasodilation, natriuresis, and diuresis. However, the clearance of natriuretic peptides by neprilysin and other enzymes can limit their protective effects, further exacerbating heart failure symptoms.[6] This is the basis of sacubitril, a neprilysin inhibitor in the combination drug sacubitril/valsartan, a first-in-class angiotensin receptor/neprilysin inhibitors (ARNI).[6]

Inflammation plays a pivotal role in both HFrEF and HFpEF. Cytokines such as tumor necrosis factor, transforming growth factor beta (TGF-β), interleukin-6, and interleukin-1 contribute to

Box. Abbreviations

EF: ejection fraction
HFrEF: heart failure with reduced ejection fraction
HFmrEF: heart failure with mid-range ejection fraction
HFimpEF: heart failure with improved ejection fraction
HFpEF: heart failure with preserved ejection fraction
GDMT: guideline-directed medical therapy
MI: myocardial infarction
RAAS: renin-angiotensin-aldosterone system
VTE: venous thromboembolism
ARNI: angiotensin receptor/neprilysin inhibitors
ACEI: angiotensin converting enzyme inhibitor
ARB: angiotensin II receptor blocker
MRA: mineralocorticoid receptor antagonist
SGLT2i: sodium-glucose cotransporter 2 inhibitors
RALES: Randomized Aldactone Evaluation Study
PARADIGM-HF: Prospective Comparison of ARNI With ACEI to Determine Impact on Global Mortality and Morbidity in Heart Failure
NYHA: New York Heart Association
LVEF: left ventricular ejection fraction
DAPA-HF: Dapagliflozin and Prevention of Adverse Outcomes in Heart Failure
EMPEROR-Reduced: Empagliflozin Outcome Trial in Patients With Chronic Heart Failure and a Reduced Ejection Fraction
EMPEROR-Preserved: Empagliflozin Outcome Trial in Patients With Chronic Heart Failure With Preserved Ejection Fraction
TRED-HF: Withdrawal of Pharmacological Treatment for Heart Failure in Patients With Recovered Dilated Cardiomyopathy
EPHESUS: Eplerenone Post–Acute Myocardial Infarction Heart Failure Efficacy and Survival Study
HF-ACTION: Heart Failure: A Controlled Trial Investigating Outcomes of Exercise Training
CHAMPION: CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in NYHA Class III Heart Failure Patients
GUIDE-HF: Hemodynamic-GUIDEd Management of Heart Failure

Table 1. Heart Failure Classification

Heart Failure Type	Ejection Fraction	Key Characteristics
HFrEF (Reduced EF)	EF ≤40%	Impaired systolic function: Heart cannot pump blood effectively. Commonly caused by ischemic heart disease or MI.[2]
HFmrEF (Mid-Range EF)	EF 41%-49%	Intermediate group with both systolic and diastolic dysfunction. Etiology and treatment often overlap with HFrEF.[2,3]
HFimpEF (Improved EF)	EF >40% after being ≤40%	Indicates improvement in systolic function; typically seen in patients with effective medical or device therapy.[2]
HFpEF (Preserved EF)	EF ≥ 50%	Predominantly diastolic dysfunction; normal pumping but impaired filling. Common in older adults and women.[4,5]

endothelial dysfunction, pulmonary edema, and left ventricular impairment.

Additionally, comorbidities such as diabetes, obesity, and chronic kidney disease contribute to chronic low-grade inflammation, further perpetuating worsening heart failure. The research into anti-cytokine and anti-inflammatory therapies is ongoing.[7]

MANAGEMENT OVERVIEW

Inpatient Heart Failure Management

Effective inpatient heart failure management begins with a comprehensive clinical evaluation to assess hemodynamic profiles, evaluate congestion severity, and determine perfusion adequacy. Cardiogenic shock necessitates immediate multidisciplinary intervention and adherence to established guidelines. Timely identification of acute coronary syndrome is critical, as urgent revascularization may be required. In cases without ischemic disease, inflammatory heart conditions should be considered—particularly those presenting with conduction blocks or ventricular arrhythmias. Most heart failure admissions result from gradual worsening of preexisting structural heart disease, often triggered by factors such as arrhythmias, ischemia, or comorbidities. Patients presenting with pulmonary edema and severe hypertension require rapid blood pressure reduction, especially those with HFpEF.[8] Care plans should prioritize addressing precipitating factors, managing comorbidities, and optimizing GDMT to improve outcomes.

Hospitalization is a pivotal opportunity to initiate, maintain, or adjust GDMT—particularly for patients with HFrEF. Continuing GDMT during hospitalization reduces postdischarge mortality and readmission risks, while initiating GDMT during the hospital stay provides significant clinical benefits.[9] Intravenous loop diuretics remain the cornerstone of congestion management, with dose adjustments or the addition of thiazide diuretics or mineralocorticoid receptor antagonists (MRAs) when needed.[8]

Resolving congestion before discharge is crucial, as persistent congestion increases the risks of rehospitalization and mortality. Patients who were started on loop diuretics during hospitalization and were prescribed loop diuretics at discharge had a significantly lower risk of 30-day readmission.[10] Heart failure hospitalization also significantly increases the risk of venous thromboembolism (VTE), particularly within the first 30 days post-discharge but also long term.[11] Prophylactic anticoagulation with agents such as low-molecular-weight heparin, unfractionated heparin, or direct oral anticoagulants is recommended to prevent deep vein thrombosis and pulmonary embolism in high-risk patients.[12]

Monitoring serum electrolytes is a critical component of acute heart failure management, as imbalances are common and closely linked to adverse outcomes. Both hypokalemia ($K^+ < 4.0$ mmol/L) and hyperkalemia ($K^+ > 5.5$ mmol/L) are independently associated with increased morbidity and mortality. Hyperkalemia has become more prevalent since the introduction of RAAS inhibitors, particularly following the RALES trial, which highlighted the benefits of spironolactone in severe heart failure.[13] The availability of newer potassium-lowering agents, such as patiromer and sodium zirconium cyclosilicate, offers promising options to manage hyperkalemia and facilitate the initiation or up-titration of RAAS inhibitors.

Sodium levels also warrant careful attention—hyponatremia ($Na^+ < 135$ mEq/L) is associated with a higher risk of complications, including cognitive impairment, falls, prolonged hospitalization, readmission, and all-cause mortality. Similarly, hypomagnesemia ($Mg^{2+} < 1.9$ mg/dL), which affects up to one-third of patients with heart failure, is a significant risk factor for ventricular arrhythmias and sudden cardiac death.[14] Given these risks, routine electrolyte monitoring and timely correction during acute heart failure hospitalization are essential to improve clinical outcomes and ensure the safe implementation of GDMT. Combining comprehensive hemodynamic assessment, optimization of GDMT, effective congestion management, and preventive measures for VTE forms the foundation of effective inpatient heart failure management.

Pharmacologic Management by Subtype

HFrEF

Management of HFrEF has advanced significantly, with contemporary GDMT emphasizing a quadruple therapy approach: ARNI, β-blockers, MRAs, and sodium-glucose cotransporter 2 (SGLT2) inhibitors.[2,15,16] Evidence strongly supports initiating all four drug classes in patients with HFrEF due to their additive life-saving effects. A 2020 analysis showed that 65-year-old patients receiving all four classes gained 4.4 additional life-years compared to those treated with only an angiotensin converting enzyme inhibitor (ACEI)/angiotensin II receptor blocker (ARB) and β-blocker.[17] Similarly, a 2022 systematic review and network meta-analysis found that combined treatment with all four drug classes was the most effective in improving outcomes among therapy combinations and extended life expectancy by 7.9 years in 50 years compared to no treatment.[18] For a 70-year-old patient, the use of all four therapies added 5 life-years compared to no treatment. These findings highlight the compounding benefits of comprehensive GDMT and underscore the urgency of initiating and optimizing all four therapies to maximize survival and quality of life for patients with HFrEF.

ARNI—particularly sacubitril/valsartan—has demonstrated superiority over ACEIs in reducing cardiovascular death and hospitalization for heart failure in the PARADIGM-HF trial and is now first-line treatment.[2,19,20] Patients receiving ACEIs or ARBs should transition to ARNI. However, 36 hours should pass before switching from ACEIs due to the risk of angioedema. ACEIs and ARBs are alternatives for patients unable to tolerate ARNI. Caution is required in patients with severe renal impairment or hyperkalemia, and regular monitoring of renal function and electrolytes is necessary.

β-blockers—specifically bisoprolol, carvedilol, and sustained

release metoprolol succinate—have proven mortality benefits in HFrEF, which are observed within weeks of initiation and include reduced risk of death and hospitalization.[21] Importantly, β-blockers should be rapidly up-titrated to optimal doses as tolerated.[22] Potential side effects include bradycardia, fatigue, hypotension, and worsening heart failure in the initial stages. They should be avoided in patients with bradycardia and second- or third-degree heart block in the absence of a pacemaker.[23] Monitoring heart rate and blood pressure is essential during initiation and titration.

MRAs such as spironolactone and eplerenone reduce mortality and hospitalization in patients with New York Heart Association (NYHA) class II–IV HFrEF.[24] They are recommended for patients with an estimated glomerular filtration rate > 30 mL/min/1.73 m² and serum potassium < 5.0 mEq/L. Potential side effects include hyperkalemia—particularly in patients with impaired renal function—and gynecomastia with spironolactone. Potassium levels should be monitored, and potassium binding agents can be used to mitigate hyperkalemia when necessary. MRAs should be discontinued if serum potassium exceeds 5.5 mEq/L.[2] In addition to the steroidal MRAs, finerenone—the first US Food and Drug Administration-approved nonsteroidal MRA—has shown efficacy in heart failure and chronic kidney disease, with significant improvements in both kidney and cardiovascular outcomes.[25]

SGLT2 inhibitors, including dapagliflozin and empagliflozin, are a major addition to HFrEF treatment. The DAPA-HF trial and the EMPEROR-Reduced trial demonstrated that these agents reduce the risk of cardiovascular death and hospitalization by approximately 25%.[26] However, potential side effects include urinary tract infections, dizziness, hyperkaliemia, edema, and kidney failure.[27] The high cost of these medications also may limit accessibility for some patients.[28] Hospitalists and outpatient clinicians should carefully monitor patients for these adverse effects and educate them about recognizing early signs of complications.

Hydralazine and isosorbide dinitrate H-ISDN remains a class I treatment recommendation for African American patients with NYHA class III–IV HFrEF. However, these therapies should be initiated only after optimizing the quadruple GDMT regimen.[2] The push to initiate all four pillars of GDMT as rapidly as possible is grounded in evidence showing that benefits accrue within days to weeks of initiation. Clinicians should prioritize up-titrating each medication to the target or maximally tolerated doses to achieve optimal outcomes. Coordination across care teams and patient education about adherence and side effects are essential to the therapy's success.

Intravenous (IV) ferric carboxymaltose (FCM) has been shown in some trials to improve NYHA functional class, 6-minute walk distance, and quality of life in patients with iron deficiency anemia and chronic heart failure,[29] whereas other studies have not demonstrated significant improvements in these functional outcomes. However, all trials consistently show that IV FCM significantly reduces the risk of total heart failure hospitalizations.[30]

HFmrEF

There are no prospective RCTs specifically targeting patients with HFmrEF. Current evidence for managing HFmrEF comes primarily from post hoc analyses and subsets of data from heart failure trials, where patients were retrospectively categorized as having HFmrEF. Left ventricular ejection fraction (LVEF) exists on a continuum, and among individuals with LVEF within the range of 41% to 49%, those with lower values appear to respond to GDMT similarly to patients with HFrEF. Therefore, it is reasonable to apply HFrEF treatment protocols to patients in this subgroup, including SGLT2 inhibitors (SGLT2i), β-blockers, ARNI/ACEI/ARB, and MRAs.[2,15] Supporting this approach, the EMPEROR-Preserved trial demonstrated significant clinical benefits of the SGLT2i empagliflozin in patients with symptomatic heart failure and a LVEF greater than 40%.[31]Additionally, post hoc analyses of trials for HFrEF that included patients with LVEF of 41% to 49% suggest that these individuals may derive benefit from GDMT traditionally used in HFrEF management.[32] Repeat assessments of LVEF are recommended for patients with HFmrEF to monitor disease progression and guide therapy adjustments.

HFpEF

HFpEF has historically been challenging to manage pharmacologically due to limited evidence of benefit from many therapies. However, recent clinical trials have provided guidance on effective strategies for treatment of HFpEF, emphasizing GDMT.[33] Primary goals include managing hypertension by titrating blood pressure within an appropriate target range and addressing associated conditions, such as atrial fibrillation, to improve symptoms and outcomes. Managing atrial fibrillation in patients with HFpEF can improve symptoms and overall quality of life. Chronic anticoagulant therapy is recommended for patients with chronic heart failure and permanent, persistent, paroxysmal atrial fibrillation and a CHA_2DS_2-VASc score of 2 or greater for men and 3 or greater for women.[34] Additionally, direct oral anticoagulants are generally preferred over warfarin in eligible patients, based on cost, drug-drug interactions, or other indications.[35] Rhythm control strategies, including catheter ablation or anti-arrhythmic therapy, may be considered based on individual patient characteristics and symptom burden. In the 2 largest RCTs comparing ablation to either amiodarone or standard medical therapy, catheter ablation resulted in absolute risk reductions in death or hospitalization of 10% and 16.5%, respectively.[36,37] Diuretic agents should be used judiciously to alleviate congestion and improve symptoms in patients with HFpEF. The goal is symptom relief while minimizing the risk of volume depletion, electrolyte imbalances, or worsening kidney function.[2]

SGLT2 inhibitors have a Class 2a recommendation and should be initiated in all individuals with HFpEF barring contraindications. These agents have demonstrated significant cardiovascular benefits, including reduced hospitalization for heart failure and

cardiovascular death across all EF subgroups.[31] SGLT2 inhibitors are effective in both ambulatory patients with HFpEF and those with acutely decompensated heart failure. Evidence suggests their benefit is additive to other GDMT, including MRAs and ARNIs.[38] Meta-analyses indicate a consistent reduction in the composite endpoint of heart failure hospitalization and cardiovascular death (hazard ratio [HR], 0.80; 95% CI, 0.73-0.87) in individuals with HFmrEF and HFpEF.[39]

MRAs, ARNIs, and ARBs each have a Class 2b recommendation—particularly for patients with LVEF at the lower end of the HFpEF spectrum.[33] MRAs, such as spironolactone, may reduce hospitalizations in selected subsets of patients with HFpEF. While they have not consistently shown improvements in quality of life or exercise tolerance, MRAs provide balanced diuresis, hypertension control, and reduction in hospitalization rates.[39] ARNIs, such as sacubitril/valsartan, inhibit neprilysin, which augments natriuretic peptides, bradykinin, and substance P to counteract heart failure progression. Although the primary composite endpoint of total heart failure hospitalizations and cardiovascular death was numerically lower with sacubitril/valsartan versus valsartan (HR, 0.87; 95% CI, 0.75-1.01), it did not reach statistical significance, but ARNIs are recommended for their comprehensive cardiovascular effects.[40] ARBs, such as valsartan, serve as a viable alternative when ARNIs are contraindicated or not feasible (eg, due to history of angioedema or financial constraints). Though less effective than ARNIs, ARBs can aid in hypertension control and reducing heart failure-related hospitalizations.[41] For all three classes, careful titration based on patient tolerance, symptoms, blood pressure, potassium levels, and renal function is essential. The management of HFpEF has evolved significantly, with evidence supporting the use of SGLT2 inhibitors, MRAs, ARNIs, and ARBs. These therapies, tailored to individual patient profiles and contraindications, form the cornerstone of modern HFpEF treatment strategies. Achieving optimal blood pressure control and addressing comorbid conditions—such as atrial fibrillation—are critical for improving outcomes. Careful titration and monitoring are essential to maximize therapeutic benefits and minimize adverse effects.

HFimpEF

In patients with HFimpEF, GDMT should be continued. The TRED-HF trial showed that 44% of patients who recovered, became asymptomatic, and were weaned off therapy experienced a relapse, compared with none of the patients who remained on treatment.[42] Improvement in symptoms, cardiac function, and biomarkers after therapy indicates remission rather than complete and sustained recovery, emphasizing the importance of maintaining treatment to prevent relapse.

Diuresis in Heart Failure

Diuretic therapy is essential in the management of heart failure because of its role in alleviating congestion by reducing fluid retention. Loop diuretics, such as furosemide, bumetanide, and torsemide, are the cornerstone of therapy because of their potent natriuretic effects.[8] They act on the thick ascending limb of the loop of Henle, inhibiting the sodium-potassium-chloride cotransporter to enhance sodium and water excretion. In heart failure, neurohormonal activation and hemodynamic changes promote sodium retention, making loop diuretics crucial in overcoming these compensatory mechanisms.[43] Despite their efficacy, prolonged use may lead to diuretic resistance, characterized by increased sodium reabsorption in the distal nephron. The addition of thiazide diuretics, such as hydrochlorothiazide or metolazone, can enhance diuresis in resistant cases.[8] Furthermore, adding 50 mg per day of hydrochlorothiazide to usual care of patients with acute decompensated heart failure has been shown to improve diuretic response in the first few days of therapy, with patients experiencing fewer symptoms, less congestion, and lower mortality.[44] Loop diuretic dosing should be tailored to clinical status, with hospitalized patients typically requiring higher IV doses. Careful monitoring of urine output and volume status is necessary to prevent excessive depletion while GDMT. By integrating diuretic therapy with GDMT, clinicians can improve symptom control and patient outcomes.

Sequencing/Implementation Strategies of GDMT in HFrEF

The traditional approach to implementing GDMT in heart failure has involved starting each drug class consecutively and gradually up-titrating to the maximally tolerated dose before moving to the next class. Historically, this sequence began with an ACEI, followed by a β-blocker, MRA, and eventually switching ACEI to ARNI and adding SGLT2i. This method, endorsed by earlier guidelines, emphasized stabilization and symptom monitoring at each stage before progressing to additional therapies. For example, the 2008 European Society of Cardiology guidelines recommended up-titrating.[45] However, emerging evidence suggests that a faster approach to initiating and titrating GDMT may provide superior outcomes. Rapid initiation and up-titration have been shown to achieve significant clinical benefits as early as 2 to 4 weeks after therapy initiation. An analysis by Shen et al using data from large RCTs found that faster sequencing strategies reduced cardiovascular death or hospitalizations by as much as 47 events per 1000 patients compared to slower sequencing.[46]

Starting Two Drugs Simultaneously

Packer and McMurray advocate for initiating 2 drugs at once, such as a β-blocker and SGLT2i, followed by ARNI and MRA within 2 weeks. This approach seeks to balance rapid optimization with tolerability, leveraging the early benefits of key therapies.[43]

Starting All Four Drugs Simultaneously at Low Doses

An alternative proposed by Greene et al involves initiating all four major drug classes—β-blocker, ARNI, MRA, and SGLT2i—simultaneously at low doses, followed by gradual up-titration to target doses.[47] This strategy builds on evidence from the EPHESUS trial, which demonstrated that patients

with de novo heart failure could tolerate simultaneous initiation of ACEI, β-blocker, and MRA therapy after acute myocardial infarction.[48] The authors argue that tolerability for other patients with HFrEF should be comparable.

Tailored Sequencing Based on Patient Profiles

Rosano et al suggest adjusting the sequencing strategy based on patient-specific physiological profiles. For example, patients with low blood pressure and heart rate might benefit from starting with SGLT2i and MRA, whereas those with normal blood pressure and higher heart rates could begin with a β-blocker and ARNI.[49] Traditional sequential GDMT implementation allows for careful monitoring and adjustment but delays the introduction of potentially life-saving therapies. In contrast, faster or simultaneous initiation strategies prioritize early comprehensive treatment, which may reduce mortality and hospitalization. Tailored approaches further enhance therapy sequencing by incorporating patient-specific factors, such as blood pressure, heart rate, and comorbidities. These newer strategies challenge the stepwise approach by emphasizing the urgency of initiating multiple therapies early, with the choice of method guided by patient characteristics, clinical stability, and tolerability to achieve optimal outcomes.

Dietary/Lifestyle Recommendations

Lifestyle and dietary changes are key components in the management of heart failure, helping to alleviate symptoms, improve quality of life, and potentially reduce hospitalizations. While pharmacological treatments remain central to management of heart failure, appropriate modifications to diet and physical activity can enhance patient outcomes.

The AHA recommends a general sodium intake limit of <2300 mg/day for cardiovascular health, though there is insufficient evidence to support this level of restriction specifically for patients with heart failure. While sodium restriction is commonly advised, studies have shown mixed results regarding its impact on clinical outcomes in patients with heart failure.[50] The Dietary Approaches to Stop Hypertension (DASH) diet, which is rich in antioxidants and potassium, can help achieve sodium restriction without compromising nutritional adequacy. The DASH diet also may be associated with reduced hospitalizations for heart failure. A registered dietitian- or nurse-coached intervention that included a sodium restriction of 2-3 g/day improved NYHA functional class and reduced leg edema in patients with HFrEF.[51] However, extreme sodium restrictions (eg, <2.5 g/day) have not demonstrated consistent benefits in terms of clinical outcomes, such as mortality or hospital readmissions. Recent pilot studies have explored the effects of different levels of sodium restriction, including providing meals with 1.5 g/day sodium. Some studies suggest that such interventions can reduce urinary sodium excretion and improve quality of life but have not led to improvements in clinical outcomes.[52] Additionally, patients with heart failure often find it challenging to adhere to dietary sodium restrictions—even with prepared meals or home visits. These findings highlight the complexity of sodium restriction and the need for individualized dietary counseling to optimize management.

Fluid restriction is another important consideration in managing heart failure, particularly for patients experiencing symptoms of volume overload. While there is some evidence suggesting that fluid and sodium restriction interventions can improve symptoms such as leg edema and NYHA functional classification in patients with HFrEF, the overall clinical impact on hospitalization and mortality rates remains uncertain.[2] A meta-analysis of RCTs examining fluid restriction in heart failure found no significant benefit in terms of reduced hospitalizations or mortality. Similarly, fluid restriction did not substantially improve other markers, such as serum sodium levels, serum creatinine, or the duration of IV diuretic use.[2] Despite these mixed results, careful fluid management remains a cornerstone of symptom control in heart failure, particularly in patients with significant volume overload.

