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Trends in e-cigarette use

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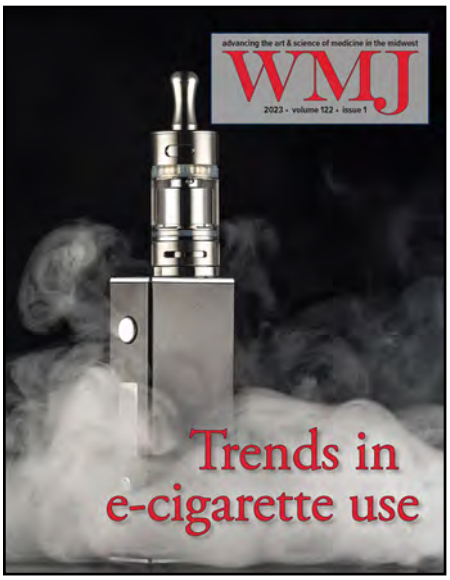

COVER THEME

Trends in E-cigarette Use

Cigarette smoking has been on the decline for decades among all age groups, both in Wisconsin and the United States. However, e-cigarette use—or vaping—has increased markedly since its introduction over 10 years ago. A study in this issue of WMJ *seeks to characterize trends in e-cigarette use among callers to the Wisconsin Tobacco Quit line, to better inform strategies to assist with e-cigarette cessation.*

Cover design by Kendi Neff-Parvin

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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WMJ

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EDITORIAL

ORIGINAL RESEARCH

The *WMJ* (ISSN 1098-1861) is published by the Medical College of Wisconsin and the University of Wisconsin School of Medicine and Public Health and is devoted to the interests of the medical profession and health care in the Midwest. The managing editor is responsible for overseeing the production, business operation and contents of the *WMJ.* The editorial board, chaired by the medical editor, solicits and peer reviews all scientific articles; it does not screen public health, socioeconomic, or organizational articles. All articles and artwork published herein, including commentaries, letters to the editor, and editorials represent the views of the authors, for which neither *WMJ* nor the publisher take responsibility, unless clearly stated. Advertising content is the responsibility of the advertiser and does not imply an endorsement or sponsorship by *WMJ* or the publsiher and its affiliates unless specified. *WMJ* is indexed in Index Medicus, Hospital Literature Index, and Cambridge Scientific Abstracts.

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BRIEF REPORTS

CASE REPORTS

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Do Internal Medicine Hospitalists and Advanced Practice Providers Desire Training in Diagnostic Point- Of- Care Ultrasound? A Cross Sectional Survey

Dear Editor:

Point-of-care ultrasonography (POCUS), especially that of heart, lungs, deep vein thrombosis, volume status, and free fluid assessments, is a great adjunct to bedside clinical examination for inpatient medical care. Its diagnostic accuracy, reduced time to diagnosis, prognostic significance, and favorable impact on physician-patient interactions is reverberating in our industry.[1] In recent studies, emergency department POCUS led to a change of diagnosis in 30% of cases and change in management in 89% of life-threatening situations.[2] In critical care and anesthesia cases, it changed diagnosis and management in 41% to 51% and 43% to 82%, respectively.[3] Although established in the specialties of emergency, critical care, and anesthesia, internal medicine is relatively new to POCUS.[4] And now there seems to be a widening knowledge gap between faculty and trainees, as undergraduate and graduate medical education programs incorporate POCUS training into their curricula.

In November 2022, we conducted a cross sectional survey to assess the level of exposure, perceptions, and interest towards POCUS training. An anonymous 13-question Qualtrics survey was sent to all Medical College of Wisconsin faculty and advanced practice professionals (APP) in the divisions of Hospital and Perioperative Medicine.

A total of 59 faculty and APPs completed the survey, with a response rate of 41% (60% were hospitalists; 40% were APPs). Thirty-three percent of respondents had more than 3 years of experience in their field. Around 24% of respondents had completed a POCUS training course: the majority had in-person hands-on training, and 2 had full certification. Sixty-six percent of the POCUS-trained faculty had less than 3 years' experience performing POCUS, whereas 33% had more than 3 years' experience. Seventeen percent reported using POCUS in routine clinical practice; 77% perceived benefit to diagnostic POCUS in clinical practice and teaching learners. Most respondents highlighted the importance of POCUS as a bedside tool, especially in volume status assessment. Eighty percent of respondents were interested and willing to commit time up to 40 hours for a longitudinal training program with an online precourse, a hands-on workshop, and then a longitudinal mentored portfolio creation for practice.

This survey highlights the glaring knowledge gap among faculty and the need for a well-structured longitudinal training program. A focused curriculum, Faculty for longitudinal assessment, image archiving, quality assessment, and devices are key for its success.[4,5] Our future efforts will be to secure support from leadership and funding and partnering with local physician organizations.

—Anu Taylor, MD; Abhilash Koratala, MD; Pinky Jha, MD

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Lessons in a Loss

continued from page 7

Program. My research focused on optimizing preoperative care for cancer patients undergoing surgery. While I had always been interested in cancer research, my work took on a whole new meaning. Starting research early in the morning suddenly felt less early and there was an overflow of motivation to continue working into the evening. Dedicating my summer to this research was so abundantly meaningful when the patients I hoped to help became so familiar.

At times I wish I could harness my 10-year-old naivety again; 23-year-olds are not supposed to die from cancer. Only now I know too well they can. Andrew is dearly missed, and as I reflect on his arduous journey, below are a few observations I wish to share and will carry with me throughout my medical career.

First, appreciate the little things in life. The last time I spoke to Andrew, he explained how difficult it was for him to see a world so full of complaints. This is as good of a reason as any to find the positives—no matter how small—in every moment.

Second, we must hold tightly to the things in life we value most. While the world of medicine is unbelievably interesting and engaging, it is only part of our identity. We are sons, mothers, friends, authors, artists, and, above all, humans. Finally, adversity is inevitable throughout our lives, so I will conclude with the motto Andrew found strength in throughout his journey: Be courageous, stay strong, keep faith.

• • •

Acknowledgement: The family of Andrew Wernicke gives their full support and permission to publish this manuscript in his memory and hopes his story inspires the readers of *WMJ*. More information about Andrew and the Andrew Wernicke Courage Foundation can be found at https://www.andrewwernicke.com/

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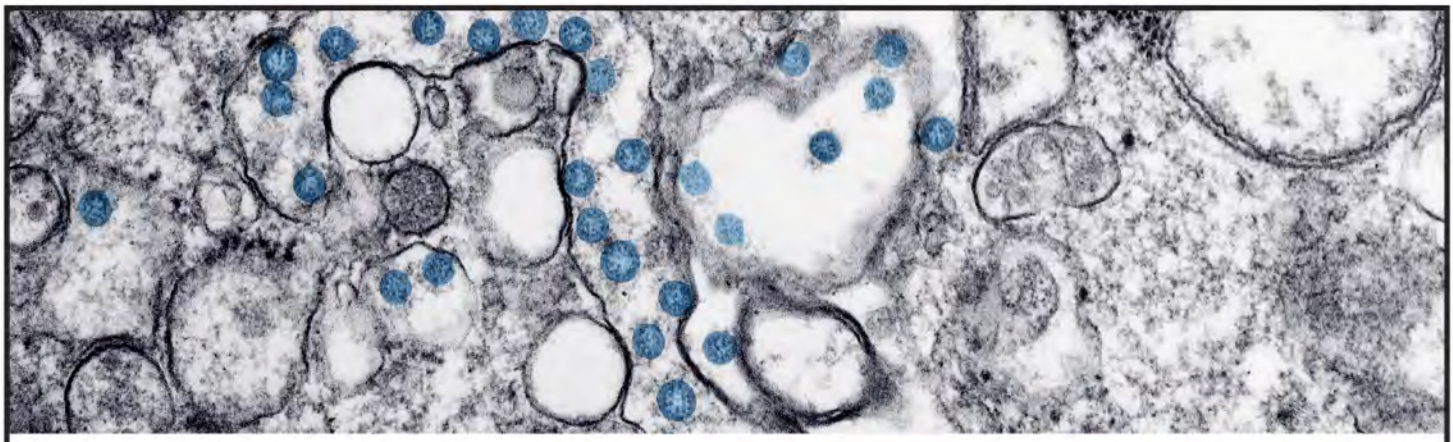

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OCTOBER 2023

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

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- Long-term changes to health care delivery as a result of the pandemic
- Were we ready for the pandemic? What steps we should take to prepare for another pandemic
- How effective were efforts to fight the pandemic

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WMJ

Fahad Aziz, MD, FASN

The Power of Shared Decision-Making in Medical Settings

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

Shared decision-making is a process where a health care provider and a patient work together to make the best decision for the patient. It is a crucial component of patient-centered health care. Sharing our expert, honest opinions with patients helps to strengthen our connection, and difficult medical decisions are more manageable when the patient fully understands the problem and shares in the decision-making. It's our nature to accept the decisions in which we have ownership.

The patient-clinician relationship is one of the most meaningful experiences shared by humans. It's a consensual relationship where the patient voluntarily seeks the clinician's assistance, and the clinician knowingly accepts that person as a patient. However, this relationship can be very complicated and is not always perfect. Good patient-clinician relationships go beyond excellent bedside manner and are built on trust.

MODELS OF THE DOCTOR-PATIENT RELATIONSHIP

In 1956, Szasz et al described three basic models of the doctor-patient relationship:[1]

1. **Active-passive model:** This model is based on the physician acting on the patient without input. It may be appropriate during an emergency where the physician act quickly and the patient is not in a state to make any critical decisions.
2. **Guidance-cooperation model:** In this model, the physician decides, based on their medical knowledge, what's best for the patient. The clinician makes a recommendation, and the patient is expected to comply.
3. **Mutual participation model:** This model is based on equal participation between the clinician and the patient and requires that both parties engage in activities that they find satisfying.

Each model has utility in specific situations; however, due to its tremendous advantages, there has been considerable support for the mutual participation model over the last few decades.

ADVANTAGES OF SHARED DECISION-MAKING

A shared decision-making approach can provide a readily understandable roadmap to keep clinicians moving toward success in clinical scenarios. It is the key to handling complex, emotion-laden situations with transparency and confidence and includes the following benefits.

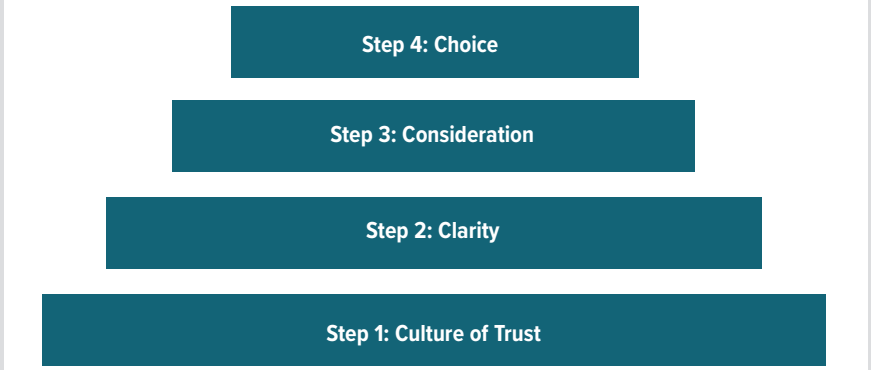
A. Patient and clinician satisfaction: Giving patients a chance to describe their preferences and then helping them understand the risks and benefits of their decisions increases their satisfaction with the care they are receiving. Several studies have shown that patients who were more involved in the decisions made by their clinicians were more knowledgeable about their condition and were more satisfied with their medical care[2] and clinicians feel satisfied when they provide high-quality care with the support of their patients.[3]

> Good patient-clinician relationships go beyond excellent bedside manner and are built on trust.

B. Better outcomes: Shared decision-making reduces patient anxiety and improves patient compliance with their treatment plan. They have more knowledge of their medical conditions and have a better understanding of the potential risks and benefits of the treatment, which plays an essential role in physicians' job satisfaction and reduces clinician burnout.[3]

C. Better connection between patients and clinicians: As clinicians, we know that connecting with our patients is a powerful tool.[4] Listening to the their concerns, giving them an honest opinion, and then answer-

Figure. 4-C Stepwise Model for Shared Decision-Making



ing their questions helps them understand the clinical situation and the risks and benefits of treatment options. Sharing in decision-making forges a strong connection between patients and clinicians and ensures the decision is one patients can own and respect.