Exercise training provides numerous benefits for patients with heart failure and is safe when appropriately implemented. The HF-ACTION trial, which included 2331 patients with a LVEF of 35% or less, demonstrated that exercise training combined with usual care led to modest reductions in cardiovascular mortality and hospitalizations, particularly after prespecified adjustments.[53] Meta-analyses of several smaller trials have shown that exercise training improves functional capacity, exercise duration, and health-related quality of life and reduces the frequency of hospitalizations for heart failure.[54] Cardiac rehabilitation programs, which incorporate medical evaluation, education, psychosocial support, and structured exercise, are recommended for stable patients stable patients receiving optimal GDMT and able to participate in physical activity.[55] Dietary and lifestyle modifications, such as sodium restriction, fluid management, and exercise, are important adjuncts to pharmacologic therapy. Although evidence for strict sodium restriction is mixed, adherence to dietary recommendations such as the DASH diet and moderate sodium restriction can help improve symptoms and reduce hospitalizations. A tailored approach that combines dietary guidance from a registered dietitian with participation in cardiac rehabilitation can significantly enhance outcomes and quality of life for patients with heart failure.

CardioMEMS

CardioMEMS has emerged as a transformative tool in heart failure management, advancing beyond traditional noninvasive monitoring methods such as weight, heart rate, blood pressure, and subjective symptoms like dyspnea. Based on microelectromechanical systems (MEMS) technology, CardioMEMS directly targets hemodynamic congestion, which often precedes clinical symptoms by several weeks. The device consists of a small sensor implanted in the pulmonary artery that enables continuous,

real-time measurement of pulmonary artery pressures. Data are wirelessly transmitted to clinicians, allowing proactive therapy adjustments before decompensation occurs. This preemptive strategy has demonstrated substantial clinical impact; studies show CardioMEMS significantly reduces heart failure–related hospitalizations, with real-world data suggesting a 57% reduction – surpassing outcomes observed in controlled settings such as the CHAMPION trial and the GUIDE-HF trial.[56] Reflecting its clinical utility, the AHA and American College of Cardiology have granted a Class IIb recommendation for CardioMEMS use in select adults with heart failure.[2]

Despite these benefits, limitations remain. Safety is a concern; within the first 3 years of approval, more than 5500 devices were implanted in the United States, with at least 155 unique adverse events reported, reflecting a complication rate of approximately 2.8%. Patient selection is critical because certain populations are contraindicated for implantation, including those with active infection, history of pulmonary embolism or deep vein thrombosis, congenital heart disease, indwelling mechanical right heart valves, or coagulation disorders.[56] Furthermore, the procedure requires right heart catheterization, which some patients may not tolerate because of comorbid conditions or procedural risk. Cost also presents a barrier; CardioMEMS is substantially more expensive than standard care, with reported costs ranging from approximately $25 963 in the United Kingdom to $201 437 in the United States, limiting accessibility in resource-constrained settings.[56] These factors underscore the need for careful patient selection and cost-benefit evaluation when considering CardioMEMS in routine heart failure management.

CONCLUSIONS

Heart failure remains a major clinical challenge, requiring patient-centered, evidence-based management. Advances in classification and therapy have led to the "four pillars" approach in HFrEF, improving survival and reducing hospitalizations. Hospitalists play a key role in optimizing inpatient care, ensuring effective decongestion, timely GDMT initiation, and smooth transitions to outpatient management. Although SGLT2 inhibitors show promise across EF ranges, HFpEF and HFmrEF lack well-defined treatments, necessitating further research. Emerging strategies in HFrEF emphasize earlier and more aggressive GDMT implementation to enhance outcomes. Beyond pharmacologic therapy, lifestyle modifications such as sodium restriction and structured exercise improve quality of life. Future heart failure management will incorporate novel pharmacotherapies, regenerative medicine, and artificial intelligence-driven precision care to address treatment gaps, particularly in HFpEF.

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Table 2. Heart Failure Management Summary

Type	Management	
HFrEF	Quadruple therapy: ARNI (or ACEI/ARB if intolerant), β-blockers, MRAs, and SGLT2i[2,15,16,27]	Rapid initiation and up-titration are recommended
HFmrEF	Treated similarly to HFrEF with the same quadruple therapy[2,15]	
HFpEF	2A: SGLT2i.[31,57] 2B: MRAs, ARNis, and ARBs[33]	Key goals: managing hypertension, addressing comorbidities (eg, atrial fibrillation), and relieving congestion
HFimpEF	Continuation of HFrEF therapies is crucial[42]	

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Hepatitis C in Wisconsin Jails: Barriers to Testing and Treatment During Incarceration

Emily Hacker, MPH; Kailynn Mitchell, MPH; Caroline Mohr, MPH

ABSTRACT

Background: Justice-involved individuals are disproportionately affected by hepatitis C virus (HCV) infection. Wisconsin's viral hepatitis elimination plan prioritizes this population, yet little is known about jail capacity for testing and treatment.

Methods: A 10-item survey was emailed to administrators of 71 county jails and 1 Tribal detention facility to assess HCV testing and treatment practices and barriers. Responses were analyzed descriptively.

Results: Thirty facilities (41.7%) responded. Ten jails (33.3%) offered HCV testing; 15 (51.7%) provided treatment. Common barriers to testing included lack of contracted services (40%) and staffing constraints (23.3%). Barriers to treatment included financial restrictions (66.7%) and short incarceration periods (33.3%).

Discussion: Limited testing and treatment capacity persists despite Medicaid coverage and effective therapies.

Conclusions: Partnerships with local health agencies and policy changes addressing cost and contractual limitations are essential to expand HCV services in Wisconsin jails.

BACKGROUND

Hepatitis C is a bloodborne virus that causes liver inflammation. If left untreated, the hepatitis C virus (HCV) can cause cirrhosis of the liver, hepatocellular carcinoma, and liver failure. Hepatitis C is not transmitted through casual contact; it is transmitted primarily through sharing injection drug use equipment, sharing household items such as razors or nail clippers, receiving tattoos or piercings in unregulated settings, or through blood transfusions and organ donations received before 1992. HCV also can be transmitted through sexual activity with a person who has hepatitis C.[1]

While hepatitis C is not a vaccine-preventable condition like hepatitis A and B, it can be cured. Direct-acting antiviral (DAA) medications, such as glecaprevir/pibrentasvir (Mavyret) and sofosbuvir/velpatasvir (Epclusa), cure more than 95% of HCV infections. Treatment typically takes 8 to 12 weeks, depending on the medication prescribed,[2] and can be cost-prohibitive for patients who are uninsured or underinsured. Wisconsin lifted its Medicaid restrictions for hepatitis C treatment in 2019, eliminating prior authorization, sobriety requirements, and disease severity limitation.[3] Despite advances in both medication efficacy and access to treatment, certain populations remain disproportionately affected by HCV infection and barriers to care. Justice-involved individuals (those who are incarcerated or on probation or parole) have been identified as a priority population in Wisconsin's Viral Hepatitis Elimination Plan. Approximately 30% of people diagnosed with HCV spend at least part of each year incarcerated.[4]

Wisconsin has 72 counties, 71 of which operate a county jail. The Menominee Indian Tribe of Wisconsin operates a separate detention facility. All county facilities operate independently of the Wisconsin Department of Corrections, and each jail is responsible for the health care of individuals in its custody. Most jails in Wisconsin contract with third-party health care providers to oversee medical services. Limited county budgets can make implementing new programs difficult. For many justice-involved individuals, jail or prison facilities are their only access to medical services. Because of uncertain or brief incarceration periods,

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Figure 1. Average Length of Incarceration

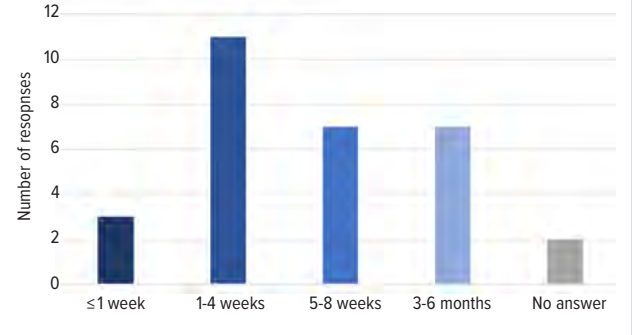
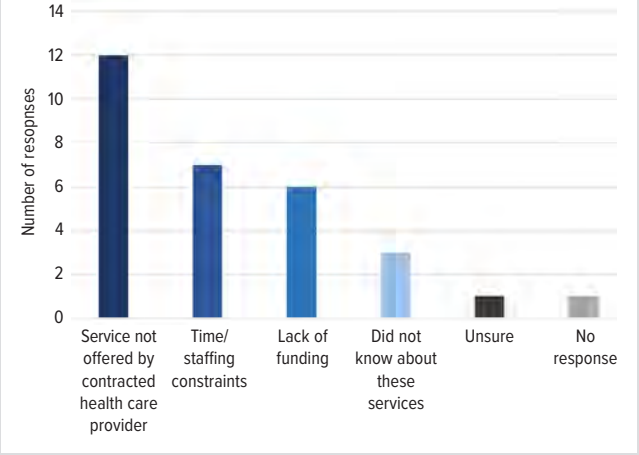


Figure 2. Barriers to Hepatitis C Testing in County Jails



Respondents could select more than 1 option.

initiating hepatitis C treatment in jails is challenging. However, hepatitis C testing requires relatively little time – approximately 20 minutes for a rapid antibody test and 2 to 7 days for an RNA confirmatory test. Assessing jail capacity and interest in providing hepatitis C testing and treatment aligns with viral hepatitis elimination planning as directed by the World Health Organization.[5]

METHODS

A 10-item survey was developed to assess which county jails in Wisconsin provide hepatitis C testing and treatment and to identify barriers to providing these services. This survey was emailed to each jail administrator in the state. Two weeks after the initial email, follow-up requests were sent to administrators who had not yet responded. After 1 month, the survey was closed, and responses were analyzed.

RESULTS

One survey was sent to each jail administrator for the 71 county jails across Wisconsin and to the Tribal detention facility. Of the 72 surveys sent, 30 responses were received. The survey included questions about each jail's provision of hepatitis C testing and treatment, barriers to testing and treatment, and average length of incarceration.

Eleven jails (36.7%) reported an average length of incarceration of 1 to 4 weeks. Seven (23.3%) jails reported an average length of 5 to 8 weeks, and 7 jails reported an average length of 3 to 6 months. Three county jails reported an average length of incarceration of 1 week or less, and 2 facilities did not provide an answer.

Ten facilities (33.3%) reported offering hepatitis C testing, while 20 jails (66.7%) indicated that testing was not offered. Of the 30 responses received, 12 jails (40%) reported that their contracted health services provider did not offer hepatitis C testing, 7 (23.3%) reported time and/or staffing constraints as barriers to testing, 6 (20%) cited lack of funding, and 3 (10%) reported being unaware of testing services. Respondents were allowed to select more than one response.

Fifteen facilities (51.7%) reported offering hepatitis C treatment, and 14 (48.3%) reported that treatment was not provided. One respondent did not answer this question. Of the 15 jails that provided hepatitis C treatment, 12 (80%) reported that individuals receiving treatment prior to incarceration were allowed to continue treatment upon admission, 8 (53.3%) reported that a contracted health care provider would prescribe DAAs, and 6 (40%) reported that treatment would be provided if the person was incarcerated for the duration of treatment. Respondents were allowed to select more than one response.

Ten (66.7%) jails reported that hepatitis C treatment was not offered due to financial restrictions, 8 (53.3%) reported that treatment was not a service offered by their contracted health care provider, and 5 (33.3%) reported that inmates were not in custody long enough to complete treatment. Five facilities also reported that providers were hesitant to start treatment for individuals with an unknown length of incarceration, 4 (26.7%) reported insufficient staff capacity to monitor or administer the medication, 1 facility (6.7%) reported that health care staff were unfamiliar with treatment protocols, and 1 facility (6.7%) did not provide a response. Respondents were allowed to select more than one response.

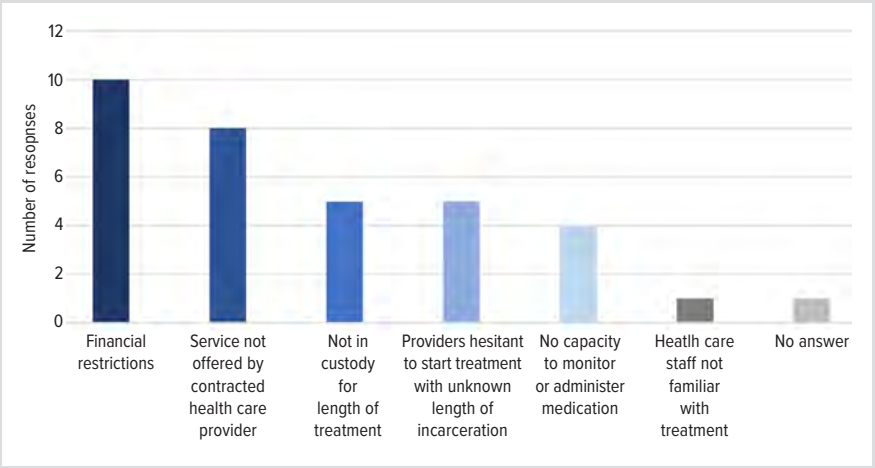
DISCUSSION

Jails hold individuals in custody for shorter periods than state correctional institutions, making initiation of hepatitis C treatment difficult. Once started on a treatment regimen, a person should complete it without interruption. For jails with an average length of incarceration of less than 8 to 12 weeks, effective completion of HCV treatment is unlikely. Pre-release referrals to treatment providers can be made, or individuals may be transferred to state custody based on sentencing; the Wisconsin Department of Corrections provides hepatitis C testing and treatment.[6] Seven county jails reported an average length of incarceration of 3 to

6 months (Figure 1). These facilities could be prioritized for discussions about HCV treatment implementation.

Fourteen county jails were unable to offer hepatitis C testing services, largely due to existing agreements with contracted health care providers. Lack of funding and time and staffing constraints were also reported as limiting factors (Figure 3). Wisconsin DHS can assist local and Tribal health departments in implementing rapid and confirmatory hepatitis C testing in county jails.

Figure 3. Barriers to Offereing Hepatitis C Treatment



Respondents could select more than 1 option.

Wisconsin county jails incarcerate approximately 12 000 individuals at any given time.[7] To receive hepatitis C treatment while incarcerated, 80% of responding facilities reported that individuals must already be receiving treatment prior to incarceration and provide the medication to be administered. This may explain the disparity between the 10 facilities providing testing and 15 facilities providing treatment. While Wisconsin Medicaid covers the cost of hepatitis C treatment,[3] coverage is suspended during incarceration, and the cost-prohibitive nature of DAAs means many county inmates will be unable to complete treatment. Additionally, lack of insurance coverage prevents jails from generating revenue through the 340B Drug Pricing Program.[8] Financial restrictions and service exclusions from third-party health care contractors further impede treatment for incarcerated individuals. Without addressing these policy barriers, hepatitis C treatment for inmates in county jails is unlikely to become widely available in Wisconsin.

CONCLUSIONS

While the provision of hepatitis C treatment for individuals in jail custody remains a significant challenge, testing provided by outside agencies eliminates cost barriers and limitations imposed by existing contracts with third-party health care providers. Wisconsin DHS will continue to engage community partners, including jails, as part of viral hepatitis elimination planning. Individuals who know their hepatitis C status can receive counseling on prevention measures to reduce transmission and can be connected with treatment navigation resources upon release. Ongoing surveillance of hepatitis C and the development of new partnerships among the Wisconsin Department of Health Services, local and Tribal health departments, and county jails across Wisconsin align directly with the State's viral hepatitis elimination plan.

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The Demographics of Whole-Body Donors in Wisconsin

Sarah Traynor, PhD; Christine Egede, MD; Ryan E. Hillmer, PhD; Scott J. Hetzel, MS; Meghan M. Cotter, PhD

ABSTRACT

Background: Individuals who donate their bodies to academic, whole-body donation programs support health science education, training, and research. This is the first report on Wisconsin whole-body donor demographics and the extent to which donors represent the state population.

Methods: Donor demographic data from 2016 through 2021 were collected from death certificate worksheets and compared with Wisconsin population data from the US Census Bureau and state health statistics.

Results: Most donors were non-Hispanic White individuals, did not have a college degree, and did not work in health care. The median age at death was 86 years. Twenty-eight percent of donors served in the armed forces. Donors were not representative of the Wisconsin population in age, race, ethnicity, or military service.

Discussion: Whole-body donors provide an invaluable resource for health science education and research. Understanding donor demographics is an important first step in examining diversity and representation within Wisconsin's body donation programs.

BACKGROUND

Whole-body donation is a critical component of health professions education. Thousands of health science students, researchers, and professionals learn from whole-body donors during their training and careers. In Wisconsin, there are 2 academic, whole-body donor programs to which individuals may donate: the University of Wisconsin School of Medicine and Public Health Body Donor Program (UWBDP) in Madison and the Medical College of Wisconsin Anatomical Gift Registry (AGR) in Milwaukee.

Both programs serve as educational and biomedical research resources for health science students at public and private colleges and universities in Wisconsin. Anatomy and physiology courses that utilize donated bodies educate medical, physician assistant, dental, pharmacy, physical therapy, occupational therapy, and undergraduate students, as well as medical residents. Both programs greatly value the individuals who donate their bodies, and every year, faculty, staff, and students at each program express their gratitude during body donor memorial ceremonies attended by donors' families and loved ones.

Like standardized patients in simulated clinical scenarios, whole-body donors are an important population who represent students' future patients. Despite the tremendous gift that body donors provide, little is known about the population of individuals who donate their bodies to these programs and how representative they are of the Wisconsin population. This collaboration between UWBDP and AGR is the first study on the demographics of whole-body donors in Wisconsin.

METHODS

Donor demographic data were collected from the death certificate worksheet (DCW) for each Wisconsin resident who died from January 1, 2016, through December 31, 2021, and donated their body to UWBDP or AGR. All personally identifiable information was removed from datasets prior to analysis. Wisconsin population data were collected from the US Census Bureau 2020 Decennial Census,[1] the 2020 American Community Survey 5-Year Estimate,[2] and the Wisconsin Interactive Statistics on Health Query System.[3]

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Table. Decedent (Donor) Statistics and Results (n = 1224)

Decedent Statistic	How Statistic Is Reported	Donor Sample Data	Wisconsin Census Data	*P* value
Sex	F or M	Female, 662 (54.1%); male, 562 (45.9%)	Female, 50.2%; male, 49.8%	.0007
Age at death	Individuals must be 18 years or older to donate male, 84 (74-89)	All, 86 (76-91); female, 87 (78-93);	All 78; female 82; male 75	<.001
County of residence	County in which the donor was living at time of death	Top 3: Milwaukee County, 293 (23.9%); Waukesha County, 164 (13.4%); Dane County, 140 (11.5%)	—	—
Hispanic/ Spanish/ Latino origin (ethnicity)	Check 1 or more boxes: Not Hispanic/Spanish/Latina(o); Mexican/Mexican American/Chicana(o); Puerto Rican; Unknown; Cuban; Other Hispanic/Spanish/Latina(o)	Not Hispanic/Spanish/Latina(o), 1206 (99.5%); of Hispanic/Spanish/Latina(o) origin, 6 (0.5%)	Not Hispanic/Spanish/Latina(o), 92.4%;of Hispanic/Spanish/ Latina(o) origin, 7.6%	<.001
Race[a]	Check 1 or more boxes: White, Black or African American, American Indian or Alaskan Native, Asian Indian, Chinese, Filipino, Japanese, Korean, Vietnamese, Laotian, Hmong, Other Asian Specify, Native Hawaiian, Guamanian or Chamorro, Samoan, Other Pacific Islander, Other, or unknown	White 1196 (98.8%); Black or African American, 11 (0.9%), Asian 4 (0.3%)	White, 80.4%; Black or African American, 6.4%; Asian, 3%	<.001
Education	Check a box: 8th grade or less; 9th-12th grade no diploma; high school graduate or GED completed; some college credit, but no degree; associate degree; bachelor's degree; master's degree; doctorate or professional degree; or unknown	Associate degree or less, 844 (69.6%); bachelor's degree or more, 368 (30.4%)	Bachelor's degree or more, 30.8%; associate degree or less, 69.2%	.765
Usual occupation	Write-in: Occupation held for the longest period of time; cannot use "Retired"	Top 2: Office and Administration, 17.6%; Construction and Trades,[b] 14.6%; and Healthcare,[c] 7%	—	—
Armed forces service	Check a box: Yes, no, unknown	Yes, 344 (28.1%); no 880 (71.9%)	Yes 5.9%; no 94.1%	<.001

Donor sample data is reported as N (%) or median (IQR).
[a]*P* values are Holm-adjusted for multiple testing within the same variable.
[b]Construction and Trades includes 3 major groups:[5] Construction and Extraction; Installation, Maintenance, and Repair; and Production Occupations.
[c]Healthcare includes 2 major groups:[5] Healthcare Practitioners and Technical Occupations, and Healthcare Support Occupations.

Figure 1. County of Residence of Wisconsin Whole-Body Donors

Modified from The Wisconsin Maps PowerPoint (Public Domain License).[6]

The demographic data, reported as decedent statistics on the DCW, included sex, age at death, county of residence, Hispanic/Spanish/Latino ethnicity, race, education, usual occupation (occupation held for the longest period of time; not "Retired"), and armed forces service. Demographic variables are not self-reported because the DCW is completed by a funeral director in consultation with the decedent's responsible party, typically the legal next of kin. The DCW forms are completed through the Statewide Vital Records Information System (SVRIS).[4] The DCW cannot be submitted if any decedent information is reported in an incorrect format or if a box is left blank.