Shared Decision-Making Process

To develop a shared decision-making process, I propose the 4-C stepwise model (see Figure).

Step 1: Develop a culture of trust: In the pyramid shared decision-making, the culture of trust between a clinician and patient always comes first. Building trust takes time, and with repeated displays of their integrity, clinicians can create a relationship of trust with their patients.

Step 2: Clarity: One of the most critical components of shared decision-making is adding clarity to the situation. I have seen outstanding physicians use paper and pen or a whiteboard while discussing complex issues and possible solutions with their patients.

Complex medical problems can be made more accessible by adding clarity, which has two components:

1. ***Listen carefully.*** With their busy schedules, many clinicians don't have much time to spend with each patient, and patients too often feel rushed through their visits. Patients must not feel rushed; instead, they should be given time to share their and concerns. There is an old saying: "Fifty percent of medical problems would be cured if your physician just listened to your problems."[4]
2. ***Allow ample time for questions.*** Patients should be given enough time to think through the issue, and clinicians should make themselves available to answer any questions. It's important to remember that all questions are valid, and patients should be encouraged to ask anything--no matter how minor or straightforward it may seem. Making patients feel comfortable and answering their questions helps clinicians earn their patient's confidence—a crucial component of shared decision-making.

Step 3: Consideration: After the patient understands their medical issue(s), clinicians should explain all possible treatment options and the risks and benefits of each, and patients should be encouraged to ask questions about those treatment options.

Step 4: Choice: After understanding the process and available treatment options, patients should be encouraged to make decisions with their clinician. Ownership boosts a patient's confidence and adherence to their treatment plan.

If we wish to be clinicians who are "connecting" and "influencing," it's essential that we make shared decisions with our patients--and that we teach and demonstrate the power of shared decision-making to future health care professionals.

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Lessons in a Loss: A Journey Through Friendship, Cancer, and Medical School

Nathaniel B. Verhagen, BS

During my transition to middle school, my friend Andrew was diagnosed with brain cancer. I recall my parents reassuring me that he would be receiving world-class care at the Children's Hospital of Wisconsin. Ten-year-old kids aren't supposed to die from cancer I thought, and thankfully, he didn't. However, the gauntlet of surgery and chemotherapy greatly weakened Andrew. The star athlete, student, and friend became restricted by his debilitating illness, but his optimism and carefree attitude always seemed untouched.

Andrew's mom recently shared a story about when he finished his first round of chemotherapy that perfectly captures his positive demeanor. She described the great joy in the hospital on the day that Andrew rang the bell, signifying the end of his chemotherapy. However, this moment of relief was quickly replaced by fear as Andrew later developed pneumonia. Andrew's doctors were concerned that he may not make it through the infection. Visibly upset and stricken with fear, Andrew's dad entered the hospital room to check on him. This was when Andrew—in his witty, nonchalant manner that everyone loved—asked, "Dad are you really crying? I am going to be fine." And he was.

As I went on to live out a normal middle and high school experience, Andrew's cancer recurred, and he was in and out of treatment. His illness kept him from enjoying the milestones kids our age were supposed to, like attending high school graduation. When it came time for me to go off to college, he was pursuing a hopeful clinical trial. We both had dreams of a brighter future.

> While the world of medicine is unbelievably interesting and engaging, it is only part of our identity. We are sons, mothers, friends, authors, artists, and, above all, humans.

This year, I started medical school at the same institution where Andrew began his cancer journey nearly 12 years ago. Every time I enter Children's Hospital, memories of first visiting Andrew's hospital room flood my mind. When Andrew was first diagnosed, a group of our friends went to visit him in the hospital. We were all given visitor bracelets and went up to his room to find him smiling in his hospital bed. My initial worry of seeing Andrew for the first time since he was diagnosed disintegrated immediately. We began doing what you might expect middle school boys to do--recklessly tossing a ball around his hospital room. His baseball prowess continued to shine through as the ball zipped around the room; however, we were all unable to comprehend the hardship he was enduring. Thinking of these moments with Andrew have added so much purpose to my medical education. He has fueled my passion for cancer research, and during a hectic exam week, the thought of Andrew adds an obvious relevance to my field of study and the patients I hope to care for.

Only when I began learning how to save a life, Andrew finally lost his. After over 10 years of highs and lows, his journey concluded. He had endured two brain surgeries, six port placements, lost his hair six different times, took over 100,000 pills, and boarded 62 flights for a clinical trial in a span of 2 years, while also managing to attend college for five semesters. To this day, I do not think he complained once.

This summer, I was fortunate to conduct research through the Medical College of Wisconsin's Medical Student Summer Research

continued on page 3

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Living Donor Protection Act: A Call to Action

Kurtis J. Swanson, MD

Chronic kidney disease and end-stage kidney disease are serious, emerging problems nationally and for our patients here in Wisconsin. In its most recent annual report, the National Kidney Foundation of Wisconsin contextualizes the burden of kidney disease in Wisconsin: 84,000 patients and families live with the diagnosis of chronic kidney disease. Over 6,800 people in Wisconsin are on dialysis. Over 1,300 men and women are waiting for a kidney transplant.[1] These numbers have only increased since this report was published in 2019. Yet, there is hope.

Kidney transplantation—particularly living donor kidney transplant—provides the gift of life for Wisconsinites afflicted with kidney disease. According to the Scientific Registry of Transplant Recipients, nearly 120 living donor transplants are performed in adult and pediatric patients in Wisconsin annually.[2-3]

Prospective living donors face many barriers to providing the gift of life, including financial challenges such as loss of income/employment and difficulties securing life, disability, and long-term care insurance. In a multicenter study performed by the Kidney Donor Outcomes Cohort, Rodrigue et al noted that 92% of donors incurred direct costs (median $433, range $6–$10,240), and more than one third (36%) reported lost wages in the first year after donation (median $2,712, range $546–$19,728).[4]

In response to these substantial hindrances, policymakers have crafted bipartisan legislation—the Living Donor Protection Act (HR 1255/S 377)—which would serve to protect living donors from wage loss by organizing Family Medical Leave Act protections and preventing insurance denials/conditions. As described in its recent statement, the National Kidney Foundation summarizes how this act will protect living donors and promote live organ donation in three primary ways:[5]

1. Prohibit life, disability, and long-term care insurance companies from denying and/or limiting coverage, as well as charging higher premiums for living donors.
2. Amend the Family and Medical Leave Act of 1993 to specifically identify living organ donation as a serous health condition for private and civil service employees.
3. Direct the US Department of Health and Human Services to update materials on live organ donation to reflect these new protections and promote living organ donation.

As members of our medical community in Wisconsin, as well as our statewide constituency, we can use our collective voice to advocate for the health and well-being of our living donors and recipients of these gifts. I urge you to reach out to our congressional representatives to make the Living Donor Protection Act a reality.

For more information or if you would like to get involved , visit the American Transplant Foundation Living Donor Laws guide (www.americantransplantfoundation.org/wp-content/uploads/2022/11/Living-Donation-Laws.pdf) and the Voices for Kidney Health website supported by the National Kidney Foundation (https://voices.kidney.org/ldpa/).[6,7]

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Trends in E-cigarette Use in Callers to the Wisconsin Tobacco Quit Line

Brian S. Williams, MD; Megan Piper, PhD; Thomas M. Piasecki, PhD; Jesse Kaye, PhD; Michael Fiore, MD, MPH, MBA

ABSTRACT

Introduction: E-cigarette use has been increasing for years with a limited understanding of how to help users quit. Quit lines are a potential resource for e-cigarette cessation. Our objective was to characterize e-cigarette users who call state quit lines and to examine trends in e-cigarette use by callers.

Methods: This retrospective study examined data from adult callers to the Wisconsin Tobacco Quit Line from July 2016 through November 2020, including demographics, tobacco product use, motivations for use, and intentions to quit. Descriptive analyses were performed by age group with pairwise comparisons.

Results: A total of 26,705 encounters were handled by the Wisconsin Tobacco Quit Line during the study period. E-cigarettes were used by 11% of callers. Young adults aged 18-24 had the highest rates of use at 30%, and their use rose significantly from 19.6% in 2016 to 39.6% in 2020. E-cigarette use among young adult callers peaked at 49.7% in 2019, coinciding with an outbreak of e-cigarette-related lung injury. Only 53.5% of young adult callers used e-cigarettes to "cut down on other tobacco," compared to 76.3% of adult callers aged 45-64 ($P < 0.05$). Of all callers using e-cigarettes, 80% were interested in quitting.

Conclusion: E-cigarette use among callers to the Wisconsin Tobacco Quit Line has increased, driven largely by young adults. Most e-cigarette users who call the quit line want to quit. Thus, quit lines can serve an important role in e-cigarette cessation. A better understanding of strategies to help e-cigarette users quit is needed, particularly in young adult callers.

INTRODUCTION

Cigarette smoking has been on the decline for decades among all age groups in Wisconsin and the United States.[1-3] However, e-cigarette use—or vaping—has increased markedly since its introduction over 10 years ago. As of 2019, 4.5% of all adults (18 and older) in the US reported current e-cigarette use.[4] Among all age groups, young adults aged 18-24 reported the highest rates of e-cigarette use, with 9.3% reporting that they used e-cigarettes in 2019.[4]

E-cigarettes represent a potential public health benefit if used exclusively to help people quit combustible tobacco cigarette use.[5] However, most young adult e-cigarette users report that they never previously smoked cigarettes,[4,6] thus they are not using e-cigarettes for combustible tobacco cessation. Given the risks of negative health consequences with e-cigarette use among young adults,[7-10] the rising rates of e-cigarette use among this population[4] mandates a better understanding of how to help e-cigarette users to quit.

State tobacco quit lines serve as an important resource to connect tobacco users with free, evidence-based treatment for nicotine addiction.[11] Given their established infrastructure and broad reach, quit lines are poised to play a major role in helping e-cigarette users quit vaping. Studies examining e-cigarette use among quit line callers have focused largely on how e-cigarettes impact cigarette smoking cessation[12-14] rather than on e-cigarette cessation. One recent study evaluating e-cigarette use in callers across 24 public quit lines noted a rise in e-cigarette use in quit line callers from 12.3% in 2016 to 14.7% in 2018, with highest rates of use among young adult callers at 25.2% reported in 2018.[15] As e-cigarette use increases, more information is needed regarding use patterns (exclusive vaping vs dual use with cigarettes), trends by age group, motivations for use, and interest in quitting e-cigarettes among callers to quit lines, with a particular focus on young adults given

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their higher rates of use. Such information can help quit lines to better develop treatment services for e-cigarette users and help clinicians better understand the potential of quit lines to assist their patients who use e-cigarettes.

The Wisconsin Tobacco Quit Line (WTQL) receives approximately 5,000 to 10,000 calls per year. Its core program provides a single counseling session and 2 weeks of over-the-counter nicotine replacement therapy. The goal of this study is 2-fold: to characterize e-cigarette users who call state quit lines and to examine the trends, by age, in quit line use among people who vape. The current study used data from calls to the WTQL from July 2016 through November 2020 to characterize callers' demographics, use patterns of e-cigarettes and other tobacco products, and desire to quit e-cigarettes, overall and by age groups. Trends over time in call volume and e-cigarette use among callers also were examined. Given the rise in e-cigarette use overall during this period, we expected reports of e-cigarette use among WTQL callers to have increased substantially, especially among young adult callers. The late portion of 2019 was a period of particular interest, as a nationwide, highly publicized outbreak of e-cigarette or vaping product use associated lung injury (EVALI) occurred during this time,[16] potentially driving increased interest in e-cigarette cessation.

METHODS

This study was a retrospective analysis of data from the WTQL from July 2016 through November 2020. July 2016 was chosen as the starting point as this was when the WTQL updated its intake call screening language to ask, "Have you used an e-cigarette or other electronic vaping product in the past 30 days?" During this time period, there were 26,705 treatment encounters. Treatment encounters were identified by the intake assessment call, and data from these intake assessment calls were used in the current analyses, regardless of how many additional calls occurred during the treatment encounter. It should be noted that 92% of the 26,705 calls were from unique individuals and that among individuals with repeated treatment encounters, most (89%, n = 1791) had 2 unique encounters (range = 2-14; mean = 2.16; SD = 0.62). We opted to include all treatment encounters in our analysis, even if they were from someone who had more than 1 treatment encounter, in order to capture who is using WTQL services. Results were very similar when analyses were limited to the first treatment encounter from unique individuals (see Appendix). We hereto refer to treatment encounters as calls.