Due to the variety of occupations reported on the DCW, we sorted usual occupation into broader categories based on the US Bureau of Labor Statistics Standard Occupational Classification System.[5]

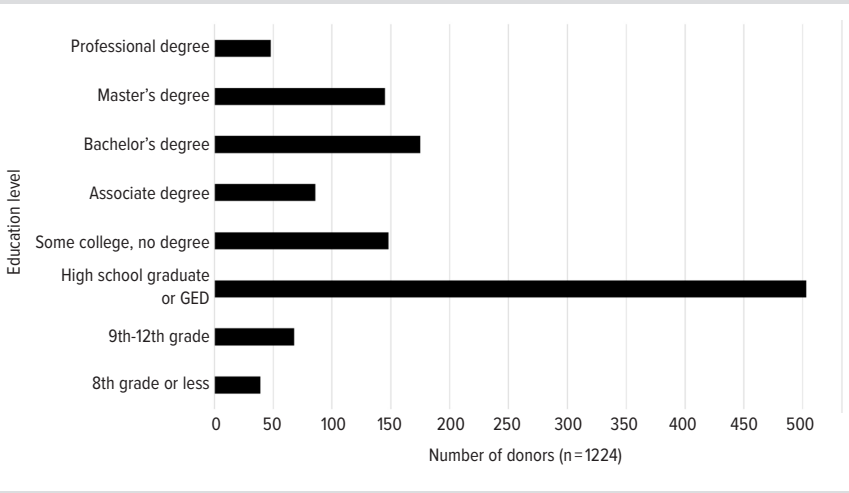
P values are reported from tests of a single proportion or Wilcoxon signed rank test against the Census data statistic as the null hypothesis for the following donor variables: sex, age at death, ethnicity, race, education, and armed forces service. The significance threshold was set at $P < .001$. County of residence and occupation were not directly compared in this study.

RESULTS

From 2016 though 2021, 1224 whole-body donations were accepted: 565 individuals donated their bodies to UWBDP and 659 to AGR.

Females accounted for 54% of the donor sample; males accounted for 46% (Table). This female-to-male ratio is not significantly different from the Wisconsin population (Table). The median age at death was 87 years for female donors and 84 years for male donors—both significantly higher than the median age at death in Wisconsin (78 years; Table). Whole-body donors came from across the state, with many having resided in the 3 most populous counties: Milwaukee (24%), Waukesha (13%), and Dane (12%; Figure 1). Almost all donors (99.5%) were of non-Hispanic/Spanish/Latina(o) ethnicity (Table). The majority of donors (98.8%) were White, 0.9% were Black or African American, and 0.3% were Asian (Table). The Asian racial categories listed on the DCW (eg, Asian Indian, Chinese, Filipino; Table) were combined into a broader Asian category so that the donor data could be compared directly to state Census data. No other racial categories were represented among donors during 2016-2021. This racial distribution is significantly different from that of the Wisconsin population, which is approximately 80.4% White, 6.4% Black or African American, and 3% Asian.

Figure 2. Education Level of Wisconsin Whole-Body Donors



Most whole-body donors did not have a college degree or work in health care; 41% graduated high school or completed a GED (Figure 2). Additionally, 30% attained a bachelor's degree or higher, which is not significantly different from the 30% of Wisconsinites who hold a bachelor's degree or higher (Figure 2; Table). The top 2 occupation categories were office and administrative support (17.6%) and construction and trades (14.6%), with only 7% of donors having worked in health care (Table). Lastly, 28% of Wisconsin whole-body donors were reported to have served in the armed forces, significantly more than the approximately 5.9% of Wisconsinites who served (Table).

DISCUSSION

This is the first report on Wisconsin whole-body donors and the extent to which they represent the state population. Individuals who donate their bodies to the 2 academic programs—UWBDP and AGR—are socially and economically diverse but not ethnically or racially diverse. The statewide impact of willed body donation is clear, as donors resided in nearly every county in Wisconsin. Donors were representative of the state population in terms of female-to-male ratio and some aspects of educational attainment; however, they were not representative in age at death, ethnicity, race, and armed forces service.

Our data indicate that students are learning from donors who represent an older population. We suspect this is because younger individuals may choose organ donation rather than whole-body donation. The older age of donors presents opportunities to discuss with students postmenopausal and other age-related changes in the body, as well as care-related needs of older populations.

Similarly, students are learning from donors who are predominantly non-Hispanic White individuals. Health professions students can make value judgements about the bodies they dissect in the anatomy lab[7] and may hold false beliefs about biological differences among socially defined racial groups.[8] To address ethnic and racial diversity in the anatomy lab, we recommend reinforcing that students should expect to see anatomical variation among donors and that this variation does not align with racial categories. Additionally, this presents an opportunity to discuss with students the many historic, cultural, religious,[9] and personal factors that influence decisions about body donation.

More than a quarter of the donors were veterans, many of whom served in World War II, the Korean War, or the Vietnam War. Median donor age suggests that donors were too young for service in World War I. However, men aged 18 to 45 years were required to register for the first peacetime draft starting in 1940, and military conscription continued until 1973.[10] We suggest that historic wartime induction into military service and the age of many of our donors from 1940 through 1973 account for the large percentage of veterans in the donor sample.

CONCLUSIONS

Whole-body donors serve as unparalleled educators for the training of health science students in Wisconsin. Their immense gifts benefit thousands of students, residents, and medical profession-

als each year. Body donation also helps drive advances in biomedical research focused on mechanisms of disease and injury and the development of clinical and surgical techniques. We aim to increase awareness of body donation to better serve both our community of learners and the Wisconsin population. A goal of health care education is to train a diverse group of students and trainees reflective of the diverse patient populations they will serve. Analyzing the demographics of body donors is a first step toward understanding diversity and representation within this unique population in Wisconsin.

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A Statewide Approach to Collaboratively Improve Access to Medical Genetics Services in Wisconsin

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ABSTRACT

Background: In the absence of a state-led initiative to monitor and address medical genetics issues affecting Wisconsin, a collaborative approach among stakeholders was implemented to identify and address service needs.

Methods: Surveys and consensus-building tools were employed to identify priority service-access needs and establish strategies to address these needs.

Results: Four statewide medical genetics priorities were identified: (1) improved coordination and collaboration, (2) increased funding for the Newborn Screening Program, (3) Medicaid policy changes regarding inpatient genomic testing and reimbursement for outpatient genetic counseling services, and (4) educational opportunities for nongenetic providers to incorporate genomic medicine into practice. Three workgroups were formed and remain active in advanced efforts in these areas.

Discussion: A stakeholder-driven process supported engagement, shared communication, and collaboration within the Wisconsin medical genetics community. Workgroups facilitated measurable progress, including increased newborn screening funding, advancement of administrative rules, expanded educational opportunities, and ongoing policy advocacy. Survey findings underscore the need for improved statewide communication and continued attention to funding and telehealth policy.

Conclusions: This initiative demonstrates an efficient and effective approach to advancing statewide collaboration and policy change in medical genetics. Sustained engagement will be critical to ensure equitable access to genetic services across Wisconsin.

BACKGROUND

Medical genetics is a subspeciality field with an accelerating impact on patient care. In Wisconsin, the field has expanded over the past several decades to include 3 Centers for Human Genomics and Precision Medicine; expanded newborn screening; additional health care systems offering medical genetics services; multiple residency, fellowship and genetic counseling training programs; continuing education (CE) conferences; a professional genetic counselor organization (Wisconsin Genetic Counselors Association [WIGCA]); and several commercial businesses competing in the genetic testing global market.

Medical genetics knowledge, technology, and capabilities are advancing rapidly, as are public awareness and demand for genetic services, testing, and information.[1] However, acute and chronic challenges to the national and statewide genetics community continue to raise concerns regarding sustainability, widening access barriers, and inequity gaps.[2] The chronic national workforce shortage is well documented.[3,4] In Wisconsin, approximately 10 geneticists (about 5 full-time equivalents [FTEs]) serve the state, and nearly half are approaching retirement age. Workforce shortages directly affect access to care, strains training programs that rely on these professionals for education and clinical supervision, and can lead to fewer outreach clinics serving rural areas. Mitigation efforts include increasing genetic counselor capacity; implementing alternate service models, such as genetic counselor-only clinics; pairing genetic counselors with advanced

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practice providers for specific indications or management of established patients with known diagnoses and protocols; utilizing genetic counseling assistants and medical assistants to support administrative needs (eg, prior authorizations, genetic test coordination);[5] and educating primary and specialty providers.

The field of medical genetics straddles the public and private domains of medicine and arguably should have sustained involvement from the public sector. In 2000, the Maternal and Child Health Bureau funded a workgroup of 34 Wisconsin stakeholders (genetic and nongenetic health care professionals, state agency staff, legislators, educators, and third-party payers) to review the status of genetics in Wisconsin and develop a "Genetics Services Plan for Wisconsin" with recommendations and guidance.[6] Among its recommendations were creation of a legislatively mandated standing advisory council modeled after the Newborn Screening Advisory Group and Birth Defects Prevention and Surveillance, establishment of an autonomous state genetics program, and improvement in statewide collaboration. However, many of the recommendations did not materialize.

Table 1. Current Areas of Need in Policy, Funding, and Education (2022 and 2023)

	Funding			Policy			Education		
Issue	2022 n=24	2023 n=28		2022 n=24	2023 n=28		2022 n=24	2023 n=28	
Outpatient genetic test coverage	63%	46%	↓	75%	42%	↓	63%	42%	↓
Inpatient exome/genome	50%	38%	↓	63%	46%	↓	46%	35%	↓
GC reimbursement (public and private)	50%	38%	↓	75%	58%	↓	25%	19%	↓
Newborn Screening Program	29%	58%	↑	4%	27%	↑	21%	38%	↑
Permanent telehealth insurance coverage	54%	23%	↓	71%	62%	↓	25%	15%	↑
Capacity to address genetic return of results from research	29%	38%	↑	4%	15%	↑	21%	35%	↑

Abbreviation: GC, genetic counselor.

For this matrix question, included in the 2022 and 2023 surveys, respondents were asked to indicate the current area(s) of need (funding, policy change, or education of decision-makers) for each issue facing medical genetics service. Respondents could select as many as they thought applied.

Table 2. Current Areas of Need in Public Health, State Infrastructure, and Leadership (2022 and 2023)

	Funding			Policy			Education		
Issue	2022 n=24	2023 n=28		2022 n=24	2023 n=28		2022 n=24	2023 n=28	
Statewide genetics coordinator	33%	43%	↑	17%	14%	↓	58%	61%	↑
WI sudden unexplained death in the young	25%	25%	=	0%	4%	↑	21%	18%	↓
Newborn Screening Program	42%	57%	↑	4%	32%	↑	21%	36%	↑
Birth Defects Registry	21%	18%	↓	8%	4%	↓	21%	21%	=
Population screening for genetic conditions	42%	18%	↓	21%	11%	↓	29%	29%	=
Family advocacy and engagement	17%	21%	↑	8%	4%	↓	33%	43%	↑

Abbreviation: WI, Wisconsin.

For this matrix question, included in the 2022 and 2023 surveys, respondents were asked to indicate the current area(s) of need (funding, policy change, or collaboration) for each public health-related issue. Respondents could select as many as they thought applied.

State funding for genetics programs or initiatives has largely remained level or decreased. Until 2023, the Wisconsin newborn screening bloodspot card fee – which is used to fund the Newborn Screening Program – remained unchanged ($109/card) for more than 10 years, despite screening expansion and increased operational costs. A state genetics coordinator position was eliminated, and funding for the Genetic Systems Integration (GSI) Initiative, created to improve access to genetics services, decreased. The Health Resources and Services Administration-funded Regional Genetics Networks were defunded in 2024. Public and private payer reimbursement policies for genetic testing and services have improved over the past decade yet continue to trail advances and practice guidelines.

In the absence of a state-led initiative to monitor and address medical genetics issues affecting the entire state, from 2018 to 2020 an ad hoc professional group collaborated with Wisconsin Medicaid and several local insurers to improve access to outpatient genomic testing, including exome sequencing, considered standard of care for patients with congenital anomalies or intellectual disability.[7,8] Exome sequencing prior authorization approvals through Medicaid increased significantly – from zero to 76 during 2017-2021.[8] This successful process and outcome greatly influenced the GSI Initiative to address continuing statewide medical genetics service needs through formation of the Wisconsin Medical Genetics Stakeholder Group (WMGSG). This brief report describes the group's collaborative process and outcomes.

METHODS

Forty-eight and 52 thought leaders and stakeholders in the Wisconsin medical genetics community were invited to participate in the 2022 and 2023 WMGSG meetings, respectively. Invitees included clinical and laboratory geneticists, genetic counselors, advanced practice providers, metabolic dieticians, referring providers, administrators, and public health representatives.

The purpose of the 2022 meeting was to identify priority service-access needs within the collective sphere of influence and to establish strategies to address the needs. The 2023 meeting aimed

to continue statewide communication, collaboration, and cooperation in assessing and addressing statewide needs.

Prior to both meetings, invitees completed a survey using Qualtrics Survey Software (Qualtrics, Provo, Utah). Both surveys collected respondent demographics. The 2022 survey contained additional questions in 2 domains: (1) Service Access Issues and Needs, and (2) Resources. Domain 1 categories included workforce; training programs; continuing education; policy, funding and education; and public health, state infrastructure, and leadership. Domain 2 categories included funding sources, staff, and partners. The 2023 survey contained 2 Domain 1 questions from the 2022 survey (policy, funding, and education; and public health, state infrastructure, and leadership).

Survey results were presented and discussed in facilitated, large- and small-group sessions at each meeting. Participants achieved consensus on 3 priority needs and self-selected into small groups to consider resources and strategies to address each need. This report reflects the ideas and areas of consensus documented by a dedicated notetaker. Three workgroups were established to implement strategies and effect change in each area.

Table 3. Workgroup Purposes and Outcomes (2023 to Present)

Workgroup	Strategies and Outcomes
Newborn Screening *Purpose* Develop a coordinated plan and message among stakeholders to support newborn screening funding and sustainability	*Strategy* • Facilitate statewide inter and intra institution communication regarding strategies and actions to educate legislative decision-makers on the NBSP during the 2023 biennium budget process (raising the blood spot card fee to $195) and the 2025 DHS rulemaking process (CR024-25} *Outcomes* • Contributed to a coordinated plan and message to decision-makers • Contributed to the furtherance of the rulemaking process which proposes an increase in the NBSP blood spot card fee to $223/card and the addition of two conditions to the newborn screening panel (rule modifications in Senate and Assembly committee review at the time of submission)
Policy and Advocacy *Purpose* Advocate for improved genetic testing policy for Wisconsin Medicaid beneficiaries and direct billing for genetic counseling services	*Strategies* • Identify state and federal pathways for policy change • Identify and compare genomic testing policies for regional and national large private payers and public payers *Outcomes* • Ongoing engagement with WI Medicaid to develop a genomic testing policy • WI Medicaid does not have the resources to create the enrollment pathway and define and implement covered services for GC direct billing
Workforce and Training *Purpose* Create and offer educational opportunities (with CME) for nongenetic providers to integrate genetics into their practice	*Strategy* • Work with partners to improve CME for genetics and nongenetics providers *Outcomes* • Contribution to provider training series and parent educational resources on genomic testing • Enhancement of the Genetics in Wisconsin website with more educational materials and resources

Abbreviations: NBSP, Newborn Screening Program; DHS, Department of Health Services; WI, Wisconsin; GC, genetic counselor; CME, continuing medical education.

Each workgroup consists of volunteers from multiple institutions across the state. Both authors are members of all workgroups. The lead author chairs the Newborn Screening and Workforce and Training workgroups, and the senior author chairs the Policy and Advocacy workgroup.

RESULTS

Needs and Resources Survey

The survey response rate was 52% (25/48) in 2022 and 53.8% (28/52) in 2023. Results from Domain 1 (service-access issues and needs) showed that 80% and 60% of repondents, respectively, indicated insufficient physician and genetic counselor FTEs to meet the genetic service needs in Wisconsin. Thirty-four percent and 56.5%, respectively, indicated that there are sufficient training programs for physicians and genetic counselors; however, none agreed that sufficient training programs exist for advanced practice providers. Eighty percent responded there are enough continuing education opportunities for genetic professionals, while only 16% agreed that there are enough opportunities for nongenetic providers (data not shown).

In 2022, most participants identified a need for policy change in outpatient genetic testing, inpatient exome/genome testing, reimbursement for genetic counselor outpatient services, and permanent telemedicine coverage, in addition to a need for education and funding for outpatient genetic testing (Table 1).

Several notable differences emerged between the 2022 and 2023 survey results. In 2023, the percentage of respondents indicating a need for Newborn Screening Program funding and policy changes increased, and 62% identified a need for permanent telemedicine insurance coverage – down from 71% in 2022.

In 2022, 58% respondents identified a need for statewide genetics coordination and collaboration, and 42% identified a need for additional funding for newborn screening and population screening for genetic conditions (Table 2). In 2023, respondents indicating a need for statewide collaboration and coordination remained stable.

Meeting Outcomes

Fifty-two percent of invitees attended the 2022 and 2023 WMGSG meetings (25/48 and 27/52, respectively). At the 2022 WMGSG meeting, the following priority needs were identified:

1. Statewide collaboration and coordination to address issues impacting the entire state
2. Increased funding for the Newborn Screening Program
3. Improved payer policies regarding inpatient and outpatient genetic testing and reimbursement for genetic counselor services

4. Education opportunities for nongenetic providers

Three workgroups were established: Newborn Screening, Policy and Advocacy, and Education (see Table 3 for workgroup goals and outcomes).

DISCUSSION

This brief report demonstrates an efficient approach to supporting engagement, shared communication, consensus building, and collaboration within the Wisconsin medical genetics community, with the goal of guiding and effecting positive change. The 3 workgroups established in 2022 remain active and continue to advance efforts in the prioritized areas.

The Newborn Screening workgroup facilitated statewide communication and coordinated action to educate decision-makers about newborn screening and the critical funding issues during the Wisconsin 2023 biennium budget process, resulting in an increased bloodspot card fee ($195/card). Additionally, in 2025, the workgroup supported advancement of the CR024-25, an administrative rule that raises the bloodspot card fee to $223 per card.[9]

The Workforce and Training workgroup contributed to continuing education opportunites for genetic and nongenetic providers in partnership with other educational initiatives. The Policy and Advocacy workgroup continues to engage with Wisconsin Medicaid, WIGCA, and other stakeholders to create an inpatient genomic testing policy and advocate for a genetic counselor professional fee.

Survey results demonstrated the need for improved statewide communication regarding relevant policies and issues. Most respondents indicated a need for permanent telehealth policy in 2023, even though Wisconsin transitioned to a permanent policy in 2022 that allows for reimbursement of functionally equivalent health care services provided via telehealth.[10] Additionally, the 2023 survey indicated increased concern about newborn screening funding despite state legislature approval of an increased bloodspot card fee earlier that year.

Medical genetics services, as well as existing and emerging public health programs, rely on the medical genetics community. The public sector should have a significant role in monitoring and supporting this community. Until that role is realized, identifying and addressing statewide needs will depend on grassroots collaborative approaches.

CONCLUSIONS

This collaborative initiative demonstrates that a stakeholder-driven approach can effectively identify and address critical gaps in statewide medical genetics services. Sustained engagement through workgroups has led to measurable progress in funding, policy development, and education. Continued collaboration will be essential to maintain momentum and ensure equitable access to genetic services across Wisconsin.

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Correlating Ultrasound Echogenicity of the Abductor Pollicis Brevis and Median Nerve Cross-Sectional Area in the Setting Carpal Tunnel Syndrome: A Pilot Study

Ragav Sharma, DO; Peter Kane Connelly, MD

ABSTRACT

Introduction: Carpal tunnel syndrome is the most common peripheral entrapment neuropathy, often associated with structural and functional changes in the median nerve and thenar muscles. Neuromuscular ultrasound is increasingly used to complement nerve conduction studies in carpal tunnel syndrome evaluation, yet its potential for assessing muscle integrity remains underexplored. This pilot study examined correlations between median nerve cross-sectional area (MNCSA) and abductor pollicis brevis (APB) muscle characteristics on ultrasound.

Methods: Veterans were enrolled at the Clement J. Zablocki VA Medical Center from July to November 2023. Inclusion criteria were age ≥18 years, carpal tunnel syndrome confirmed by nerve conduction studies, and planned carpal tunnel release. Exclusion criteria included prior carpal tunnel release, upper limb trauma or surgery, hand deformities, peripheral neuropathy, and diabetes. Ultrasound images of the median nerve and APB were obtained. Using Adobe Photoshop, APB echogenicity (grayscale value, black/white ratio) and cross-sectional area in longitudinal and transverse views were calculated and analyzed for correlation with MNCSA.

Results: Ten participants were included. Strong negative correlations were observed between MNCSA and APB cross-sectional area in longitudinal and transverse views (Pearson coefficients, –0.51 and –0.50, respectively). Weak to moderate positive associations were found between MNCSA and APB echogenicity values (0.32 and 0.24, respectively).

Conclusions: APB characteristics on ultrasound, including echogenicity and cross-sectional area, may serve as complementary indicators of carpal tunnel syndrome. Future research should include larger samples, control groups, and assessment of correlations with carpal tunnel syndrome severity on nerve conduction studies.