Measures

During intake calls, the WTQL collected month and year of call, demographic information, method of entry (phone, fax, e-referral, web enroll, other), and tobacco-specific questions (tobacco type[s] used, age at first use). For approximately 1 month twice each year when callers reported e-cigarette use, they were asked (1) "How many days did you use an e-cigarette or e-vaping product in the last 30 days?"; (2) "Are you using e-cigarette/e-vaping products to quit smoking?"; (3) "Do you intend to completely quit using e-cigarettes/e-vaping products within the next 30 days?'

Statistical Analyses

Descriptive analyses and pairwise comparisons were performed to examine demographic characteristics of the sample overall and by age group (18-24 years, 25-44 years, 45-64 years, and 65+ years). These age groups were chosen as they represent the standard age groups defined by the Centers for Disease Control and Prevention in reporting smoking prevalence.[3,4]

To characterize WTQL callers, they were classified according to patterns of product use: e-cigarette only, combustible cigarette only, dual use of e-cigarettes and combustible cigarettes, or neither e-cigarette nor combustible cigarette use (eg, smokeless tobacco). Rates of each use pattern were calculated overall, and the proportions of each use pattern were compared across age groups. The frequency of vaping, use of e-cigarettes to quit smoking, and motivation to quit vaping were analyzed similarly and followed by pairwise comparisons between age groups.

To examine trends over time, descriptive analyses examined the total call volume and investigated how the age structure of the callers varied over time. Pairwise tests were performed to identify changes in quit line utilization over time within each age group. Next, we examined the proportion of callers in each age group reporting e-cigarette use in each year. Trends were tested using a logistic regression analysis predicting e-cigarette use from year (coded linearly from 2016 = 0 to 2020 = 4), a categorical age group variable, and their interaction. To permit a closer look at a potential influence of the 2019 EVALI outbreak, we plotted e-cigarette use over time by quarter-years for the whole set of calls and within each age group.

This study was approved by the University of Wisconsin-Madison Health Sciences Institutional Review Board.

RESULTS

Characterizing WTQL Callers

From July 2016 through November 2020, there were 26,705 calls to the WTQL. Table 1 describes demographic and tobacco use characteristics of the callers. The majority of callers were >44 years old (67.9%), female (59.9%), White (73.9%), first used tobacco prior to age 18 (62.8%), and used cigarettes (95.8%). E-cigarettes were used by approximately 11% of all callers during the study period. Most of contacts with WQTL were initiated by tobacco users calling the WTQL (71.5%).

Tobacco product use patterns and assessments of e-cigarette use characteristics are given in Table 2. Of the 2,969 callers reporting e-cigarette use, 93.2% (n = 2,768) reported being "dual users" (using both e-cigarettes and cigarettes), while the remaining 6.8% used e-cigarettes alone. E-cigarette use was most common among young adults aged 18-24 (30.1%). The proportion of dual users

Table 1. Demographics of Wisconsin Tobacco Quit Line Callers by Age Group, 2016-2020

	Total N (%)	18-24 years N (%)	25-44 years N (%)	55-64 years N (%)	65+ years N (%)
Total Callers	26,705 (100)	730 (2.7)	7,848 (29.4)	13,276 (49.7)	4,851 (18.2)
Sex					
Male	10,694 (40.0)	301 (41.2)[a,b]	3,193 (40.7)[a]	5,317 (40.0)[a,b]	1,883 (38.8)[b]
Female	15,979 (59.8)	427 (58.5)[a,b]	4,644 (59.3)[a]	7,944 (59.8)[a,b]	2,964 (61.1)[b]
Race					
American Indian/Alaska Native	400 (1.5)	19 (2.6)[a]	146 (1.9)[a]	191 (1.4)[b]	44 (0.9)[c]
Arab/Arab American	31 (0.1)	3 (0.4)[a]	18 (0.2)[a]	8 (0.1)[b]	2 (0.04)[b]
Asian	104 (0.4)	4 (0.5)[a,b]	68 (0.9)[a]	28 (0.2)[b,c]	4 (0.1)[c]
Black/African American	4514 (16.9)	99 (13.6)[a,c]	1,232 (15.7)[a]	2,523 (19.0)[b]	660 (13.6)[c]
Native Hawaiian/Pacific Islander	21 (0.1)	2 (0.3)[a]	9 (0.1)[a,b]	8 (0.1)[b]	2 (0.04)[b,c]
White	19,738 (73.9)	543 (74.4)[a]	5,725 (72.9)[a]	9,609 (72.4)[a]	3,861 (79.6)[b]
Other	1,008 (3.8)	44 (6.0)[a]	388 (4.9)[a]	468 (3.5)[b]	108 (2.2)[c]
Ethnicity					
Hispanic or Latino	1,041 (3.9)	44 (6.0)[a]	457 (5.8)[a]	461 (3.5)[b]	79 (1.6)[c]
Non-Hispanic or Latino	24,738 (92.6)	664 (91.0)[a]	7,138 (91.0)[a]	12,358 (93.1)[b]	4,578 (94.4)[c]
Education					
<High school	3,741 (14.0)	121 (16.6)[a]	826 (10.5)[b]	2,152 (16.2)[a]	642 (13.2)[c]
High school/GED	9,737 (36.5)	367 (50.3)[a]	2,837 (36.1)[b,c]	4,728 (35.6)[b]	1,805 (37.2)[c]
Some college or technical/trade school	7,927 (29.7)	184 (25.2)[a]	2,469 (31.5)[b]	3,812 (28.7)[c]	1,462 (30.1)[b,c]
College or university degree	4,451 (16.7)	36 (4.9)[a]	1,474 (18.8)[b]	2,157 (16.2)[c]	784 (16.2)[c]
Entry method					
Phone	19,098 (71.5)	539 (73.8)[a,c]	5,363 (68.3)[b]	9,475 (71.4)[a]	3,721 (76.7)[c]
Fax referral	2,901 (10.9)	91 (12.5)[a]	892 (11.4)[a]	1,559 (11.7)[a]	359 (7.4)[b]
E-referral	2,471 (9.3)	64 (8.8)	696 (8.9)	1,232 (9.3)	479 (9.9)
Web enroll	1,189 (4.5)	32 (4.4)[a]	693 (8.8)[b]	393 (3.0)[c]	71 (1.5)[d]
Other	1,046 (3.9)	4 (0.5)[a]	204 (2.6)[b]	617 (4.6)[c]	221 (4.6)[c]
Tobacco used (not mutually exclusive)					
Cigarette	25,584 (95.8)	684 (93.7)[a]	7498 (95.5)[b]	12,749 (96.0)[b]	4,653 (95.9)[b]
E-cigarette	2,969 (11.1)	220 (30.1)[a]	1,260 (16.1)[b]	1,152 (8.7)[c]	337 (6.9)[d]
Cigar	1,476 (5.5)	73 (10.0)[a]	474 (6.0)[b]	690 (5.2)[c]	239 (4.9)[c]
Smokeless tobacco	843 (3.2)	63 (8.6)[a]	453 (5.8)[b]	268 (2.0)[c]	59 (1.2)[d]
Pipe	196 (0.7)	13 (1.8)[a]	71 (0.9)[b]	66 (0.5)[c]	46 (0.9)[b]
Other	544 (2.0)	42 (5.8)[a]	197 (2.5)[b]	240 (1.8)[c]	65 (1.3)[d]
Age at first tobacco use					
5-12 years	3,098 (11.6)	86 (11.8)[a,b]	898 (11.4)[a]	1,714 (12.9)[b]	400 (8.2)[c]
13-17 years	13,671 (51.2)	457 (62.6)[a]	4,273 (54.4)[b]	6,822 (51.4)[c]	2,119 (43.7)[d]
18-20 years	5,229 (19.6)	154 (21.1)[a]	1,565 (19.9)[a]	2,292 (17.3)[b]	1,218 (25.1)[c]
21-24 years	1,675 (6.3)	17 (2.3)[a]	532 (6.8)[b]	757 (5.7)[c]	370 (7.6)[b]
25+ years[†]	2,212 (8.3)	0 (0.0)	345 (4.4)[a]	1,281 (9.6)[b]	586 (12.1)[c]