INTRODUCTION

With an estimated incidence of 1 to 5 per 1000 person-years, carpal tunnel syndrome (CTS) is the most common peripheral entrapment mononeuropathy in humans.[1] The condition results from compression of the median nerve at the carpal tunnel.[2] Patients often experience sensory paresthesia, pain, and functional deficits of the affected hand.[1,2] Known risk factors include female sex, diabetes, obesity, pregnancy, hypothyroidism, and multiple environmental factors.[3] Diagnosis is typically made based on clinical history and physical examination, followed by confirmatory nerve conduction studies, the current clinical gold standard.[4]

A growing number of physicians recognize that neuromuscular ultrasound provides a painless, efficient evaluation of the median nerve at the carpal tunnel.[5] Consequently, neuromuscular ultrasound is increasingly being used in conjunction with nerve conduction studies to evaluate for CTS.[5] Commonly cited diagnostic indicators include median nerve cross-sectional area (MNCSA) at the wrist, median nerve vascularity, and median nerve structural changes at the carpal tunnel.[5] Of these, MNCSA demonstrates the best sensitivity and specificity.[6,7] A MNCSA of 10 mm^2 is generally accepted as the upper limit of normal, beyond which CTS may be suspected.[8]

Though less commonly appreciated, neuromuscular ultrasound also enables assessment of muscle health and integrity.[9] In CTS, this information may prfigureovide valuable clinical and diagnostic data. Specifically, echogenicity of thenar muscles increases in

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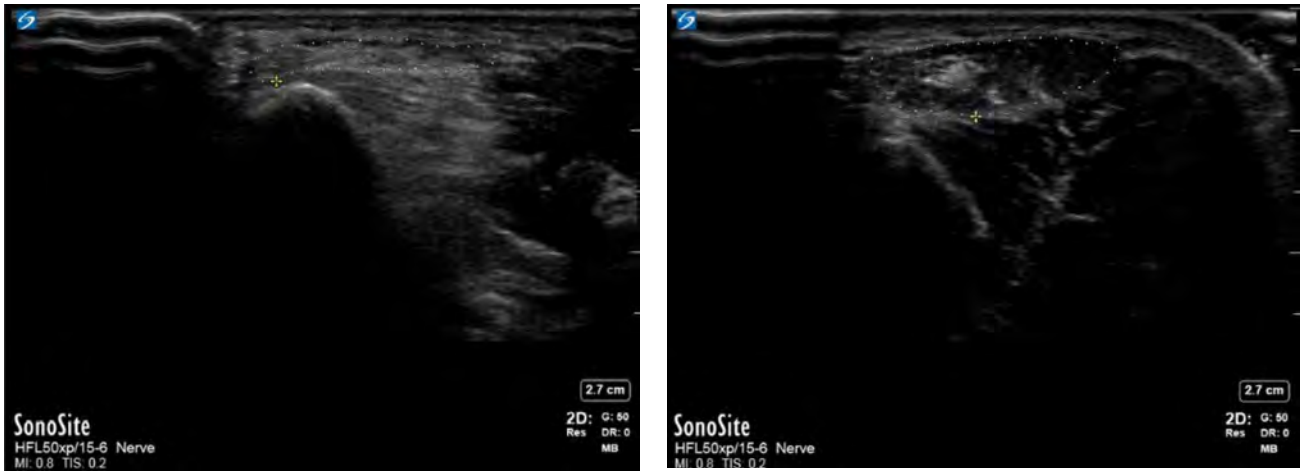
Figure 1. Cross Section of the Abductor Pollicis Brevis Demonstrating Differences in Echotexture Including Hypoechoic Versus Hyperechoic Areas



advanced CTS cases,[10] These changes likely occur due to increased tissue density from neurogenic denervation, producing a brighter ultrasound appearance, referred to as increased echogenicity.[9] Differences in echotexture are shown in Figure 1.

Building on this knowledge, our pilot study investigated potential correlations between abductor pollicis brevis (APB) muscle characteristics on ultrasound and MNCSA in patients with CTS confirmed by nerve conduction studies. This information may improve understanding of CTS pathophysiology and expand the diagnostic applications of neuromuscular ultrasound.

METHODS

This pilot study was conducted at the Clement J. Zablocki Veterans Affairs Medical Center (CJZVA) in Milwaukee, Wisconsin. After institutional review board (IRB) approval, eligible patients were identified through chart review of referrals to Physical Medicine and Rehabilitation, Orthopedic Surgery, and Plastic Surgery for CTS evaluation and management. Inclusion criteria were age >18 years and CTS confirmed by nerve conduction studies. Exclusion criteria were prior carpal tunnel release, upper limb trauma or surgery, hand deformities, peripheral polyneuropathy, and diabetes. Patients meeting inclusion criteria were approached by phone or in person. After informed consent per IRB protocol, patients were enrolled and scheduled for neuromuscular ultrasound evaluation at the CJZVA Translation Research Unit.

All ultrasounds were performed by a board-certified physiatrist with additional qualifications in electrodiagnostic medicine and neuromuscular ultrasound, as recognized by the American Board of Electrodiagnostic Medicine. Images were obtained using a Sonosite X-porte machine with a 5-12 Mhz linear probe. All images were deidentified and saved to an IRB-approved encrypted USB drive, stored securely at CJZVA per protocol.

Table. Calculated Pearson Coefficients Between Median Nerve Cross-Sectional Area and Abductor Pollicis Muscle Brevis (APB) Echogenicity Values (EV) and Echogenicity Ratios (ER)

Muscle	Pearson Coefficient
APB Longitudinal EV	0.32
APB Longitudinal ER	-0.11
APB Transverse EV	0.24
APB Transverse ER	-0.07

Subjects were examined in a seated position with the wrist supinated and elbow fully extended. Using the linear probe, the median nerve was identified in cross-section immediately ventral to the pronator quadratus muscle, then traced distally to the carpal tunnel entrance, identified by the scaphoid and pisiform bones. Still images of the median nerve were captured in transverse and longitudinal views, and the MNCSA in the transverse view was calculated using Sonosite software. The probe was then moved to the thenar eminence, where APB was identified via anatomic landmarks. APB was selected for analysis due to its limited ulnar nerve innervation compared with other thenar muscles. Still images of APB were captured in transverse and longitudinal views.

Image and Data Analysis

APB echogenicity was analyzed using Adobe Photoshop (Adobe Inc). The lasso tool was used to isolate the APB from surrounding structures. As shown in Figure 2, echogenicity was assessed by calculating black and white pixels and mean brightness on a scale of zero (black) to 255 (white). Mean brightness was obtained from the histogram function and termed echogenicity value. Ratios of black pixels to total were calculated and termed echogenicity ratio. Both metrics were calculated for each subject. APB cross-sectional area was also measured in longitudinal and transverse views.

Statistical analysis was completed using Pearson's coefficient due to the paired nature of the data. Normal distribution was confirmed with the Shapiro-Wilk test. Pearson coefficients were calculated between MNCSA and APB echogenicity ratio/value, and MNCSA and APB cross-sectional area. Power analysis was not performed due to limited sample size.

RESULTS

After inclusion criteria were met, 13 patients were enrolled; 3 did not attend the initial visit and were excluded. Thus, 10 patients were analyzed.

The mean MNCSA was 17 mm^2. Strong negative correlations were found between MNCSA and APB cross-sectional area in longitudinal and transverse views (Pearson coefficients, -0.51 and -0.50, respectively). Weak to moderate associations were found between MNCSA and APB echogenicity value in longitudinal and transverse views (Pearson coefficients, 0.32 and 0.24, respectively). All Pearson coefficients are shown in the Table.

DISCUSSION

This pilot study sought to identify associations between MNCSA and APB muscle changes on ultrasound in patients with carpal tunnel syndrome. Although limited by sample size, several important findings emerged. Specifically, the data demonstrate correlations between MNCSA and APB echogenicity and cross-sectional area.

The strong inverse relationship identified between APB cross-sectional area and MNCSA aligns with previous reports of muscular atrophy on ultrasound in CTS.[10] Although CTS severity was not measured, prior studies have correlated MNCSA with severity; thus, APB cross-sectional area may serve as a useful metric for gauging severity. Awareness of this potential association is important for clinicians using neuromuscular ultrasound to evaluate CTS.

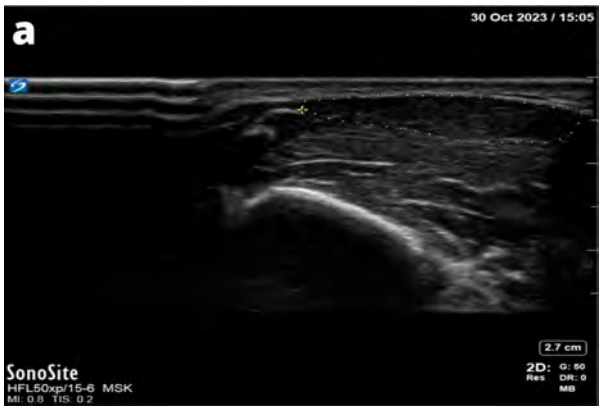
Associations between MNCSA and APB echogenicity ratio/value, though weaker, confirm previously described ultrasound findings of neurogenic denervation. Specifically, increased muscle echogenicity reflects intramuscular fibrosis and fatty infiltration in CTS. While routine calculation of these values may be impractical, recognition of muscular changes on ultrasound remains critical for clinicians performing neuromuscular ultrasound.

Study limitations include the small sample size (n = 10), recruitment from a veteran population (limiting generalizability), and potential variability in ultrasound technique, intraoperator reliability, and patient comorbidities. The absence of a control group without CTS further limits comparisons.

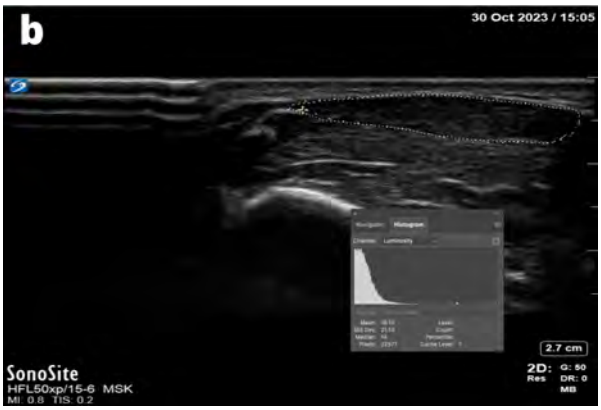
CONCLUSIONS

The findings of this study support the use of neuromuscular ultrasound to enhance understanding of carpal tunnel syndrome pathophysiology, particularly regarding abductor pollicis brevis muscle changes. More specifically, APB evaluation may complement more established CTS diagnostic methods. Future research should include a larger sample size, addition of a control group, and exploration of correlations with CTS severity on nerve conduction studies.

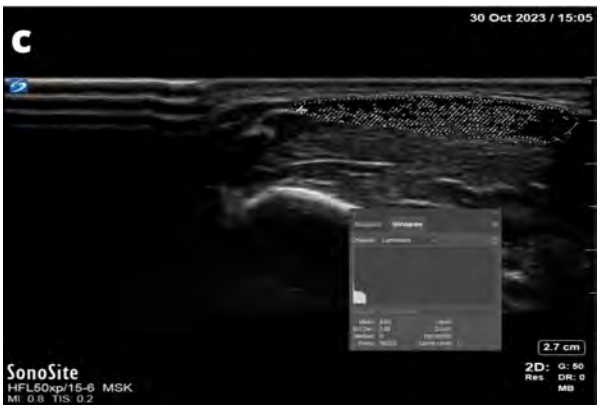
Figure 2. Calculating Echogenicity Values and Ratios of the Abductor Pollicis Brevis (ABP) Muscle in Short Axis Utilizing Adobe Photoshop



A. Image of the APB exported directly from ultrasound.



B. Lasso tool on Photoshop selecting the muscle and the histogram feature displaying values.



C. Selection of only black pixels within the muscle and the histogram feature displaying values.

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The Impact of Individual Exercise Versus Large and Small Group Exercise in Community-Dwelling Adults

Reid Pietila, BS; Derek Olson, DPT

ABSTRACT

Background: Exercise offers multiple health benefits, and improving adherence may positively influence community health. Thus, improving exercise adherence is likely to have a positive impact on community health. The YMCA, a longstanding community resource, provides exercise opportunities ranging from individual workouts to large-group classes. Group cohesion may enhance adherence; however, the effect of group size on cohesion is not well understood.

Methods: This study at the Greater Green Bay YMCA examined the impact of individual, small-group (<12 participants), and large-group (≥12 participants) exercise on adherence, frequency, satisfaction, confidence in safe exercise, and self-perceived health. An online survey distributed via the YMCA newsletter collected data on exercise preferences, membership duration, and related factors.

Results: Fifty-six members completed the survey: 14 exercised exclusively in large groups, four in small groups, 20 individually, and 18 used multiple methods. Large-group participants reported the highest satisfaction (8.8/10) and exercised most frequently, with 64% attending three or more times per week. Large-group and individual exercisers reported the highest confidence in safety (8.3/10). Combination exercisers had the highest self-perceived health (7.9/10). Among long-term members, 73% participated in some form of group exercise.

Discussion/Conclusions: Exercising in groups of at least 12 participants was associated with greater satisfaction and more frequent exercise compared with smaller groups or exercising alone. Participation in any group exercise was linked to higher self-perceived health. These findings suggest that group cohesion may influence adherence and health perceptions, providing a foundation for future research and program development.

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BACKGROUND

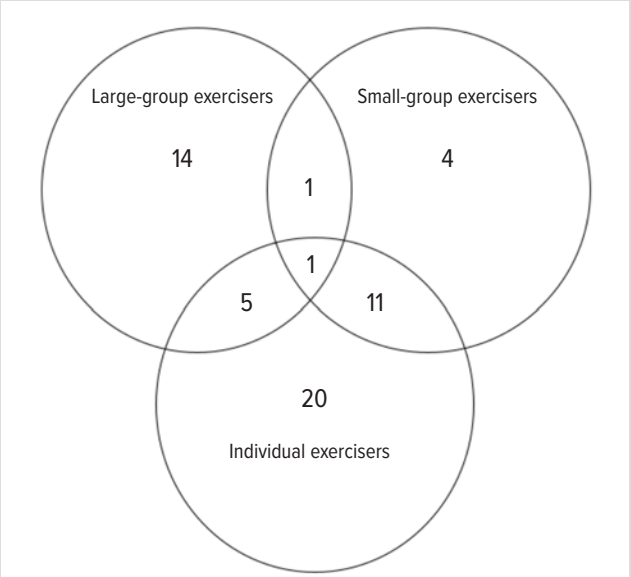
The benefits of exercise are multifactorial, encompassing several aspects of health, and exercise capacity may be inversely related to mortality risk.[1] Knowing this, optimizing exercise adherence could profoundly affect mortality prevention. The YMCA has been a community pillar in the United States since 1851, promoting healthy living and community engagement. It offers various exercise opportunities across different degrees of group involvement, ranging from individual exercise to large group classes. Perception of group cohesion may be associated with improved exercise adherence in a structured exercise setting.[2-5] However, additional research is needed to understand the effect of group size on overall group cohesion and how this may impact exercise adherence and satisfaction over time. Additionally, no data suggest an ideal group size to optimize cohesion and exercise adherence over time.

We sought to investigate the impact of individual, small-, and large-group exercise on adults at the Greater Green Bay YMCA and to determine participants' adherence to various exercise methods. We also aimed to help the YMCA improve program offerings to maximize member retention.

METHODS

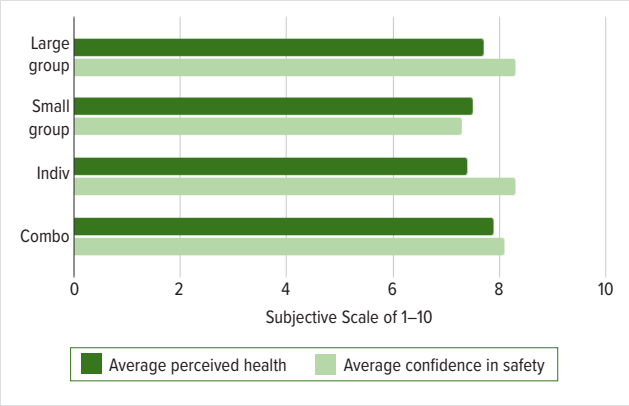
A 12-question survey was created to assess exercise preferences among YMCA members. After Institutional Review Board approval, members of the Greater Green Bay YMCA (N = 13 000)

Figure 1. Exercise Preferences of All Participants, N = 56



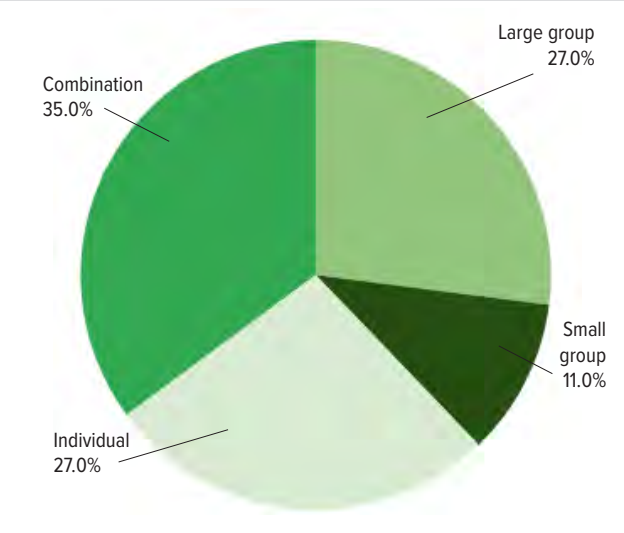
Overlapped areas indicate combination exercisers.

Figure 2. Average Perceived Health and Confidence in Safety Per Group



Abbreviations: Indiv, individual; Combo, combination.
Overlapped areas indicate combination exercisers.

Figure 3. Long-term Members in Each Exercise Group



Long-term members defined as > 2 years.

were invited to participate in the study via an online survey included in the YMCA monthly newsletter email. Participants voluntarily completed the survey, which assessed various aspects of their exercise involvement with the YMCA.

The survey included questions on age, sex, length of membership, frequency of YMCA exercise per week, members' primary reason for exercising, exercise method of choice, favorite aspect of chosen exercise method, satisfaction with exercise routine (0-10 scale), self-perceived health (0-10 scale), and confidence in performing exercise techniques safely (0-10 scale). All in-person exercise classes offered at the YMCA were included in the study, including weightlifting, cardio, cycling, Pilates, water aerobics, and cross-training. Virtual exercise classes and online coaching were excluded from the study. Members were designated as individual exercisers, small-group exercisers (<12 members), or large-group exercisers (≥12 members). The cutoff of 12 members to distinguish small from large groups was determined in consultation with YMCA exercise program directors, based on the prevalence of classes exceeding 12 participants. Those participating in multiple exercise methods were termed combination exercisers. Members were further categorized based on the length of their membership: short-term (< 6 months), intermediate (6 months - 2 years), and long-term (>2 years).

RESULTS

A total of 56 members participated in the study: 45 females and 11 males. The average participant age was 59.4 years. The study included 37 long-term, 13 intermediate, and 6 short-term members. Of the 56 participants, 14 participated exclusively in large-group classes, 4 in small-group classes, 20 in individual exercise, and 18 in more than one method (Figure 1). Ninety percent of males exercised individually as part of their routine, and 50% incorporated group exercise. Sixty-six percent of female participants engaged in group exercise, and 30% participated exclusively in large-group exercise.

Large-group exercisers reported the highest average satisfaction (8.8/10), followed by combination exercisers (8.2/10), individual exercisers (7.7/10), and small-group exercisers (7.5/10) (Appendix Supplemental Figure 1). Large-group exercisers worked out at the YMCA most frequently, with 64% exercising 3 or more times per week, followed by individual exercisers (55%), combination exercisers (50%), and small-group exercisers (50%) (Appendix Supplemental Figure 2). Combination exercisers reported the highest average self-perceived health (7.9/10), followed by large-

group exercisers (7.7/10), small-group exercisers (7.5/10), and individual exercisers (7.4/10) (Figure 2).

Large-group exercisers and individual exercisers reported the highest average confidence in safety (8.3/10) (Figure 2). Combination exercisers and large-group exercisers most valued socialization as part of their exercise routine (50% and 36%, respectively). Seventy-five percent of small-group exercisers, 53% of combination exercisers, and 50% of large-group exercisers reported workout quality as their favorite aspect of their routine, whereas 65% of individual exercisers cited convenience. Among long-term members, 35% were combination exercisers, 27% were large-group exercisers, 27% were individual exercisers, and 11% were small-group exercisers. Overall, 73% of long-term members participated in some form of group exercise (Figure 3).

DISCUSSION

Socialization and group cohesion may influence exercise adherence, as 73% of long-term members participated in some form of group exercise. Interestingly, small-group exercisers represented the smallest proportion of long-term members, which may reflect the limited availability of small-group classes. The study included only 4 participants who exercised exclusively in small groups, suggesting either low interest in small-group classes or limited offerings. This finding may indicate that large-group exercise is more likely to support long-term exercise adherence.

Large-group exercisers were most likely to exercise at the YMCA at least 3 times per week, followed by individual exercisers. Small-group and combination exercisers were least likely to exercise at the YMCA at this frequency, which may suggest decreased adherence among members who rely solely on small-group exercise. Participants involved in any form of group exercise reported higher levels of self-perceived health, with combination and large-group exercisers reporting the highest scores. This trend suggests that group cohesion may positively influence self-perceived health and that large-group exercise may have a greater impact than small-group exercise.

As expected, individual exercisers placed less importance on socialization and valued convenience most highly. In contrast, group exercisers prioritized socialization and most enjoyed workout quality. Large-group and individual exercisers reported the highest confidence in exercising safely, which is notable. We anticipated that small-group and individual exercisers would report the highest confidence because small-group classes offer more direct instruction, and individual exercisers typically have sufficient experience to function independently in a gym. Participants in the large-group category demonstrated the highest satisfaction, likely related to a sense of group cohesion. This trend aligns with the value placed on socialization in large-group exercise. Participant demographics may further explain this finding, as most participants were of retirement age, and exercise classes may serve as a source of social engagement.

This study had several limitations. First, participation in multiple exercise methods introduced confounding variables. Second, the small sample size of small-group exercisers (n = 4) limits analysis. Third, the overall sample size and descriptive nature of the data precluded statistical significance. Finally, the average participant age was 59.4, limiting generalizability to a younger population.

Next Steps

The YMCA may encourage participation in group exercise through incentives such as discounts for members attending group classes or waiving fees for special offerings. These strategies may increase member retention and ultimately benefit public health. Although conclusions are limited, this study provides a foundation for further investigation. Future studies should aim to clarify the relationship between group size and exercise adherence, ideally with greater statistical power and balanced representation across groups. Additional research should identify an optimal group size for adherence and satisfaction and explore age-related differences in exercise preferences.

CONCLUSIONS

Because members participated in several different exercise modes, we could not determine a specific group size that optimizes cohesion and exercise adherence over time. However, our results suggest that exercising in groups of at least 12 participants is associated with more frequent exercise, better long-term adherence, and greater satisfaction compared with exercising in groups of fewer than 12 participants or exercising alone. Our data also suggest that participants involved in any form of group exercise report higher self-perceived health than those who exercise exclusively alone.

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Appendix: Available at wmjonline.org

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Abdominal Cocoon Syndrome Secondary to Signet Ring Cell Adenocarcinoma: A Rare Diagnostic Challenge

Umbish Dino, MBBS; Ahamed Lazim Vattoth, MD; Jeremy Smith, MD

ABSTRACT

Introduction: Abdominal cocoon syndrome, or sclerosing encapsulating peritonitis, is a rare condition characterized by the encasement of the small bowel in a dense fibrocollagenous membrane, often mimicking symptoms of bowel obstruction. Secondary ACS associated with malignancy is exceptionally uncommon.

Case presentation: A 44-year-old man with a history of ascites presented with intractable nausea, vomiting and severe cachexia. The diagnostic process posed significant challenges, requiring advanced imaging and invasive interventions to uncover the underlying malignancy.

Discussion: This case highlights the diagnostic challenges of secondary abdominal cocoon syndrome, emphasizing the importance of maintaining high clinical suspicion and utilizing advanced diagnostic tools in complex presentations.

Conclusions: Early recognition, advanced imaging, and a multidisciplinary approach are critical to optimizing outcomes in rare and challenging conditions.

INTRODUCTION

Abdominal cocoon yndrome (ACS), or sclerosing encapsulating peritonitis, is a rare condition characterized by partial or complete encapsulation of the small bowel by a dense fibrocollagenous membrane.[1] Most cases are idiopathic, but secondary causes include infections (eg, tuberculosis), malignancies, peritoneal dialysis, and postsurgical adhesions.[2] The incidence of ACS is challenging to estimate because of its rarity, but it has been reported more frequently in men in their 30s through 50s – particularly in regions where tuberculosis is endemic.[1,3] Case reports suggest that secondary ACS associated with malignancies, as observed in this case, is even rarer, making its diagnosis particularly challenging.[4] Existing literature reveals two such malignancy-associated cases: a 49-year-old man with liver cirrhosis and diffuse large B-cell lymphoma who had imaging and autopsy evidence of ACS, and a 16-year-old girl with extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue who had intraoperative findings of ACS.[5,6]

The clinical presentation of ACS often mimics bowel obstruction, with symptoms such as nausea, vomiting, abdominal distension, and cachexia.[1] Diagnostic delays are common because of the nonspecific nature of these symptoms and the lack of clear radiological markers, particularly in cachectic patients in whom reduced intra-abdominal fat can obscure key findings on conventional imaging modalities such as abdominal computed tomography (CT).[4,7] This case underscores the importance of maintaining a high index of suspicion, especially when conventional diagnostic methods fail to yield a clear etiology.

CASE PRESENTATION

A 44-year-old man presented with a 2-month history of intractable nausea and vomiting, accompanied by a 44-pound weight loss and profound cachexia. He reported an inability to tolerate both solids and liquids, necessitating initiation of a nasogastric tube with continuous suction and total parenteral nutrition for nutritional support. His social history included past smoking (10 pack-years), alcohol use, occasional marijuana use, and a lifelong career in roofing. His family history was unremarkable, and his medical history included ascites of unknown etiology, extensively evaluated 2 months earlier at an outside hospital.

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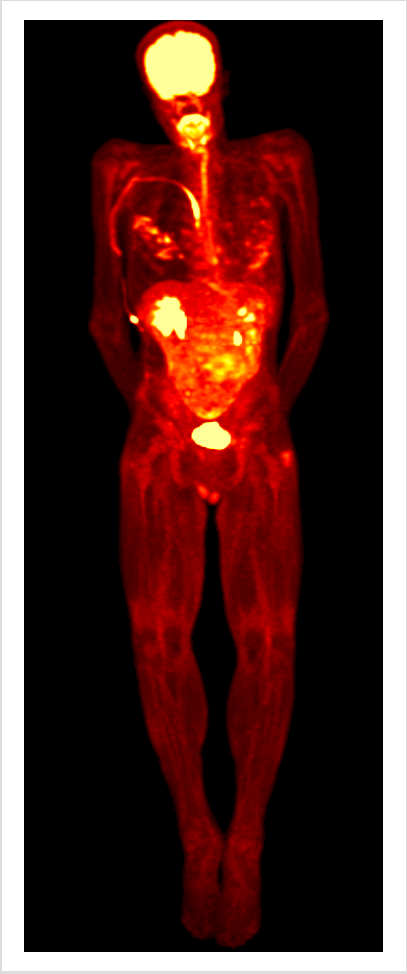
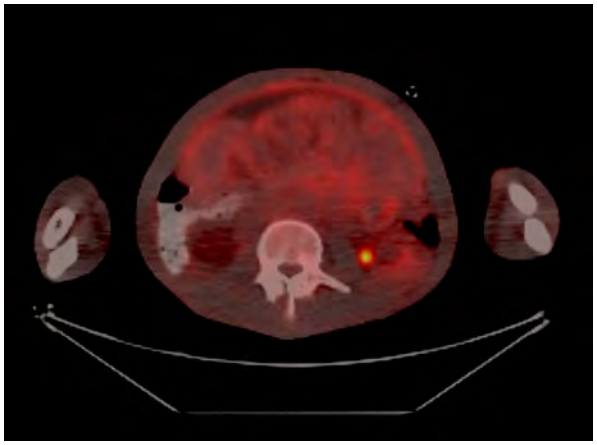
Figure 1. Three-Dimensional MIP PET–CT Image (Coronal View) Demonstrating Abnormal FDG Uptake Around the Peritoneum



Abbreviations: MIP, maximum intensity projection; PET, positron emission tomography; CT computed tomography; FDG, fluorodeoxyglucose.

Figure 2. Axial PET-CT Image Demonstrating Increased FDG Uptake in the Small Bowel With Surrounding Encapsulation



Abbreviations: PET, positron emission tomography; CT computed tomography; FDG, fluorodeoxyglucose.

Investigations at that time included ascitic fluid analysis, which revealed a high protein content (>2.5 g/dL) and a borderline serum-ascitic albumin gradient (SAAG) of 1.2. Cytology was negative for malignancy, and hepatitis and autoimmune panels were unremarkable. A transthoracic echocardiogram showed a normal left ventricular ejection fraction. Microbiological and cytological studies ruled out tuberculosis. Despite these efforts, no definitive cause for the ascites was identified. Abdominal ultrasound revealed mild nodular changes on the liver with otherwise normal morphology, and CT of the abdomen showed no cirrhotic changes. He was discharged with a diagnosis of idiopathic ascites and managed with spironolactone and furosemide.

At the time of the current presentation, the patient exhibited persistent nausea and vomiting, profound temporal wasting, and severe malnutrition. Physical examination revealed a cachectic male with a firm, nontender abdomen and minimal distension. Cardiovascular, respiratory, neurological, and extremity examinations were unremarkable. Laboratory findings showed elevated tumor markers, including CA-125, CA 19-9, and CEA; elevated alkaline phosphatase; and hypoalbuminemia. Endoscopic evaluation was pursued. Esophagogastroduodenoscopy (EGD) revealed Los Angeles (LA) grade B esophagitis, a 6-cm hiatal hernia, congested gastric mucosa, and poor gastric distension attributed to presumed extrinsic compression. Biopsy specimens taken during EGD were negative for malignancy. Endoscopic ultrasound (EUS) demonstrated diffuse gastric wall thickening and abnormal echotexture of the left hepatic lobe but was not conclusive. Of note, multiple EUS attempts were required because of resistance to insufflation. A CT scan of the abdomen and pelvis revealed diffuse peritoneal thickening, bowel wall edema, and nodular liver changes (Figure 1). However, the lack of intra-abdominal fat due to severe cachexia obscured key findings. Given the elevated alkaline phosphatase and nodular changes raising concern for a progressive fibrotic or malignant process, a liver biopsy was performed, which showed no significant fibrosis, cirrhosis, or malignancy.

With no clear etiology identified, the oncology service was consulted, and advanced imaging was pursued. A positron emission tomography (PET)-CT scan revealed fluorodeoxyglucose (FDG)-avid diffuse peritoneal thickening and abdominal cocooning (encasement of the small bowel in a dense fibro-collagenous membrane), suggestive of peritoneal malignancy (Figure 2). However, the primary source of malignancy remained elusive.

To establish a definitive diagnosis, a peritoneal biopsy was performed, which revealed signet ring cell adenocarcinoma of gastrointestinal origin with metastasis to the peritoneum. The final diagnosis of abdominal cocoon syndrome secondary to metastatic signet ring cell adenocarcinoma was established. Unfortunately,

Figure 3. Axial Computed Tomography Image Demonstrating Edema and Thickening of Peritoneum With Compartmentalization of Bowel Loops

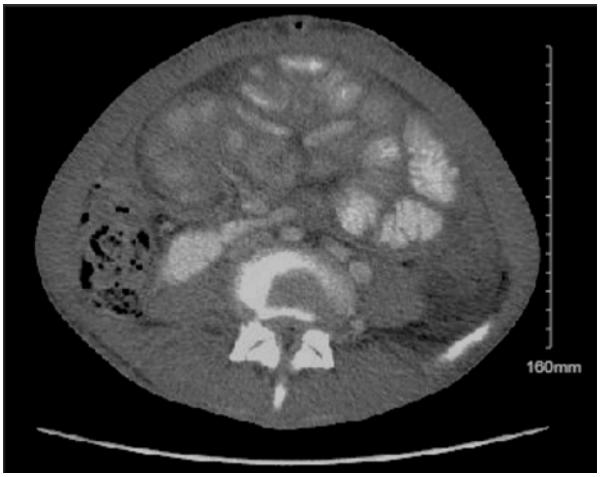
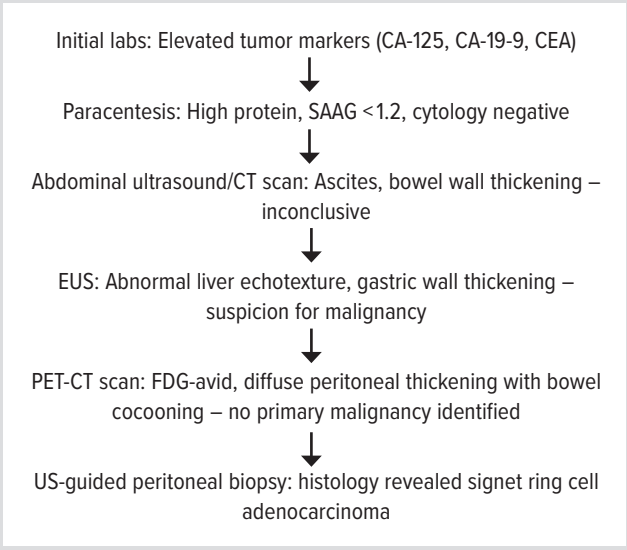


Figure 4. Flowchart Demonstrating Diagnostic Steps Leading to Final Diagnosis



Abbreviations: SAAG, serum-ascitic albumin gradient; EUS, endoscopic ultrasound; CT, computed tomography; PET, positron emission tomography, FGD, fluorodeoxyglucose.

the disease was advanced and deemed inoperable at the time of diagnosis. Due to the diffuse nature of the cancer, oncology considered surgery or radiation therapy unlikely to be helpful and systemic chemotherapy to be the only treatment option. Based on his severely malnourished state, frailty, poor performance status, and disease extent, systemic chemotherapy was cautioned to potentially aggravate the patient's symptoms without a clear idea whether the cancer would respond. He transitioned to palliative care, focusing on symptom management and quality of life. The nasogastric tube was kept in place for decompression, and while vomiting improved during hospital course, he was provided as-needed antiemetics on discharge.

DISCUSSION

Abdominal cocoon syndrome (ACS), also referred to as sclerosing encapsulating peritonitis, is a rare clinical entity typically presenting as intestinal obstruction. While idiopathic cases predominate, secondary causes such as tuberculosis, prior abdominal surgeries, peritoneal dialysis, and malignancy are well-documented.[1,2] This case, highlighting ACS secondary to metastatic signet ring cell adenocarcinoma, underscores unique diagnostic and therapeutic challenges, particularly in the context of severe malnutrition and advanced malignancy.

The rarity of ACS, particularly its secondary form associated with malignancies, poses diagnostic difficulties. Most documented cases are idiopathic or linked to tuberculosis in endemic regions, with reports predominantly involving men in their 30s through 50s.[1,3], In this case, the patient presented with nausea, vomiting, weight loss, and ascites of unknown etiology – symptoms that, while suggestive of gastrointestinal and hepatobiliary disorders, contributed to diagnostic delays because of their nonspecific nature. Although nausea and vomiting are consistent with obstructive symptoms, the presence of weight loss and ascites further complicated the clinical picture, obscuring the underlying cause.[4]

Imaging plays a critical role in diagnosing ACS. CT scans are often instrumental, revealing characteristic findings such as peritoneal thickening, encapsulation of bowel loops, and cocooning.[7] However, in this case, the diagnostic utility of CT imaging was hindered by the patient's severe cachexia, which led to a lack of intra-abdominal fat. Intra-abdominal fat typically acts as a natural contrast against surrounding tissues, making it easier to delineate anatomical landmarks and structures.[8,9] This allows for highlighting abnormalities such as peritoneal thickening or encapsulation with greater ease. The absence of fat in this patient resulted in reduced contrast, making it difficult to differentiate structures and interpret findings accurately, which were largely misinterpreted as nonspecific edema and inflammation. This limitation highlights the importance of recognizing scenarios in which advanced imaging, such as PET-CT, should be expedited to overcome such diagnostic barriers. PET-CT, with its ability to detect FDG-avid peritoneal thickening, was pivotal in this case, raising strong suspicion for peritoneal malignancy causing abdominal cocooning and guiding subsequent diagnostic steps.[10]

Future cases involving malnourished patients with similar clinical presentations may benefit from the early use of advanced imaging to prevent prolonged diagnostic delays. Endoscopic evaluations, including EGD and EUS, are valuable diagnostic tools for gastrointestinal pathologies but were challenging in this case. Multiple EUS attempts encountered resistance to insufflation, initially attributed to edema and inflammation but retrospectively

linked to fibrosis and cocooning characteristic of ACS. This limitation delayed definitive diagnosis by hindering timely tissue sampling, emphasizing the need for alternative strategies or adjunct diagnostic modalities when standard techniques are unrevealing. Signet ring cell adenocarcinoma, the underlying malignancy in this case, is an aggressive cancer often associated with peritoneal dissemination.[11] The absence of an identifiable primary tumor in this patient, coupled with widespread metastatic involvement, compounded diagnostic complexity.

Cases like this highlight the critical role of histopathological confirmation, which ultimately establishes the diagnosis through peritoneal biopsy. This case contributes to the growing literature on secondary ACS, offering valuable lessons for clinical practice. First, while advanced imaging modalities are resource-intensive, their early implementation in malnourished patients with diagnostic uncertainty may expedite diagnosis and improve outcomes. Second, the multidisciplinary collaboration in this case—spanning gastroenterology, radiology, oncology, and pathology—illustrates the importance of a coordinated approach in managing complex cases. Lastly, recognizing the demographic patterns of ACS, with a predilection for males in their 30s to 50s, can guide clinical suspicion and diagnostic prioritization in similar cases.[1,3] By demonstrating the unique diagnostic challenges posed by ACS secondary to an aggressive malignancy, this case is an example of improving diagnostic strategies in rare conditions. The expedited use of advanced imaging and a multidisciplinary approach may lead to earlier diagnosis and potentially life-saving interventions in future cases.

CONCLUSIONS

This case highlights the importance of maintaining a high index of suspicion for abdominal cocoon syndrome (ACS) in patients with nonspecific symptoms and refractory presentations. In complex cases in which cachexia limits conventional diagnostic tools, the early use of advanced imaging modalities such as PET-CT and a multidisciplinary approach can expedite diagnosis and improve outcomes. Recognizing ACS in similar clinical contexts may guide timely and effective management in future cases.

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Choroidal Rupture Secondary to Treble Fishhook Ocular Injury

Patricia Siy, BS; Kevin Schneider, MD; Jennifer Larson, MD

ABSTRACT

Introduction: Choroidal rupture is a vision-threatening complication of blunt ocular trauma but is rarely reported in association with fishing-related injuries. We describe a case of choroidal rupture following ocular trauma from a fishing lure.

Case presentation: A 9-year-old boy presented with a penetrating fishhook right eye injury from a treble hook lure. Ophthalmic examination and imaging confirmed choroidal rupture. Initial visual acuity was 20/200 in the right eye and improved to 20/60 at 2 months postinjury. At 6 months, visual acuity declined to hand motions, and optical coherence tomography showed choroidal neovascularization (CNV). The patient underwent anti-vascular endothelial growth factor (VEGF) injection under general anesthesia. At most recent follow-up visual acuity was 20/50.

Discussion: Fishing injuries typically cause vision loss through penetrating or perforating ocular trauma. Although blunt trauma is a recognized cause of choroidal rupture and vision loss, this mechanism from a fishing lure is rarely described. Close monitoring for secondary CNV is essential, and anti-VEGF therapy can effectively reduce subretinal and intraretinal fluid, resolve hemorrhage, and treat choroidal neovascularization.

Conclusions: This case highlights the potential for blunt ocular trauma from fishing lures to cause choroidal rupture and vision loss. Preventive strategies, including eye protection and adult supervision, are critical to reduce the risk of similar injuries.

INTRODUCTION

Ocular injuries are a significant cause of visual impairment in the United States. According to data from 2008 in the Nationwide Emergency Department Sample, ocular injuries result in an average of over 1700 emergency department (ED) visits per day, and males are almost twice as likely to be affected as females. These injuries usually occur as a result of work- or sports-related accidents, with the majority occurring before age 44.[1] Multiple databases consistently show that ocular injuries occur more frequently in young males than in other groups.[1,2] Additionally, ocular trauma disproportionately affects rural communities, with ED visits for such injuries occurring 5.4 times more often in rural areas than in urban areas.[1] The long-term morbidity of these injuries is especially concerning, as data from the United States Eye Injury Registry (1988–2003) indicate that fewer than two-thirds of patients with severe eye trauma regain visual acuity better than 20/200 after treatment.[2]

Although rare overall, fishhook injuries represent a substantial portion of sports-related eye traumas and typically are categorized as penetrating or perforating injuries.[3] Complications such as infection, intraocular hemorrhage, traumatic cataract, corneal scarring, and retinal detachment have previously been reported in cases of penetrating fishhooks injuries;[4] however, we report a case of blunt trauma from a fishhook ocular injury that resulted in choroidal rupture and vision loss.

CASE PRESENTATION

A 9-year-old boy presented to a rural ED following penetrating ocular trauma caused by a treble hook lure. On arrival, a towel was attached to the fishhook, as the family had attempted to cover the eye. Per interview, the patient had been practicing casting with a fishing pole and treble hook lure in his driveway when he reeled back and the lure struck his right eye.

External examination revealed one hook embedded in the right upper eyelid, one free hook, and one deeply embedded hook not

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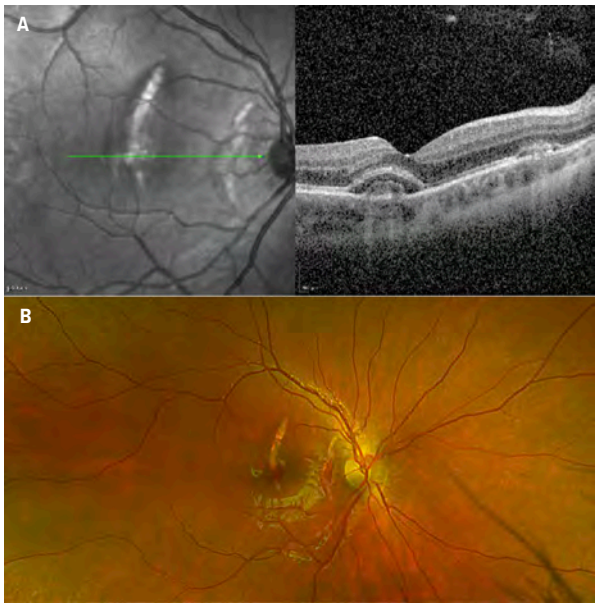
Figure 1. Initial Penetrating Injury

Penetrating treble hook injury with blunt force trauma to right upper eyelid and globe from fishing lure.

Figure 2. Images Three Days Postinjury



A. Initial orbital computed tomography 3 days after injury and open globe repair shows crescent-shaped subfoveal choroidal rupture.
B. Initial fundus photography shows subfoveal choroidal rupture 3 days after injury and open globe repair.

fully visualized. At the outside ED, an ED physician sedated the patient with ketamine and cut the lure from the hook. The hook in the eyebrow was extracted using the 18-gauge needle-over-the-barb technique. However, the final hook was found embedded in the sclera. A paper cup was placed over the eye for protection, tetanus status was reviewed, cefazolin was administered, and ophthalmology was then consulted. Ocular pressures were not checked initially due to concerns about an open globe injury.

The patient was transferred to a tertiary care hospital for specialized ophthalmologic management. Initial presentation showed a fishhook embedded in the right upper eyelid and eye (Figure 1). Orbital computed tomography (OCT) confirmed a right globe injury with a retained metallic fishhook spanning the lateral corneal limbus. Initial visual acuity was 20/200 in the right eye and 20/25 in the left eye based on a standard Snellen distance chart. He was given intravenous moxifloxacin as prophylaxis and brought to the operating room for emergent open globe repair and examination under anesthesia.

Under anesthesia, the fishhook was visualized perforating the right upper eyelid and penetrating the superolateral sclera 3 mm posterior to the limbus. The barb tip from one hook was found to penetrate the conjunctiva, Tenon's capsule, and sclera. Fortunately, the proximal barbed portion did not fully penetrate the sclera, allowing removal in the same trajectory as the injury without further damage to the underlying uveoscleral tissue. The hook was grasped with a locking hemostat and removed. The sharp end of the hook was rotated away from the globe, and a wire cutter was used to cut the barb, which was then discarded. The remaining hook was then removed from the eyelid without resistance.

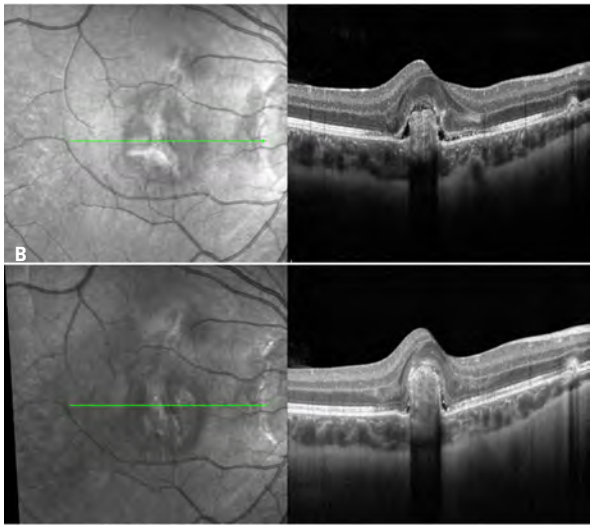
Examination of the globe using the operating microscope revealed a 1.5-mm scleral laceration with exposed pigmented uveal tissue. The globe was well-formed, including the anterior chamber. The uveal tissue was excised, and a single 9-0 nylon scleral suture was placed. Three 8-0 polyglactin 910 sutures were placed to close the conjunctiva. The wound was Seidel negative. Subconjunctival injections of cefazolin and betamethasone were administered.