Note: Within-category counts do not always sum to corresponding caller total owing to missing data on some measures. Proportions in the same row not sharing the same subscript ([a,b,c,d]) differ significantly at $P < 0.05$. Subscripts omitted for rows with no significant pairwise comparisons.

[†]The 18-24-year-old age group not included in pairwise columns comparisons owing to the structural zero in this group.

was similar across age groups. Young adults were significantly less likely to report using e-cigarettes "to cut down on other tobacco" compared to older adults aged 45-64 (53.5% vs 76.3%, OR = 0.36; 95% CI, 0.18-0.70; $P = 0.003$). Most callers in all age groups (79.6% of total sample) reported a "desire to quit e-cigarettes" in the next 30 days.

Trends Over Time

Call volume data over time are summarized in the top portion of Table 3. Calls to the WTQL peaked in 2018, with an average of 579 per month. There was a marked decrease in callers in 2020, with an average of 352 per month. Calls from young adults represented less than 5% of the total call volume in each study year and decreased over time.

Rates of reported e-cigarette use by year and age group are reported in bottom section of Table 3. The Figure depicts trends in reported use of e-cigarettes over quarter-years during the study period by age groups. E-cigarette use in young adult callers increased from approximately 20% in 2016 and 2017 to a peak of 49.7% in 2019, then fell somewhat to 39.6% in 2020. A logistic regression analysis revealed a significant linear increase with year (OR = 1.48; 95% CI, 1.30-1.68; $P < 0.001$) and an effect of age group, such that, compared to 18- to 24-year-old callers, odds of reported e-cigarette use were marginally lower in those 25-44 years old (OR = 0.72; 95% CI, 0.52-1.01; $P = 0.053$) and significantly lower in those 45-64 years old (OR = 0.53; 95% CI, 0.38-0.73; $P < 0.001$) and those 65 and older (OR = 0.44; 95% CI, 0.30-0.65; $P < 0.001$). Additionally, there was a year × age group interaction (Wald = 60.65; df = 3; $P < 0.001$). Specific interaction contrasts indicated that, relative to the increase in reported e-cigarette use among 18–24 year olds, increases over time were less pronounced among the other age groups (interaction ORs = 0.62 - 0.76; $Ps < 0.001$). Interestingly, the Figure indicates that the peak period in which young adult e-cigarette users called WQTL occurred in the third quarter of 2019, coinciding with the EVALI outbreak that began in July of 2019.[16]

DISCUSSION

The goals of this study were to better characterize e-cigarette use among callers to the WTQL from June 2016 through November 2020 and examine trends, by age, over time. We were especially interested in understanding young adult use patterns. Reported e-cigarette use during the study period increased in WTQL call-

ers overall. This is consistent with prior data[15] and likely reflects the increasing rates of e-cigarette use nationally—largely among younger adults.[3,4] This is consistent with our finding that e-cigarette use varied markedly by age, with young adults having the highest rate of e-cigarette use. Young adults, when compared to older callers, less frequently reported using e-cigarettes to "cut down on tobacco use" and more frequently reported being "e-cigarette only" users. These patterns are consistent with national population-level studies showing higher rates of dual use in older adults.[17] These differences in both use patterns and reasons for vaping based on age suggest that different approaches may be warranted for older versus young adult WTQL callers, as motivations may affect expected use duration and expectations for quitting.

Our data show that approximately 80% of callers to the WTQL who use e-cigarettes intend to quit vaping in the next 30 days. These rates did not differ markedly between age groups and were higher than prior studies that reported between 50% and 65% of adult e-cigarette users intending to quit.[18] Although callers to the WTQL aren't specifically asked if they are calling for assistance to quit e-cigarettes, their intentions to quit suggest they may view the WTQL as a quit resource. Given the lack of data on how to help e-cigarette users quit, these results highlight the importance of identifying how quit lines can best support e-cigarette cessation attempts. It is also important to understand how best to help dual users quit both cigarettes and e-cigarettes.

Finally, this study shows that tobacco product use is dynamic and requires continued monitoring to identify and respond to changes in use patterns over time. E-cigarette use in callers to the WTQL peaked in the 3rd quarter of 2019, which coincided with the EVALI outbreak during which e-cigarette users were becoming ill and occasionally died.[16] While this was ultimately determined to be related to vitamin E acetate used in counterfeit tetrahydrocannabinol (THC) vape devices,[19] the initial concern was that the disease was the result of vaping e-cigarettes, and the media extensively highlighted this possible connection. The peak in young adults calling the WTQL during this timeframe was dramatic and provides additional support to the notion that young adults identified the WTQL as a valuable resource for quitting e-cigarettes.

This study has limitations. First, we examined quit line data from a single state, thus the findings may not be generalizable to other states or regions of the country. Second, detailed e-cigarette use questions were asked only for approximately 2 months per year, resulting in a smaller number of responses for those detailed

Table 2. Tobacco Product Use Patterns and Characteristics of E-cigarette Use Among Wisconsin Tobacco Quitline Callers, 2016-2020

	Total Sample	18-24 years	25-44 years	45-64 years	65+ years
Tobacco Product Use Pattern					
E-cigarette only, N (%)	201 (0.8)	28 (3.8)[a]	77 (1.0)b	79 (0.6)[c]	17 (0.4)[d]
Dual user, N (%)	2,768(10.4)	192 (26.3)[a]	1,183 (15.1)[b]	1,073 (8.1)[c]	320 (6.6)[d]
Cigarette only, N (%)	22,816 (85.4)	492 (67.4)[a]	6,315 (80.5)[b]	11,676 (87.9)[c]	4,333 (89.3)[d]
Other tobacco, N (%)	920 (3.4)	18 (2.5)	273 (3.5)	448 (3.4)	181 (3.7)
Total	26,705	730	7,848	13,276	4,851
E-cigarette assessments					
E-cigarette frequency (days/mos), M (SD)†	11.9 (11.1)	17.1 (13.8)[a]	11.9 (11.2)[b]	11.2 (10.7)[b]	11.6 (10.0)[a,b]
E-cig used to cut down other tobacco, N (%)††	367 (68.6)	23 (53.5)[a]	132 (62.0)[a,c]	167 (76.3)[b]	45 (75.0)[b,c]
Want to quit e-cigarette, N (%)‡	401 (79.6)	32 (78.0)	168 (81.6)	158 (77.1)	43 (82.7)
E-cigarette nicotine, N (%)‡‡	452 (76.4)	39 (90.7)[a]	184 (80.3)[a]	182 (70.3)[b]	47 (77.0)[a,b]

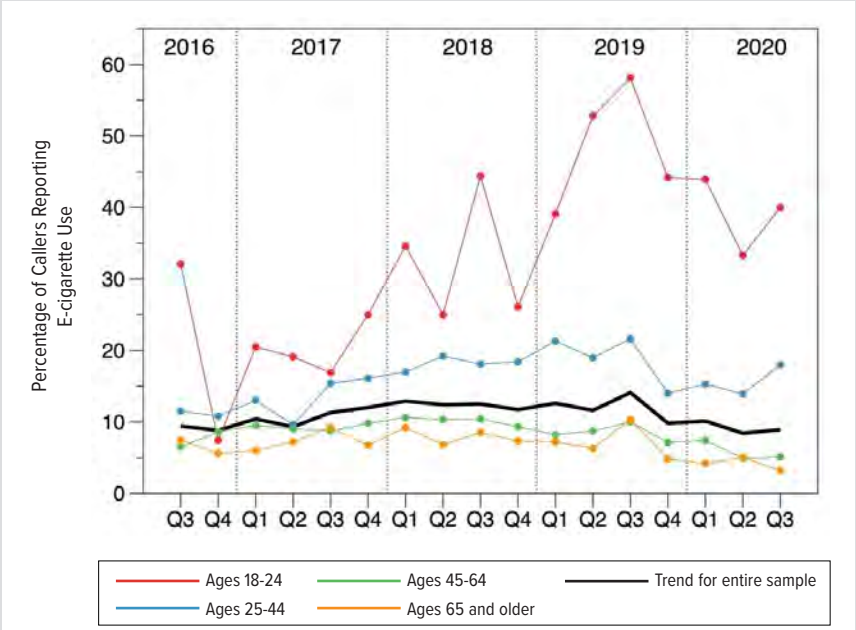
Note: Values in the same row not sharing the same subscript ([a,b,c,d]) differ significantly at $P < 0.05$. Subscripts omitted for rows with no significant pairwise comparisons.
†Limited to 313 callers administered the assessment (18-24 years, n = 21; 25-44 years, n = 118; 45-64 years, n = 132; 65+ years, n = 2).
††Limited to 535 callers administered the assessment and providing a valid response (18-24 years, n = 43; 25-44 years, n = 213; 45-64 years, n = 219; 65+ years, n = 60).
‡Limited to 504 callers administered the assessment and providing a valid response (18-24 years, n = 41; 25-44 years, n = 206; 45-64 years, n = 205; 65+ years, n = 52).
‡‡Limited to 592 callers administered the assessment and providing a valid response (18-24 years, n = 43; 25-44 years, n = 229; 45-64 years, n = 259; 65+ years, n = 61).

Table 3. Wisconsin Tobacco Quit Line Call Volume and Reported E-Cigarette Use by Year and Age Group

	2016†	2017	2018	2019	2020‡
Call Volume	**Calls**	**Calls**	**Calls**	**Calls**	**Calls**
Total (calls/month)	2,321 (387)	6,848 (571)	6,944 (579)	6,719 (560)	3,873 (352)
18-24 years (%)	107 (4.6)[a]	275 (4.0)[a]	112 (1.6)[b]	145 (2.2)[c]	91 (2.3)[c]
25-44 years (%)	776 (33.4)[a]	2,066 (30.2)[b]	2,012 (29.0)[b,c]	1,852 (27.6)[c]	1,142 (29.5)[b]
45-64 years (%)	1,159 (49.9)[a,b]	3,509 (51.2)[a]	3,406 (49.0)[b]	3,322 (49.4)[b,c]	1,880 (48.5)[b,d]
65+ years (%)	279 (12.0)[a]	998 (14.6)[b]	1,414 (20.4)[c]	1,400 (20.8)[c]	760 (19.6)[c]
Callers Reporting E-Cig Use	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**
Total	212 (9.1)[a]	724 (10.6)[b]	860 (12.4)[c]	815 (12.1)[c]	358 (9.2)[a]
18-24 years	21 (19.6)[a]	55 (20.0)[a]	36 (32.1)[b]	72 (49.7)[c]	36 (39.6)[b,c]
25-44 years	87 (11.2)[a]	274 (13.3)[a,b]	366 (18.2)[c,d]	354 (19.1)[d]	179 (15.7)[b,c]
45-64 years	86 (7.4)[a,b]	323 (9.2)[b,c]	346 (10.2)[c]	285 (8.6)[b]	112 (6.0)[a]
65+ years	18 (6.5)[a,b]	72 (7.2)[b]	112 (7.9)[b]	104 (7.4)[b]	31 (4.1)[a]

†Based on 6 months of data from 2016.
‡Based on 11 months of data from 2020.
Proportions in the same row not sharing the same subscript ([a,b,c,d]) differ significantly at $P < 0.05$.