The right upper eyelid laceration was repaired using 6-0 gut suture. Drops of phenylephrine 2.5% and cyclopentolate 1% were used to dilate both eyes prior to a dilated eye exam under anesthesia. The affected eye showed a clear lens without subluxation or evidence of traumatic cataract, and the optic nerve appeared normal. The macula exhibited two crescentic white bands, consistent with choroidal rupture. No retinal or vitreous hemorrhage was noted. Following the examination, the eye was patched and shielded for protection, and the patient was extubated.

Postoperatively, the patient continued to experience blurry vision. Visual acuity was 20/200 in the right eye and 20/20 in the left eye. Visual fields were full, and no afferent pupillary defect was noted. A handheld electronic tonometer was used to measure intraocular pressures, which were within normal limits. Retina specialist evaluation included a detailed fundus examination using a Haag-Streit slit lamp, and imaging (ultra-widefield fundus photography, OCT of the macula, and OCT angiography of the retina) confirmed choroidal rupture without choroidal neovascularization (CNV) (Figure 2).

The patient's vision improved to 20/125 at 1 month and 20/60 at 2 months postinjury. Repeat OCT and fundus photography showed resolved subretinal hemorrhage and scar formation. Notably, in the early postoperative period, the patient did not develop endophthalmitis, traumatic cataract, or retinal detachment, and there was no evidence of CNV. His visual impairment was attributed to the choroidal rupture from the blunt trauma. However, at 6 months postinjury, he developed blurred vision and presented urgently to the retina clinic. Examination and imaging demonstrated visual acuity of hand motions and a choroidal neovascular membrane (CNVM) with associated subretinal fluid in the affected eye. He underwent anti-vascular endothelial growth factor (VEGF) treatment under general anesthesia, and 1 month later, visual acuity improved to 20/60. At the most recent follow-up, 2 months posttreatment, visual acuity was 20/50 with involuted CNV and no subretinal fluid or hemorrhage (Figure 3).

Figure 3. Images at Follow-up and After Anti-Vascular Endothelial Growth Factor Injection



A. Orbital computed tomography (OCT) 6 months after injury and open globe repair shows development of choroidal neovascularization with associated subretinal fluid with visual acuity hand motions.

B. OCT approximately 2 months after anti-vascular endothelial growth factor injection with near complete resolution of subretinal fluid with improvement of visual acuity from hand motions to 20/50.

DISCUSSION

Ocular injuries are a common sports-related eye injury and cause of visual impairment. These injuries account for more than 630 000 ED visits annually, many of which could be prevented with improved safety practices.[1] In this case, the patient was not wearing eye protection while practicing casting independently. While the Wisconsin Department of Natural Resources recommends adult supervision of children while fishing, no specific guidelines address eye protection. For beginners learning to cast, safety can be enhanced by practicing without a lure or hook. Establishing clear guidelines and raising awareness of ocular injuries are important to prevent future incidents.

When ocular injuries occur, timely and appropriate initial evaluation is critical. Most often, the first assessment is conducted by nonophthalmologist clinicians.[1] Therefore, providers in primary care and the ED should be well prepared to assess and manage these cases in the early stages—especially in rural settings where access to an ophthalmologist may be limited. The assessment of ocular trauma should begin with evaluation of any life-threatening injuries. Then, a thorough history should be taken to address the mechanism of injury, setting and timing of injury, ocular review of systems, and past ocular history, including the patient's visual acuity prior to the injury. Relevant exam includes assessment of visual acuity, relative afferent pupillary defect, and confrontation visual field testing. If an open globe is suspected, an eye shield should be placed for protection, and tonometry should be deferred to avoid extrusion of ocular contents. Manipulation of the eye and removal of any visible foreign body should be deferred to an ophthalmologist.[5]

Although perforating or penetrating ocular injuries from fishhooks are the most commonly reported mechanisms, as seen in our patient, it is possible for a combined mechanism of penetrating and blunt force trauma from a fishing lure to cause ocular injury and vision impairment as well. Therefore, thorough ocular examination and imaging at follow-up are required to evaluate and manage less common fishing-related eye injuries.

One possible consequence of blunt ocular trauma is traumatic choroidal rupture, which is caused by shear stress and occurs in approximately 5% to 8% of cases. Patients may experience decreased vision, scotoma, and visual field defects.[5] The degree of visual impairment immediately following choroidal rupture depends on the location of the rupture, the degree of associated choroidal or vitreous hemorrhage, and other associated ocular injuries. Patients who sustain subfoveal choroidal ruptures, as in our patient, generally present with the worst visual acuity. In early stages of evaluation, choroidal ruptures appear as white to yellow-red crescent-shaped lesions and are often associated with retinal edema and hemorrhage. Angioid streaks and lacquer cracks have similar appearances and can be mistaken for choroidal rupture. In the weeks following choroidal rupture, a fibrotic or gliotic-appearing scar forms over the crescentic lesion, followed by hyperpigmentation at the margins of the healing lesions.[6]

In large part, the growth of CNV determines the likelihood of visual recovery. As part of the expected healing process, CNV is a normal occurrence following choroidal rupture, with 5% to 12% of patients with choroidal rupture developing CNV and 80% of CNV presenting within the first year after injury.[6,7] Newly formed blood vessels often regress once structural repair of the rupture has occurred. However, in 5% to 25% of cases, CNV persists after this

initial period of healing and can further exacerbate visual impairment by causing loss of central vision, decline in visual acuity, metamorphopsia, and scotoma.[8] During this time, careful observation and close patient follow-up is appropriate.

Most patients with a choroidal rupture do not recover a final visual acuity of 20/40 or better.[9] Long term, children may have improved visual outcomes compared with adults due to increased CNV in older ages. Thus, patients who sustain choroidal rupture injuries earlier in life may be more likely to regain visual acuity. From a histopathology standpoint, CNV in older eyes are thicker and more extensive, vascular, and cellular. The difference in CNV formation based on age is thought to be due to age-related decreased expression of angiogenic growth factors, loss of the proliferative capacity of aging endothelial cells, or loss of the expression of endothelial enzymes responsible for digesting the extracellular matrix.[10]

For some cases in which CNV persists beyond the initial stages of healing, anti-VEGF injections have been used to slow the disease process by inhibiting the progression of the CNVM. Clinical trials such as MINERVA demonstrate that anti-VEGF therapy is safe and effective for CNV treatment in adults.[11] However, there is hesitancy in using anti-VEGF in pediatric patients due to potential short-term adverse events, including endophthalmitis, other ocular inflammation, rhegmatogenous retinal detachment, ocular hypertension, cataracts, corneal opacification, and vitreous hemorrhage. Long term, anti-VEGF therapy may lead to abnormal retinal vasculature, shunt vessels, and refractive errors.[12] However, despite these potential side effects, anti-VEGF has been used in the setting of a choroidal rupture injury and posttraumatic CNV to safely provide improvement to visual acuity.[13,14] Additionally, intravitreal injection of anti-VEGF is utilized in infants with retinopathy of prematurity, Coats disease, retinoblastoma, CNV, and other advanced pediatric vitreoretinal diseases.[15] Future studies to evaluate long-term safety in pediatric populations are warranted.

CONCLUSIONS

This is the first reported case of choroidal rupture from a fishing lure injury. Given the common association of fishing injuries with globe penetration or perforation, awareness should be raised surrounding the possibility of blunt trauma and choroidal rupture, especially if a heavy lure or weight is used and strikes the eye. In these cases, thorough examination and follow-up are essential to optimize visual recovery and inform further treatment. In the event of secondary CNV, anti-VEGF injection may be warranted and requires special consideration in pediatric patients because of anesthesia requirements and limited long-term safety data.

Preventive strategies are critical. Improved guidelines that emphasize eye protection and adult supervision for children could reduce the risk of similar injuries in the future. Efforts are underway to advocate for enhanced safety recommendations through the Wisconsin Department of Natural Resources, including routine use of protective eyewear during recreational fishing.

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Gender-Affirming Self-Orchiectomy in a Nonbinary Patient

Caitlin J. McCarthy, MD; Sara S. Lindeke, MD

ABSTRACT

Introduction: Self-orchiectomy is a rare occurrence primarily documented in the context of psychosis. We present the case of a nonbinary individual without psychotic symptoms who performed self-orchiectomy to alleviate gender dysphoria.

Case presentation: An adult nonbinary individual who was assigned male sex at birth presented to the emergency department after removing their testicles several hours earlier. Psychiatry was consulted to assess capacity to refuse testicle reattachment. There was no psychosis, substance use, or suicidal ideation. The patient verbalized all necessary criteria for decision-making capacity. Urology performed wound closure, and the patient was discharged.

Discussion: Few similar cases in the existing literature discuss capacity assessment following self-orchiectomy in nonbinary patients.

Conclusions: While our patient recovered, self-surgery is dangerous. This case illustrates that self-orchiectomy is not limited to cases of psychosis or substance use and emphasizes the importance of broad access to gender-affirming care.

INTRODUCTION

Self-orchiectomy, the removal of one's own testicles, is a rare occurrence primarily documented in the context of psychosis or substance intoxication.[1-4] For transgender, nonbinary, or other gender-diverse patients with limited access to gender-affirming health care amid a constantly evolving political landscape, self-orchiectomy may feel like a last resort. We present a unique case of self-orchiectomy in a nonbinary patient without acute psychosis who demonstrated capacity to refuse urologic reattachment of testicles.

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CASE PRESENTATION

A nonbinary individual in their 30s who was assigned male sex at birth presented to the emergency department (ED) after removing their testicles several hours earlier at home. The patient applied lidocaine cream as a topical anesthetic agent, then used a zip tie as a tourniquet and a sterilized kitchen knife to remove the scrotum. They experienced significant bleeding, called emergency services, and were brought to the hospital by ambulance. The discarded scrotum was transported to the hospital separately.

Physical examination was notable for mild tachycardia with otherwise stable vital signs, absent testes, and excision of 90% of scrotal skin. Laboratory investigations, including complete blood cell count and basic metabolic panel, were unremarkable. No urine toxicology was obtained; however, there was no evidence of intoxication. The recommendation from urology was to attempt microsurgical reanastomosis of testes, which the patient declined. Consultation-liaison psychiatry was asked to assess capacity to refuse surgical reattachment of the testicles.

The patient had no significant past medical history. Psychiatric history was significant for gender dysphoria, anxiety, and depression. At the time of presentation, they were not taking any psychotropic medications and reported an extended period of stable mood and minimal anxiety prior to admission. The patient reported identifying as nonbinary for many years. They had researched treatment options to suppress testosterone for the past month because of unwanted masculine features and irritability. They felt surgical bilateral orchiectomy would be cost-prohibitive and did not obtain formal consultation for hormone-blocking medications for fear of being stigmatized by clinicians.

The patient was interviewed in the trauma bay of the ED. Mental status examiantion showed a fully oriented adult patient who was calm and cooperative with evaluation. The patient had euthymic affect, intact attention, and organized and logical thought. There was no evidence of depression, psychosis, or delusion. They were not intoxicated and did not demonstrate any cognitive impairment. They denied depressed mood, suicidal ideation, or self-harming intent. With the patient's permission, their mother was at bedside and corroborated their story. The patient accurately described the sequelae of declining testicle reattachment—specifically, sterility, reduced muscle mass, changed tone of voice, and reduced body hair; these factors were viewed positively by the patient. The patient verbalized necessary criteria for decision-making capacity and consistently chose to forego reanastomosis of their testicles. They also declined fertility preservation via sperm banking. Urology performed wound closure, and the patient was discharged the following day in stable condition. At urology follow-up 3 months later, the patient was noted to be well-healed with stable mood.

DISCUSSION

Also known as Eshmun complex, as originally described by the Greeks, self-orchiectomy has rarely been reported in the literature and almost exclusively in the context of psychosis, substance use, or delusion.[1,3-5] It also has been known as Klingsor syndrome when the motivation for castration is due to religious delusions.[6] Given the potentially stigmatizing nature of this injury, it is thought to be underreported; thus, accurate epidemiological data about self-orchiectomy are unknown.

It has been estimated that up to 87% of cases of genital self-mutilation occur in the setting of psychotic symptoms.[7] First documented in the medical literature in 1901, Stroch described a young adult man who removed his scrotum in attempt to relieve pain due to "lack of success in life" that he considered secondary to his sexual organs.[8] In 1949, Bisset documented a young man who removed both testicles as he believed it would cure his epilepsy.[9] A case report from 1979 includes a man who cut a significant distal portion of his penis "in obedience to the New Testament."[7] Also in 1979, Kalin reported a case of self-surgery by a patient who completed a bilateral orchiectomy (and later attempted adrenal gland denervation) because of the belief he needed to be saved from being "hyper-aggressive."[5] More recently, Isaacs and Kaleka (2023) reported an older man who amputated his penis in the context of schizophrenia (delusions about women arguing over his penis) and methamphetamine use.[3]

At the time of their literature review, Greilsheimer and Groves reported 40 known cases of genital self-mutilation at the time, only 6 of which involved testicle removal.[7] More recently, a systematic review by Veeder and Leo reported 173 cases of male genital self-mutilation from 1900 to December 2015, with 32.4% involving removal of the testicles.[4] They also found that for patients with gender dysphoria, inaccessibility to treatment was noted in 71% of cases.[4]

Some case reports describe attempts at castration secondary to concerns related to sexual identity and libido. One unique case report describes a middle-aged man who hired another person via an online chat room to remove his testicles; the intent was to suppress his sexual drive, to which he attributed many previous tumultuous relationships.[10] In a nonsurgical case, an adult man injected his testicles with food-grade calcium chloride in an attempt to decrease libido.[11] In both cases, neither patient was found to have acute symptoms of psychosis or depression, nor evidence of suicidality.

Few similar reports in the existing literature are in the setting of gender dysphoria, estimated to represent 15.3% of total cases.[4] McGovern documents an adult transgender woman who performed self-castration while awaiting gender-affirming surgery and cautions that if wait times for gender-affirming surgery lengthen or care becomes less accessible, the incidence of genital self-mutilation may increase.[12]

In our case, the patient was a nonbinary individual who performed a self-orchiectomy at home to remove masculinizing effects of testosterone and alleviate gender dysphoria. Consultation-liaison psychiatry was asked to determine whether the patient had capacity to refuse urological reattachment of their testicles. Their actions were not suicidal or self-harming in nature. In contrast with much of the existing literature, the patient was not psychotic, delusional, or under the influence of substances.

Few documented similar cases remark on capacity assessment in the setting of self-orchiectomy. In one case, the patient was asked to sign a statement before consenting to an operation to close the wound, describing this was intended to "prove legal cover in the event of any subsequent action after the patient had realized his deformity."[9] This patient was later described as "indeed rather proud of himself."[9] Greilsheimer and Groves posit that individuals "adamantly opposed to surgical repair" will likely dispose of the organs, while ambivalent individuals may bring the organs to the hospital.[7] They recommend that any individual who brings the severed genital organ should have surgical reattachment attempted. They also note that psychiatric consultants should prepare for negative countertransference from other team members, especially in the case of self-castration, as "he has intentionally inflicted on himself that wound Freud tells us neurotic men fear above all else and some neurotic women feel they have sustained."[7] In describing a case of a self-castration in a transgender adult woman, McGovern asserts that "people who perform self-castration usually oppose surgical repair of their genitals."[12]

The four criteria of decision-making capacity include (1) understanding of the condition including all potential risks, benefits, and alternatives; (2) ability to appreciate all relevant information and apply it to their own situation; (3) clear reasoning process; and (4) expression of a clear and consistent choice.[13] Our patient

demonstrated an understanding of their condition, including the possible effects of declining testicle reattachment and a subsequent acute drop in testosterone; in fact, they viewed potential sequelae as desirable and reported no interest in ever parenting biological children. They demonstrated appreciation of all information and a clear reasoning process, which was supported by their mother during the interview. While the patient did transport the severed testicles to the hospital, they expressed a clear and consistent choice to refuse the procedure to reattach them. We determined that they had capacity to make this decision; indeed, it was our assessment that reattaching the testicles would be more likely to cause psychological harm to this patient.

Finally, one might also consider the "four topics" or "four quadrants" ethical framework proposed by Jonsen et al, which builds on the four principles of bioethics: respect for autonomy, beneficence, nonmaleficence, and justice.[14] The first topic, medical indications, requires assessment of diagnosis, proposed treatment, and expected outcome, as well as consideration of beneficence and nonmaleficence. In this case, from a psychological standpoint, it was decided that upholding the patient's choice to remove their primary source of testosterone was both promoting their well-being and avoiding any further harm. Further, in comparison with attempted reanastamosis of the testicles, wound washout and closure was a much simpler and less invasive procedure, presenting fewer objective surgical risks. The second topic of patient preference, guided by the ethical principle of respect for autonomy, has already been discussed, as the patient was deemed to have decision-making capacity and communicated clear preference. Quality of life, the third topic, involves consideration of both respect for autonomy and beneficence in assessing how proposed treatment might impact quality of life for the patient. In our case, the patient was readily able to describe how their quality of life would be improved secondary to removal of their testicles, namely in ways that reduced their gender dysphoria and aligned with nonbinary gender identity (eg, changes in tone of voice, muscle mass, body hair). The fourth topic, contextual features, includes any psychosocial aspects that may affect patient care, such as family and relationship dynamics, economic or legal issues, or religious affiliations. Our patient described good social support in their mother and friends, no significant financial or legal issues, and gainful employment. However, the broader sociopolitical context is also relevant.

In June 2023, the Human Rights Campaign declared a state of emergency for lesbian, gay, bisexual, transgender, and queer/questioning (LGBTQ+) individuals in the United States, citing multiple restrictive legislative changes.[15] These developments have contributed to an increasingly volatile and unpredictable landscape for gender-affirming care. For some patients, barriers to accessing medically supervised treatment may lead to extreme measures such as self-orchiectomy.

CONCLUSIONS

This case contributes to the limited literature on self-orchiectomy in nonbinary patients and underscores the need for careful psychiatric evaluation in the context of gender dysphoria. Unlike most reported cases, our patient was not psychotic, delusional, intoxicated, or otherwise impaired. Their decision-making was intact, and their motivations reflected longstanding gender dysphoria and barriers to gender-affirming care.

Although the patient recovered without complication, self-surgery is dangerous and carries significant risk. Clinicians—particularly psychiatrists and emergency care providers—should be prepared to evaluate patients presenting with self-injury related to gender dysphoria. This case illustrates that self-oriectomy is not limited to cases of psychosis or substance use and underscores the importance of broad access to gender-affirming care.

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Successful Treatment of Opioid-Induced Hyperalgesia with Buprenorphine: A Case Report

Adam Clements, DO; Ben Kaster, MD, MPH; Phillip Hartfield, MD

ABSTRACT

Introduction: Opioid-induced hyperalgesia (OIH) is a paradoxical increase in pain sensitivity in patients receiving chronic opioid therapy. Many patients with OIH may be labeled incorrectly as drug-seeking or addicted. Common management strategies include opioid rotation, dose reduction, and use of N-methyl-D-aspartate receptor antagonists and/or nonsteroidal anti-inflammatory drug. However, evidence supporting these interventions is limited.

Case presentation: We report the case of a 57-year-old woman with metastatic endometrial cancer, previously treated with hysterectomy, chemotherapy, and pelvic radiation, who was receiving hospice care. Despite escalating opioid doses (240 morphine milligram equivalents daily), her pain worsened. She was discharged from hospice for opioid overuse and referred to our addiction clinic. OIH, rather than opioid use disorder, was suspected as the primary barrier to pain relief. Using a microdosing strategy, we transitioned her to buprenorphine, resulting in significant pain reduction and improved quality of life.

Discussion: Buprenorphine is an opioid widely used for the treatment of opioid use disorder, and emerging evidence supports its role in chronic pain management. However, its ability to treat OIH has not been well described. This case suggests that buprenorphine may be effective for patients with opioid tolerance and hyperalgesia and underscores the importance of considering alternative diagnoses in those who are diagnosed with opioid use disorder.

Conclusions: Buprenorphine may offer a safe and effective option for managing OIH in patients with chronic pain and high-dose opioid exposure. Further research is needed to clarify its role in treating OIH and to guide clinical practice.

INTRODUCTION

Opioid-induced hyperalgesia (OIH) is a paradoxical increase in pain sensitivity in patients receiving chronic opioid therapy, which can make managing chronic pain difficult. A hallmark feature of OIH is pain that extends beyond the original site. OIH may also include allodynia, defined as pain evoked by non-noxious stimuli.[1]

The pathophysiology of OIH is complex and not completely understood, with current evidence pointing to multiple contributing factors.[2] Chronic stimulation of μ-opioid receptors is believed to activate the central glutaminergic system and the release of pro-nociceptive spinal dynorphins, both of which enhance nociception.[3,4] The most widely researched theory of OIH is the neuroexcitatory model, which suggests that certain opioids and their metabolites activate the N-methyl-D-aspartate (NMDA) receptor. This activation leads to calcium influx, increasing neuronal excitability and facilitating pain transmission. Evidence supporting this model includes the observation that OIH is not relieved by opioid antagonists such as naloxone, which may worsen pain in patients receiving high-dose opioids by blocking μ-receptor activation while leaving hyperalgesia unopposed.[5] Multiple genetic variants encoding catechol-O-methyltransferase also appear to influence central sensitization by decreasing catecholamine breakdown.[2] This mechanism may partially explain the benefits of NMDA receptor antagonists in treating OIH.

Management of OIH can be challenging. Current pharmacological approaches include opioid, rotation, dose reduction, and use of NMDA receptor antagonists or nonsteroidal anti-inflammatory drugs (NSAIDs).[2] Studies show that OIH is more strongly associated with opioids from the phenanthrene class, such as codeine, hydromorphone, and morphine (opioid classes are listed in Table 1). Codeine is metabolized to morphine via CYP2D6,

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and morphine is primarily converted to morphine-3-glucuronide (M3G) through glucuronidation. M3G, an NMDA agonist with minimal μ-receptor affinity, is produced at a higher rate than other metabolites, contributing to neuroexcitatory effects. Switching to or initiating therapy with a structurally different opioid, such as buprenorphine, can avoid NMDA-activating metabolites and help resolve or prevent OIH.[5]

Buprenorphine is a semisynthetic opioid known for its analgesic properties and well-established role in the treating opioid use disorder (OUD). It has complex, incompletely understood effects at multiple receptors: it acts as a partial agonist at the μ-opioid receptor, antagonizes κ- and δ-opioid receptors with high affinity, and binds to the opioid receptor-like (ORL1) receptor.[6] Its ability to attenuate κ-receptor activity may reduce spinal dynorphins, which contribute to OIH pathogenesis.[7] It is theorized that buprenorphine's ORL1 activity may also reduce the risk of opioid tolerance and sensitization to painful stimuli compared with morphine.[8,9] Additionaly, buprenorphine belongs to the nonphenanthrene class of opioids, making it less likely to act as an NMDA agonist.[5]

CASE PRESENTATION

We present the case of a 57-year-old woman with endometrial cancer treated with hysterectomy, chemotherapy, and pelvic radiation in 2015, after which she developed chronic rectal and pelvic pain. When her cancer returned in 2017, she was treated at a tertiary care hospital 2.5 hours by car from her residence. Due to worsening pain, she was unable to travel this distance despite taking 240 morphine milligram equivalents (MME) daily, including fentanyl and oxycodone. Local pain management services treated her with hypogastric plexus blocks and multiple opioid pain regimens, including oxycodone, methadone, and oral hydromorphone. Her pain control was inadequate or short-lived despite several opioid rotations and high doses. She became progressively walker-dependent and exhibited significant weight loss, from 157 pounds to 98 pounds (body mass index [BMI], 15). During this period, she was hospitalized multiple times for pain control and severe opioid-induced constipation. Her pain also spread beyond the primary pelvic site including painful swallowing, headaches, generalized abdominal and back pain, and pain with defecation. Because of widespread symptoms and inability to tolerate cancer treatment, she was referred to hospice care.

While in hospice, she received long- and short-acting morphine with ketamine and diazepam. Initially, pain control was adequate; however, she began exhausting her weekly morphine supply within a few days due to escalating pain. After multiple hospitalizations for pain control and severe opioid-induced constipation, she was switched to oral morphine extended-release (MS Contin) 90 mg 3 times daily, hydromorphone 4 mg every 4 hours, and oral ketamine, which provided only temporary relief. Over 2 weeks, she again depleted her weekly supply within a few days.

Table 1. Classes of Opioids[10]

Phenanthrene Opioids	Nonphenanthrene Opioids
Codeine	Piperidine derivatives:
Hydrocodone	Fentanyl
Hydromorphine	Meperidine
Morphine	Sufentanil
Oxycodone	Other:
Oxymorphone	Buprenorphine
	Methadone
	Tramadol

Her pain worsened and spread—particularly painful swallowing and defecation—and she reported overuse of medications due to uncontrolled pain. After 6 weeks in hospice, staff determined they could no longer safely manage her pain and began tapering opioids in preparation for discharge. Her pain complaints were new and not related to cancer, and OUD was diagnosed by the hospice team. Our addiction service was consulted for pain and addiction management.

The patient reported initial relief from opioids but required progressively higher doses, eventually experiencing worsening pain regardless of dose. Pain spread to include upper abdominal pain, painful swallowing, and constant headaches. Based on these symptoms, OIH was suspected. She met fewer than 2 Diagnostic and Statistical Manual of Mental Disorders criteria for OUD. Following a microdosing strategy, we initiated a 5 mcg/hour buprenorphine patch for 7 days and escalating doses of oral buprenorphine without discontinuing long-acting morphine or hydromorphone. A patch was chosen to simplify titration; we believed she could not manage cutting films or following a complex regimen. After approximately 2 weeks of titration, a maintenance dose was achieved with a 20 mcg/hour buprenorphine patch for 7 days and 8 mg oral buprenorphine 3 times daily. We recommended continuing full opioid agonists for later tapering, but she overused them and ran out after the first week. She denied withdrawal symptoms, and her pain improved after discontinuation. After her induction, she remained on buprenorphine only, with pain controlled at approximately 3 of 10 on the pain scale. She gained 20 pounds over the next 3 months (weight, 118 pounds; BMI, 19). In the 3 months before buprenorphine induction, she was hospitalized 3 times for pain and constipation; in the 3 months after buprenorphine initiation, she was hospitalized only once for unrelated issues.

With improved pain control and overall health, she was discharged from hospice and resumed her cancer treatment. Three years after starting buprenorphine, she is in remission, weighs 130 pounds, and has not been hospitalized for pain. Pain control has remained stable on a 20 mcg/hour patch every 7 days and 8mg oral buprenorphine 3 times daily. She continues to rate pain 1 to 3 out of 10 since induction. On prior regimens, her pain never decreased below 5 and consistently worsened over time.

DISCUSSION

OIH should be considered when opioid tolerance develops and pain extends beyond the original site. Increasing opioid doses generally exacerbates pain, whereas dose reduction may improve symptoms. There are no commonly available tests to confirm the diagnosis. Patients with tolerance but without OIH typically do not improve with decreased MMEs and do not experience spreading or worsening pain with increasing dosages. An opioid rotation and/or reduction in total MME is commonly attempted to diagnose or manage OIH. This approach involves tapering the current opioid and transitioning to a different opioid with distinct pharmacokinetics and receptor activity. Case reports describe success with changing from morphine to methadone.[11]

Table 2. A Review of Evidence for Pain Control With Buprenorphine

Article	Brief Summary
Khanna et al[9]	Buprenorphine is safe and effective for chronic pain. It has a superior safety profile when compared to full opioid agonists. It can be combined with other opioids when breakthrough pain control is needed. This review covers evidence, pharmacology, and safety of buprenophine for both acute and chronic pain.
Powell et al[12]	A systematic review of 22 small studies and case reports indicates that rotating opioids to buprenorphine from other regimens maintains or improves chronic pain. The risk of precipitated withdrawal was low. The quality of evidence in this meta-analysis was limited, suggesting the need for more research on the topic.
Spreen et al[10]	Microdosing strategies for buprenorphine are safe and effective for the induction of buprenor-phine. Article reviews the evidence for buprenorphine and catalogues dosing protocols.

A 2021 systematic review examined buprenorphine rotation for patients with chronic pain and long-term opioid use. The review found opioid rotation to buprenorphine to be safe and effective without precipitating withdrawal. Patients were transitioned to buprenorphine for multiple indications, including inadequate pain control, intolerable adverse effects, risky opioid regimens, and aberrant opioid use.[12] Evidence supporting buprenorphine for pain management is summarized in Table 2.

To our knowledge, this case report is the first described example of buprenorphine treatment correlating clinically with a reduction in OIH. Our literature review identified few studies examining buprenorphine's antihyperalgesic effects. In 2005, a randomized, double-blind crossover study involving 15 patients demonstrated a greater reduction in transcutaneous stimulation-induced hyperalgesia in patients given buprenorphine compared with fentanyl.[13] No studies to date have examined buprenorphine's potential ability to attenuate hyperalgesia specifically induced by opioid therapy.

CONCLUSIONS

We present a case of a 57-year-old woman whose opioid-induced hyperalgesia was effectively treated with buprenorphine therapy. She experienced improvements in pain, ability to perform activities of daily living, and nutritional status. This case highlights the need for further clinical investigation into the relationship between buprenorphine and OIH. Given the stigma, anchoring bias, and implications of an OUD diagnosis, our case emphasizes the importance of maintaining an open mind and comprehensive differential when diagnosing and treating patients with suspected OUD.

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PAPASH Syndrome: A Case Report and Lessons for Clinical Practice

Janvi Patel, BS; Farzana Hoque, MD, MRCP

ABSTRACT

Introduction: PAPASH spectrum syndrome is a rare autoinflammatory condition encompassing psoriatic arthritis, pyoderma gangrenosum, acne, and hidradenitis suppurativa. Despite the individual prevalence of these conditions, their concurrent manifestation poses a diagnostic challenge that requires high clinical suspicion. This case illustrates the consequences of delayed recognition of this condition and underscores the crucial need for a multidisciplinary approach to optimize management.

Case presentation: We report the case of a 34-year-old African American man with a prior diagnosis of rheumatoid arthritis who developed migratory arthritis, pustular acne, and hidradenitis suppurativa. Despite suggestive clinical features, delayed access to biologic therapy contributed to disease progression and resulted in hospitalization. After extensive genetic and clinical evaluation, he was diagnosed with PAPASH syndrome.

Discussion: PAPASH syndrome is linked to mutations in the *PSTPIP1* gene and the overexpression of specific chemokines, which dysregulate interleukin-1 signaling and cause persistent inflammation. Although tumor necrosis factor-α inhibitors remain first-line therapy, limited literature exists on comprehensive treatment strategies, and further research is needed. This case demonstrates how ongoing diagnostic ambiguity and the absence of clear treatment guidelines can complicate the management of PAPASH syndrome.

Conclusions: This case emphasizes the importance of prompt identification of PAPASH syndrome in patients presenting with overlapping inflammatory conditions and highlights the need for clinical vigilance, timely initiation of biologic agents, and coordinated care to improve outcomes in this rare but serious disorder.

INTRODUCTION

PAPASH spectrum syndrome is a rare autoinflammatory condition that requires a high degree of clinical suspicion for accurate diagnosis and evaluation. It encompasses a diverse range of conditions including psoriatic arthritis, pyoderma gangrenosum, acne, and hidradenitis suppurativa (HS), each contributing to a complex clinical picture.[1] Although each of these conditions is individually common, their simultaneous occurrence poses a diagnostic and therapeutic challenge requiring individualized care. PAPASH syndrome has been linked to mutations in the *PSTPIP1* gene, which increase affinity to pyrin and upregulate caspase-1 and interleukin-1, producing a neutrophil-mediated inflammatory response.[2] We present the case of a man diagnosed with PAPASH syndrome in the setting of psoriatic arthritis, acne, and HS, highlighting the importance of recognizing overlapping symptoms to guide effective treatment.

CASE PRESENTATION

We report the case of a 34-year-old African American man with a history of rheumatoid arthritis diagnosed 6 years earlier. He had intermittently received steroid injections in both shoulders and was treated with oral prednisone at the time of diagnosis. He had received follow up from orthopedic surgery for some time due to chronic right elbow pain the previous few years. Previous management included activity modification, nonsteroidal anti-inflammatory drugs (NSAIDs), physical therapy, and bracing – none of which adequately relieved his symptoms. He was referred for fur-

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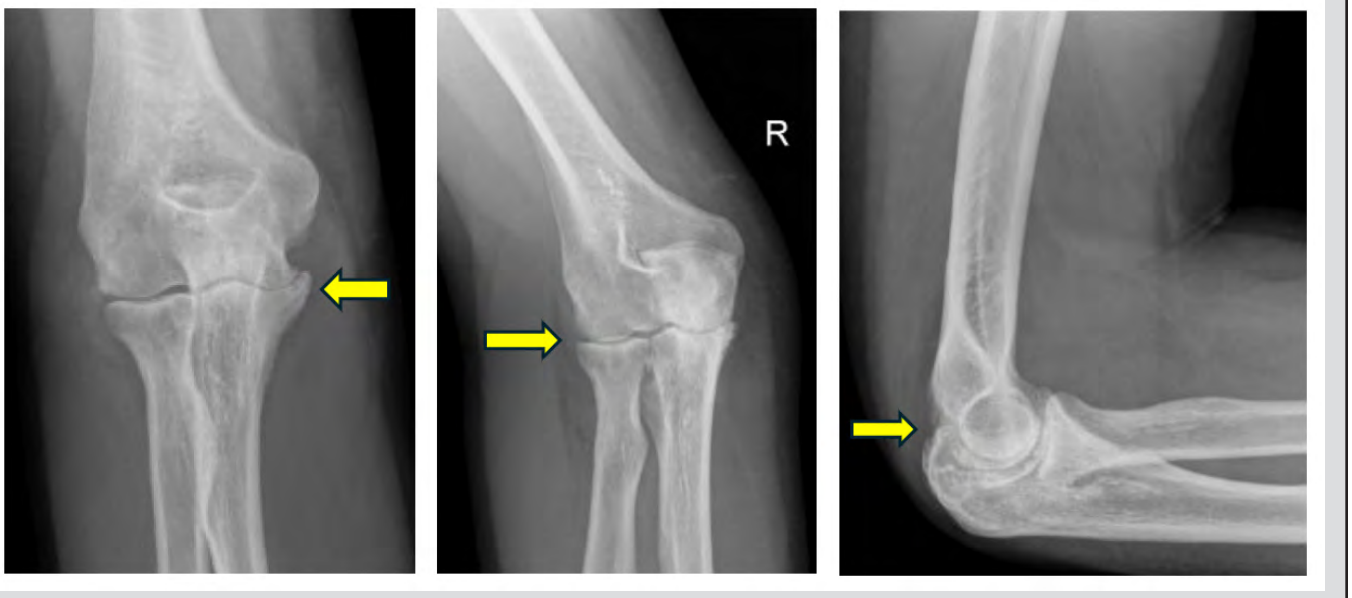
Figure 1. X-ray of Right Elbow Showing Arthritis With Moderate Joint Space Narrowing, Subchondral Sclerosis, Small Osteophytes, and Subchondral Cysts/Erosions



ther imaging, and x-ray of the elbow showed "arthritis with moderate joint space narrowing, subchondral sclerosis, small osteophytes, and subchondral cysts/erosions (Figure 1).

Magnetic resonance imaging showed severe arthritis with thinning cartilage and synovitis, prompting referral to rheumatology for evaluation of inflammatory arthritis and consideration of biologic therapy to further manage pain. At presentation, the patient reported symptoms beginning approximately 7 years earlier, initially with bilateral knee pain, followed by midfoot swelling, shoulder pain, elbow pain, and edema of the left fifth finger. He had previously established care with an outside hospital at that time and was treated with corticosteroid injections and prednisone. However, he was lost to follow-up due to his move out of state and then presented to establish care with our team.

Along with migratory arthritic pain, the patient reported frequent scaly rashes on his scalp, leading to a formal diagnosis of psoriatic arthritis. He also reported a significant smoking history (1 pack per day) and heavy alcohol use (6 drinks per day on weekends). Laboratory evaluation in anticipation of biologic therapy revealed an elevated erythrocyte sedimentation rate (ESR) of 50 mm/hour, C-reactive protein (CRP) level of 2.3 mg/dL, and cyclic citrullinated peptide (CCP) antibody IgG of 1.2 units.

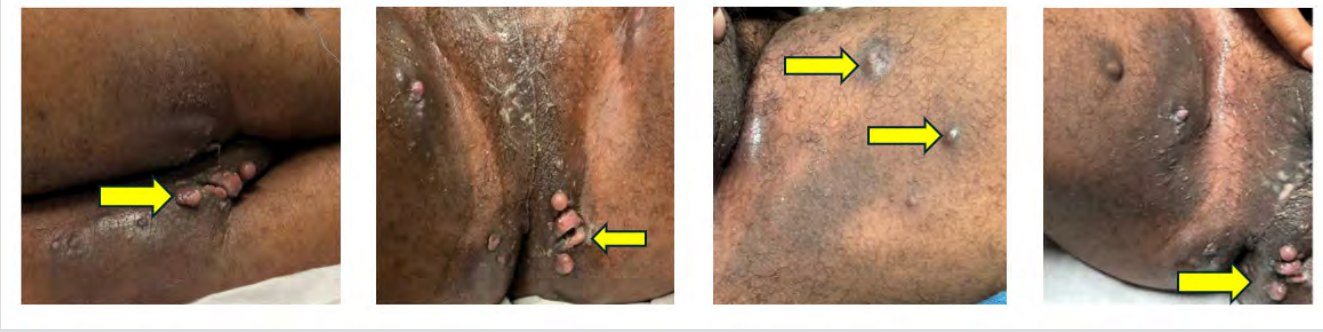
Around the same time, the patient developed erythematous papules and nodules on his face, groin, and in his armpits, prompting dermatology referral. He was diagnosed with HS (Hurley stage II) and pustular inflammatory acne. Treatment included topical clindamycin lotion to his affected areas, oral doxycycline 100 mg twice a day, and over-the-counter benzoyl peroxide wash in the shower.

Given the constellation of symptoms – including the pyogenic and psoriatic arthritis (with dactylitis, enthesitis, and synovitis), pustular acne, and HS – he was diagnosed with PAPASH syndrome by his rheumatologist. He was prescribed adalimumab 40 mg/0.4 mL subcutaneous injections every 2 weeks, prednisone for polyarthritis pain (tapered 40-30-20-10-5 mg in 5-day intervals), and continued on doxycycline. Despite urgent prior authorization for adalimumab, he was unable to obtain this medication or attend follow-up appointments. A few months later, he presented to the emergency department with worsening HS flare (Figure 2). He was admitted for evaluation, and inpatient rheumatology and dermatology were consulted. It was discovered that adalimumab had been approved by insurance but required dispensing through a specialty pharmacy, which is why he did not receive it. Rheumatology re-prescribed adalimumab and meloxicam 15 mg daily for arthritic pain. Dermatology recommended doxycycline 100 mg twice daily for 3 months, topical clindamycin, and benzoyl peroxide body wash. Soon after, he was discharged with outpatient follow-up arranged with both specialties.

DISCUSSION

Psoriatic arthritis, acne, and HS are all individual conditions that together define PAPASH syndrome, a rare disorder within the spectrum of autoinflammatory diseases characterized by genetic mutations and pathophysiologic changes.[3] In terms of genetics, various mutations – including those in the *PSTPIP1* gene – affect proteins of the inflammasome complex, which triggers autoinflammation, or proteins that regulate inflammasome function.[3] These conditions also share a common pathogenesis involving

Figure 2. Worsening Flare of Hidradenitis Suppurativa



the overactivation of the innate immune system, with abnormal interleukin (IL)-1 signaling leading to sterile, neutrophil-rich cutaneous inflammation.[4] The overexpression of chemokines such as IL-8, Fas/Fas ligand, and cluster of differentiation 40 (CD40) ligand systems also contribute to inflammation and tissue damage.[5]

Several clinically different syndromes have been described in the literature, including pyoderma gangrenosum, acne, and pyogenic arthritis (PAPA); pyoderma gangrenosum, acne, and HS (PASH); pyoderma gangrenosum, acne, and spondylarthritis (PASS); pyoderma gangrenosum, acne, pyogenic arthritis, and HS (PAPASH); psoriatic arthritis, pyoderma gangrenosum, acne, and HS (PsAPASH); and pyoderma gangrenosum, acne, and ulcerative colitis (PAC).[6] The underlying clinical features include painful arthritis and skin lesions consistent with HS and acne, as is seen in this patient. These manifestations are often accompanied by elevated systemic inflammatory markers,[6] such as an elevated ESR and CRP, which were present in this case.

Effective treatment of PAPASH syndrome requires recognition of its intersecting features–psoriatic arthritis, acne, and HS–to move beyond symptomatic relief and address underlying mechanisms. Understanding that these conditions are autoinflammatory in origin is imperative for timely initiation of biologic therapy. Tumor necrosis factor (TNF)-α is a proinflammatory cytokine, plays a pathogenetic role in many immune-mediated diseases, including psoriatic arthritis, HS, and pyoderma gangrenosum.[7] Thus, TNF-α inhibitors such as adalimumab are typically considered first-line therapy.[7] Although adalimumab has demonstrated efficacy and safety in psoriatic arthritis, evidence for its off-label use in HS and related skin disorders is limited, prompting the use of adjunctive therapies, such as antibiotics, isotretinoin, and dapsone.[7]

Emerging research on anti-IL-1 therapies for PAPASH syndrome reflects the role of IL-1 dysregulation in these disorders. Preliminary studies have shown promising results with IL-1 antagonists, including canakinumab and anakinra, in improving skin lesions such as HS, acne, and pyoderma gangrenosum.[8,9]

Although rare, it is important for clinicians to maintain awareness of PAPASH syndrome and related disorders–particularly when patients present with only some of the component conditions. Asking targeted questions about associated symptoms is critical, as patients may not volunteer what they fear may seem irrelevant. In this case, psoriatic scalp lesions were identified only through history-taking, leading to the diagnosis of psoriatic arthritis. Early recognition enables timely diagnostic evaluation and planning for biologic therapy. Along with medical management, studies support a multidisciplinary approach–including the use of systemic biologic agents, weight reduction, smoking cessation, and supportive wound care–as the most effective strategy for treating this disorder.[10,11]

CONCLUSIONS

PAPASH syndrome is a relatively rare condition with diverse presentations, typically including psoriatic arthritis, pyoderma gangrenosum, acne, and HS. The simultaneous presence of these autoinflammatory conditions challenges diagnosis and requires a nuanced management approach. Clinicians should remain attentive to the constellation of symptoms that may indicate an underlying syndrome rather than isolated conditions. The complexity of PAPASH necessitates multidisciplinary care, combining rheumatologic, dermatologic, and pharmacologic expertise. Comprehensive management and ongoing patient engagement are essential. Further research is needed to refine treatment protocols and develop new therapeutic options to better address the unique challenges posed by PAPASH syndrome.

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A Case of VEXAS Syndrome

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ABSTRACT

Introduction: VEXAS syndrome (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) is a rare disease caused by somatic mutations in the *UBA1* gene, first identified in 2020. Prevalence is unclear, and there are no established treatment guidelines, highlighting the need for disease recognition.

Case presentation: An 82-year-old man presented with hypoxic respiratory failure, fever, rash, and pancytopenia. After an extensive workup, he was diagnosed with VEXAS syndrome based on bone marrow biopsy and genomic testing.

Discussion: VEXAS syndrome results from dysregulation in the ubiquitylation pathway, causing autoinflammatory and hematologic symptoms. Diagnosis is challenging due to variable presentation. Bone marrow biopsy and genomic testing for *UBA1* mutation are crucial for diagnosis. Treatment focuses on controlling inflammation with steroids and IL-6 receptor antagonists such as tocilizumab.

Conclusions: We present this case to raise awareness of this recently established condition. Further understanding will aid in optimizing management and improving clinical outcomes.

INTRODUCTION

VEXAS syndrome (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic)—a rare systemic inflammatory disease first identified by Beck et al in 2020—is caused by somatic mutations in the *UBA1* gene in hematopoietic precursor cells.[1] Mutations in *UBA1* result in defects in the E1 enzyme, causing defective protein degradation, clonal hematopoiesis, and widespread autoinflammation. This leads to multisystem involvement characterized by overlapping hematologic and rheumatologic findings, especially in older men.[2]

DNA sequencing is used to identify the *UBA1* mutation to support the diagnosis; however, diagnosis is often delayed because of the wide spectrum of presenting symptoms and perplexing laboratory findings. The condition's low prevalence is partly due to underrecognition and underreporting. Management of VEXAS syndrome is challenging because of limited treatment options and requires a multidisciplinary approach.

Herein, we present a case of VEXAS syndrome in an 82-year-old man who presented with respiratory failure, pancytopenia, and systemic symptoms.

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CASE PRESENTATION

An 82-year-old man with a medical history of lower extremity deep vein thrombosis, splenic infarct, chronic macrocytosis, monoclonal gammopathy of undetermined significance, iron deficiency anemia, chronic kidney disease, and osteoporosis presented to the emergency department with fevers and shortness of breath. Two years prior, he had been started empirically on steroid therapy and intermittent tocilizumab for suspected giant cell arteritis (GCA) because of jaw claudication, headache, elevated C-reactive protein, and intermittent fevers. A temporal artery biopsy at that time was nonconclusive and a positron emission tomography scan was negative for large-vessel vasculitis. He continued steroid therapy but discontinued tocilizumab as the diagnosis of GCA was questioned.

On admission, the patient was febrile, hypoxic (requiring 6 L

Figure 1. Hematoxylin and Eosin-Stained Bone Marrow Core Biopsy

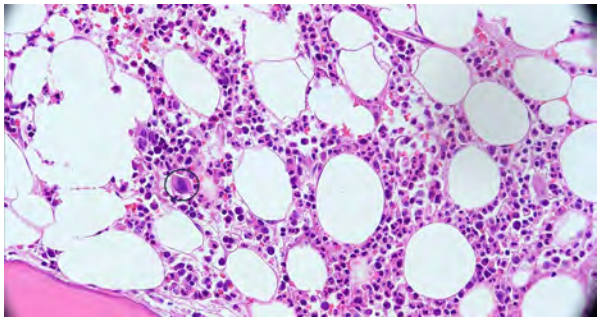
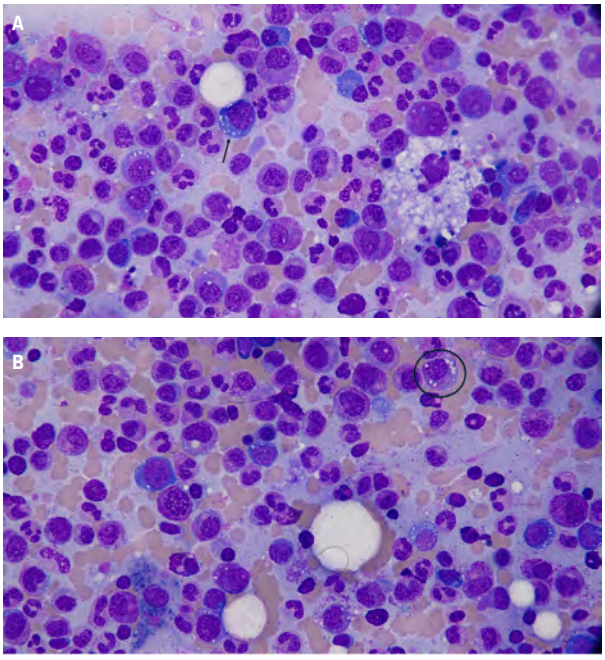


Image demonstrates a hypercellular marrow with an elevated myeloid: erythroid ratio and mild megakaryocyte atypia (black circle).

Figure 2. Wright-Giemsa-Stained Bone Marrow Aspirate



Images demonstrate a myeloid-predominant marrow with prominent cytoplasmic vacuolization in myeloid and erythroid precursors. Scattered hemophagocytic histiocytes are present.

oxygen via nasal cannula), and had acute kidney injury, thrombocytopenia, and anemia. He also had a morbilliform rash on his chest, back, and lower extremities. On hospital day 3, pancytopenia developed, with a white blood cell count (WBC) of 3.5×10^3/uL, hemoglobin (Hgb) 6.9 g/dL, and platelets (PLTs) of 160×10^3/uL (reference ranges: WBC, 4.0-15.0; Hgb, 13.7–17.5 g/dL; PLTs 165–366 K/μL). He was admitted to the intensive care unit (ICU) for acute hypoxic respiratory failure and started on intravenous antibiotics for possible pneumonia; however, the infectious workup was negative. His steroid dose was increased to 100 mg daily. A computed tomography scan of the chest ruled out pulmonary embolism and showed variable infiltrates. Bronchoscopy revealed acute alveolar hemorrhage. Prior antinuclear antibodiy (ANA) screens had been negative, but ANA titer on this admission was borderline positive at 1:80.

The patient's hospital course was complicated by intermittent worsening of acute respiratory failure when steroids were tapered, requiring multiple transfers to the ICU. Dermatology was consulted for the rash, which became diffusely red on the bilateral lower extremities, torso, and upper extremities. Hematoxylin-eosin-stained skin biopsy revealed scattered dyskeratotic keratinocytes and a sparse superficial perivascular infiltrate of lymphocytes, neutrophils, and some eosinophils.

During hospitalization, the patient also developed shingles, likely because of his immunocompromised state while on high-dose prolonged steroids, and was treated with acyclovir. Hematology was consulted, and a bone marrow biopsy was performed. Hematoxylin-eosin-stained bone marrow core biopsy and clot sections revealed a hypercellular (90%) marrow with megakaryocyte atypia characterized by small, simplified forms (Figure 1). Plasma cells were not numerically increased and were polytypic by in situ hybridization for kappa and lambda light chains. The Wright-Giemsa-stained bone marrow aspirate demonstrated an increased myeloid-to-erythroid ratio of 18.2. There was no increase in blasts. Early myeloid and erythroid precursors showed frequent cytoplasmic vacuolization (Figures 2A and 2B). Rare hemophagocytosis was observed. Cytogenetic analysis performed on bone marrow demonstrated a normal karyotype. Next generation sequencing revealed a pathogenic *UBA1* mutation (c.121A>G, p.Met41Val) at a variant allele frequency of 70.1%. No other definitively pathogenic variants were identified. Taken together, the clinical, morphologic, and molecular findings were consistent with a diagnosis of VEXAS syndrome. Hematology and rheumatology collaborated with the National Institutes of Health for a treatment plan, and the patient was placed on high-dose steroid taper and started on tocilizumab infusions. He was discharged on day 37 with supplemental oxygen. Four months after discharge, ruxolitinib (a JAK2 kinase inhibitor) was added.

Seven months after discharge, the patient continued to tolerate tocilizumab infusions. He had been on steroids for the past 2 years and was unable to wean off. He also was treated with acyclovir and atovaquone to prevent opportunistic infections while on steroids. He reported progressively worsening vision, retinal disease, and cataracts. Additionally, he developed steroid-induced diabetes and myopathy. His overall strength had not fully recovered to prediagnosis levels, although some stabilization and improvement were noted.

DISCUSSION

This case underscores the debilitating nature of VEXAS syndrome, a progressive systemic inflammatory disease predominantly affecting men older than 50 years.[2] As a recently recognized diagnosis,

its true prevalence remains uncertain. A review of health records from more than 160 000 adults by the National Heart, Lung, and Blood Institute estimated a prevalence of 1 in 4269 men older than 50.[3] A PubMed search identified only 109 reported cases globally in the past 5 years—and 25 in the United States—highlighting the need for further research to define prevalence and improve recognition.

Pathophysiology

VEXAS syndrome results from somatic mutations in the *UBA1* gene, which encodes the E1 ubiquitin-activating enzyme essential for the ubiquitin-proteasome system. The mutations impair protein degradation, leading to accumulation of misfolded proteins and chronic immune activation.[1,4] Mutated hematopoietic stem cells undergo clonal expansion, producing peripheral blood cytopenias and characteristic marrow changes.[1,5,6] Elevated cytokines—particularly interleukin-6 (IL-6)—further amplify inflammation.[7] Clinical manifestations reflect this interplay of clonal hematopoiesis and immune dysregulation, with systemic symptoms and organ involvement.[5,8] Rare dermatologic conditions such as Sweet syndrome and Kikuchi-Fujimoto disease may occur.[1,4] Additional mutations in genes like *DNMT3A* or *TET2* have been reported.[5]

Clinical Presentation

VEXAS syndrome exhibits heterogeneous features, including systemic inflammation, hematologic abnormalities, and cutaneous lesions.[2] Early symptoms may include fever, fatigue, and myalgia, with involvement of the skin, cartilage, joints, lungs, and blood vessels.[2] Common inflammatory features resemble conditions such as Sweet's syndrome, relapsing polychondritis, and polyarteritis nodosa.[1] Macrocytic anemia and other cytopenias are also prevalent.[9]

A literature review of US cases revealed presentations ranging from neutrophilic dermatitis to mediastinal lymphadenopathy and hematologic issues.[10] Notably, isolated dermatologic disease does not exclude VEXAS, emphasizing the need for genetic testing when clinical suspicion exists. The syndrome may also predispose to hematologic malignancies, including plasma cell neoplasia and myelodysplastic syndrome, though this association requires further study.[6]

Diagnosis and Treatment

Diagnosis requires correlation of clinical findings with bone marrow morphology and molecular testing. Bone marrow typically shows hypercellularity with cytoplasmic vacuoles in myeloid and erythroid precursors. Detection of a pathogenic *UBA1* variant—usually with a variant allele frequency greater than 20%—lends confidence to the diagnosis.[1]

There are no standardized treatment guidelines. Current management focuses on controlling inflammation with high-dose corticosteroids and IL-6 receptor antagonists such as tocilizumab.[11] IL-6 receptor antagonists are favored in cases with persistent inflammation but no significant transfusion-dependent cytopenias, while corticosteroids are tapered.[11] JAK inhibitors (ruxolitinib, tofacitinib) have been used in refractory cases, whereas conventional immunosuppressants (methotrexate, azathioprine, mycophenolate) are generally ineffective.[1,12] Allogeneic hematopoietic stem cell transplantation has shown success in some patients.[13,14]

Further research is necessary to optimize treatment and improve outcomes. Future strategies may include therapies targeting the ubiquitination pathway or gene editing, and clinical trials are crucial for developing evidence-based treatment algorithms.[11,12] Supportive care for complications—such as infections, cytopenias, and thrombosis—is essential, and lifelong anticoagulation therapy required for patients at risk of recurrent thrombosis.[11]

Mortality often results from respiratory failure, severe anemia, or treatment-related adverse effects.[1] This case illustrates the importance of considering VEXAS syndrome in patients with unexplained systemic inflammation, particularly when symptoms persist despite immunosuppressive therapy.

CONCLUSIONS

This case of VEXAS syndrome in a patient with pulmonary, dermatologic and hematologic manifestations demonstrates the disease's clinical complexity. Diagnosis was confirmed bone marrow biopsy showing vacuolated myeloid precursors and identification of a pathogenic *UBA1* mutation in hematopoietic cells. The underlying defect in the ubiquitination pathway drives immune dysregulation and system inflammation, explaining the broad spectrum of symptoms. Given the limited therapeutic options and recent recognition of the syndrome, further research is critical to improve outcomes. Increased awareness and early detection may help prevent disease progression and reduce morbidity and mortality.

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Wisconsin's Opportunity to Become a Beacon for the Nation in Advancing Health

Nita Ahuja, MD, MBA

On May 15, 2025, I had the great honor of becoming the 10th Dean of the University of Wisconsin School of Medicine and Public Health and Vice Chancellor for Medical Affairs at the University of Wisconsin–Madison. The writing of this column marks my 6-month anniversary as a Wisconsinite.

I am a surgeon scientist and have spent my career in multiple academic health systems. I am also a profound believer of the power of the people in academic medicine, who bring the best of science along with their heart and soul to solving critical problems while working in concert with community partners and organizations. This synergy is what attracted me here. The key question that motivates me is: How can we tap into the power of the university and our allies to help people?

In my first 6 months, I have made many connections and learnt so many amazing facts about our Badger state. I have also been impressed by seeing individual humility tempered with pride in the state, and witnessing the legendary Midwestern work ethic. These qualities have been evident throughout organizations such as UW–Madison, Medical College of Wisconsin, and leading corporations headquartered in the region. But I have also found it sobering to see some of the realities of a state where a sizable percentage of the population living in rural zones experiences a fragmented health delivery system and uneven health outcomes.

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> By working together, the physicians, health care professionals, and public health experts of Wisconsin can make a lasting impact on the challenges at hand.

I hope we can use this journal and column to connect and problem-solve together. Academic medicine's purpose is to be a catalyst, driving positive change by sparking connections between theory and practice, concepts and applications, population needs and medical discoveries.

Wisconsin's Strengths and Opportunities

Wisconsin has a proud legacy of health and public health innovations. Its medical association, the Wisconsin Medical Society, is older than the state itself. The society's founding in 1841 by an act of the Territorial Legislature signaled early interest in establishing quality standards for medical care. Wisconsin is the birthplace of clinical tests such as the Prothrombin Time/International Normalized Ratio (PT/INR) test based on work by Armand J. Quick in 1932, the first phenylketonuria test developed by Harry Waisman in the 1960s, and the first accurate rapid lead poisoning test developed by Frederic Blodgett in 1972. On the public safety front, Wisconsin was home to the first seat belt installation law in the nation in 1961. And the state has a history of innovation in health insurance, with some of the earliest examples of worker's compensation insurance, employee-sponsored health insurance, and health maintenance organizations including one described as the nation's first rural HMO.

These examples illustrate defining features of Wisconsin's approach to health: taking a systems thinking perspective, valuing quality and innovation, and showing concern not only for the individual but for all residents.

That spirit of purposeful ambition and sense of service is evident at the UW School of Medicine and Public Health. As the only public medical school in the state, and the first institution in the nation to integrate the fields of medicine and public health,[1] our actions are guided by the interests of the people of Wisconsin and the world. Our training programs and solutions seek to spark health and vitality, aligning with the school's vision of healthy people and healthy communities.

While we recently celebrated the 20-year anniversary of integrating public health into our name and missions, we have long ensured that our health professions students are training in all corners of Wisconsin.

Designating the needs of the broader community as our institution's North Star yielded discoveries such as Mohs surgery in the 1930s, which became the gold standard for skin cancer treatment, the UW Solution in the 1970s and 80s for organ preservation during transplantation, 5-fluorouracil in the 1950s as a frontline chemotherapeutic agent, tamoxifen in the 1970s for advanced breast cancer, reverse transcriptase in 1970 leading to HIV antiretroviral therapy, and the world's first derivation of human embryonic stem cell lines in 1998 and the creation of induced pluripotent stem cells in 2007 leading to regenerative medicine therapies.

We must build on this legacy to address today's health needs.

Moving Health Forward

What are the state's "burning platform" health issues today? Many signs point to variable health outcomes as causing increasing strain. Area Deprivation Index data, made available as the Neighborhood Atlas via the Center for Health Disparities Research led by Amy Kind, MD, PhD, at the UW School of Medicine and Public Health, show mixed trends across Wisconsin[2] in ADI's composite measure of factors related to income, education, employment, and housing quality. High levels of disadvantage are found in northern and northeastern regions of the state, as well as parts of central and southeastern Wisconsin. These areas correlate with measures of rurality.[3]

Variability also surfaces in population forecasts, with pockets of the state expected to shift upward in median age. A report on State and County Population Projections 2020-2050[4] predicts a 13-county region in the northern region where every county is expected to have between 27% and 45% of its population comprised of people age 65 and older by 2050. Twelve of the 13 counties are currently classified as primary care Health Professional Shortage Areas.[5] Simply put, few physicians and other health care professionals are available in the precise areas of the state where they will be needed most. We must take steps now to address this, as the impacts are already acute and will soon be critical.

A path forward can be found in the concept of healthspan, which aims to increase the number of years spent in good health and free from age-related chronic disease and disability. University of Wisconsin–Madison has committed to creating a "brain trust" of healthspan researchers through an initiative called RISE-THRIVE, standing for Wisconsin Research, Innovation and Scholarly Excellence Transforming Healthspan through Research, InnoVation, and Education. Through accelerated and strategic faculty hiring, research and infrastructure enhancement, interdisciplinary collaboration, and enhanced learning opportunities, RISE-THRIVE aims to generate discoveries in immunology and healthy aging that will inform preventive measures and lead to new treatments. This could have enormous benefits for the population by increasing quality of life and transforming the health economics of aging.[6] These efforts will also involve key partnerships, building on the university's successful track record of connecting communities and industry on collaborative solutions.

Rural health care workforce training also plays a key role in addressing population needs. As a public land grant university, our institution's commitment to rural health runs deep. We are proud to be ranked 14th by *US News and World Report* among medical schools with the most graduates practicing in rural areas.[7] The Wisconsin Academy for Rural Medicine (WARM) has added 331 MD graduates to the workforce since it launched in 2007. Eighty-two percent of WARM graduates practice in Wisconsin and about half practice in a rural area. Recently, we piloted a short-track 3-year MD program called WARMeRR as an expedited, competency-based undergraduate medical education-GME pathway to rural practice in Wisconsin.

Combined with additional rurally focused programs for precollege and bachelor's students through the Wisconsin Area Health Education Center and rural residency or fellowship programs in obstetrics and gynecology, family medicine, psychiatry, general surgery, preventive medicine and public health, we offer a comprehensive spectrum of rural health training programs. This complements our rural health services research, continuing medical education and training tailored for rural health professionals, and funding for rural health initiatives through the Wisconsin Partnership Program and the Orion Initiative.

Our internationally recognized expertise in Alzheimer's disease and related dementias research is also poised for impact. Current studies include Wisconsin Registry for Alzheimer's Prevention (WRAP), which is the largest family history study of Alzheimer's disease in the world; Clarity in Alzheimer's Disease and Related Dementias Research Through Imaging (CLARiTI), which is a nationwide study to provide state-of-the-art imaging and blood-based biomarkers for researchers around the world to use; and data and expertise that helped validate the first commercially available blood plasma test for Alzheimer's disease biomarkers. Additionally, we support a statewide network of 40 memory clinics to provide early-stage diagnosis and treatment services and support for caregivers. Broader biology of aging research programs are devoted to neurodegeneration, musculoskeletal aging, and a recently announced Wisconsin Nathan Shock Center of Excellence in the Basic Biology of Aging. This new center focuses on the intersection of metabolic dysfunction and aging-related diseases and conditions.

These are just a few examples of the research, training, care, and outreach efforts that address pressing health needs in Wisconsin. Importantly, this is a team effort. It is more critical than ever to move forward in strong partnership with private sector research collaborations. Our biohealth industry partnerships have led to several new research agreements, with more to come. Additional key relationships involve philanthropists, public health departments, community organizations, and tribal nations and communities throughout the state.

Conclusion

Forming a sense of what it means to be a Badger over the past few months has been

personally fulfilling. Former US ambassador to the United Nations Adlai E. Stevenson II summarized Wisconsin's distinctive approach well, saying, "...the Wisconsin tradition meant more than a simple belief in the people. It also meant a faith in the application of intelligence and reason to the problems of society."

I look forward to partnering with readers of *Wisconsin Medical Journal* to learn more about your good ideas addressing health needs of the state. By working together, the physicians, health care professionals, and public health experts of Wisconsin can make a lasting impact on the challenges at hand. I truly believe there is a bright future ahead, one filled with hope and promise. We have every key factor required for success: connectedness, a drive to discover, the ability to test innovative ideas and scale those that are most effective, and powerful determination reflected in strong work ethic, humility, and a sense of service to humanity. Together, we can leverage academic medicine as an engine for good.

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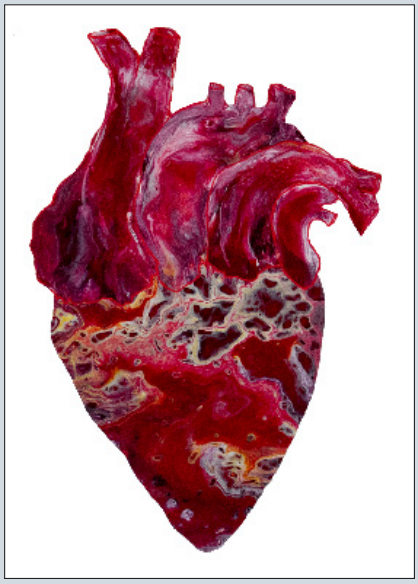

"Human Heart"

About the Artist

Drawing inspiration from her work in pathology (specifically autopsy), Emily Kammerud enjoys the rare opportunity to weigh the creative with the morose within a subject often met with intense aversion. By intermingling art and science and drawing upon an educational emphasis on anatomic pathology, disease, and human mortality, Emily conjures intense, yet provocative, more palatable visuals inspired by a subject that many viewers find themselves uncomfortable witnessing despite their morose curiosity.

www.emilykammerudart.com

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DEATHS FROM PRESCRIPTION PAINKILLERS HAVE INCREASED BY 38% IN WISCONSIN.

It's a myth that prescription painkillers are completely safe because a doctor prescribes them. The Dose of Reality is that in Wisconsin, prescription painkillers are involved in more overdose deaths than heroin and cocaine combined. In fact, 63% of opioid-related deaths in 2015 involved prescription drugs. And everyone is at risk, especially young people ages 12-25.

Working together, we can prevent prescription painkiller abuse in Wisconsin. Since 4 out of 5 heroin addicts start with prescription painkillers, we can also help to curb the statewide heroin epidemic. Go to DoseOfRealityWI.gov to learn what you can do to help.

DOSE OF REALITY
PREVENT PRESCRIPTION PAINKILLER ABUSE IN WISCONSIN.

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A message from Wisconsin Department of Justice, and the Wisconsin Department of Health Services

Wisconsin Department of Health Services

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to our Reviewers

The *WMJ* would like to thank everyone who served as a manuscript reviewer in 2024. Manuscript review is an important collegial act and is essential to the integrity of *WMJ*. We are grateful for the assistance of these individuals in ensuring authors receive objective and insightful feedback on their work.

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