Figure. Trends in Callers to the Wisconsin Tobacco Quit Line Reporting E-cigarette Use



questions. This illustrates the importance of collecting additional data on e-cigarette users who call the WTQL. Third, there was a very small number of young adult callers, highlighting need to increase cessation motivation and quit line appeal among young adults. The WTQL added a texting option as part of its services in 2021, and this may increase engagement with young adult e-cigarette users.[20] Finally, the smaller number of "e-cigarette only" users (7% of total e-cigarettes users and <1% of all callers) limited our ability to perform meaningful comparisons of this group to "dual users" or "cigarette only" users.

CONCLUSIONS

E-cigarette use increased in callers to the WTQL over the period 2016- 2020 and was highest among young adult callers. Quit lines likely can play an important role in helping e-cigarette users—particularly young adults—quit, but additional research is needed to clarify how to achieve this outcome.

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'The Biggest Problem With Access': Provider Reports of the Effects of Wisconsin 2011 Act 217 Medication Abortion Legislation

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ABSTRACT

Introduction: Abortion legislation in the United States determines people's access to services, including the abortion modality of their choice. In 2012, Wisconsin legislators passed Act 217, banning telemedicine for medication abortion and requiring the same physician to be physically present when patients signed state-mandated abortion consent forms and to administer abortion medications over 24 hours later.

Objective: No research documented real-time outcomes of 2011 Act 217 in Wisconsin; this study documents providers' descriptions of the effects of Wisconsin abortion regulations on providers, patients, and abortion care in the state.

Methods: We interviewed 22 Wisconsin abortion care providers (18 physicians and 4 staff members) about how Act 217 affected abortion provision. We coded transcripts using a combined deductive and inductive approach, then identified themes about how this legislation affects patients and providers.

Results: Providers interviewed universally reported that Act 217 negatively affected abortion care, with the same-physician requirement especially increasing risk to patients and demoralizing providers. Interviewees emphasized the lack of medical need for this legislation and explained that Act 217 and the previously enacted 24-hour waiting period worked synergistically to decrease access to medication abortion, disproportionately affecting rural and low-income Wisconsinites. Finally, providers felt Wisconsin's legislative ban on telemedicine medication abortion should be lifted.

Conclusions: Wisconsin abortion providers interviewed underscored how Act 217, alongside previous regulations, limited medication abortion access in the state. This evidence helps build a case for the harmful effects of non–evidence-based abortion restrictions, which is crucial considering recent deferral to state law after the fall of *Roe v Wade* in 2022.

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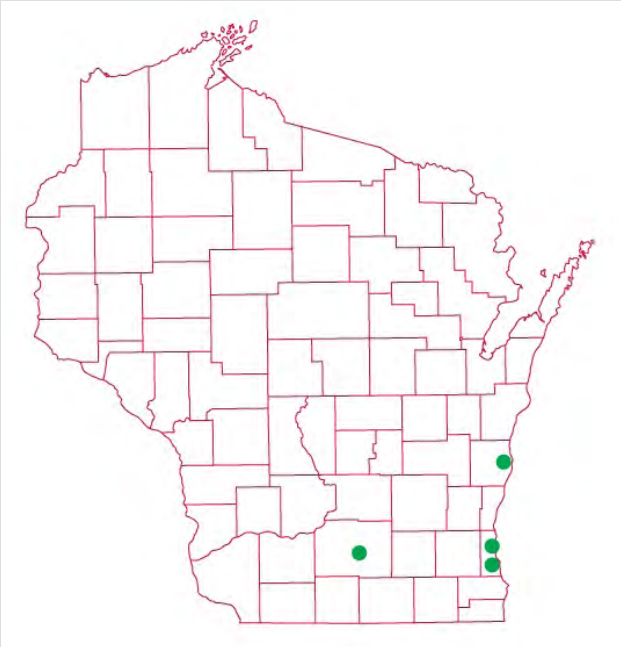
INTRODUCTION

Abortion care in the United States is at a crossroads amid changing national precedent. Increasingly, state laws rather than federal laws dictate circumstances under which people can obtain abortions.[1] Research must document how state-specific legislation affects abortion access:[2] Wisconsin's case can reveal consequences of specific medication abortion regulations.

Medication abortion using misoprostol and mifepristone is safe and effective.[3] In some settings, patients can choose between in-clinic "surgical" abortion (though in-clinic abortion does not involve surgery) and medication abortion. Few have estimated US patients' true preferences amidst limited options,[4,5] but in 2014, 45% of abortions in the United States were medication abortions, a proportion that has likely increased over time.[6] When legal and accessible, the mortality risk for abortion overall is at least 14 times lower than childbirth.[7] Over 99% of medication abortions and in-clinic abortions before 13 weeks of gestation have no adverse effects.[6,8] Federal mandates restrict pharmacists from dispensing medication abortion.[1] However, medication abortion can be administered safely through telemedicine[9]—key in states with high COVID rates, few abortion providers, and widely dispersed populations. In Wisconsin, some of the most restrictive legislation in the country has dictated how patients and providers experience abortion care.

In 2012, Wisconsin legislators passed and enacted *2011 Act 217*, containing multiple stipulations about how providers could offer medication abortion care. The bill's sponsor said it would

Figure. Locations of Clinics That Provided Abortion Services in Wisconsin, 2019



protect the "health and safety of women;" however, no evidence supports this claim.[10] Act 217 followed several other abortion restrictions enacted after Wisconsin's 2010 election, laws that contributed to closures of 40% of Wisconsin abortion clinics between 2010 and 2017.[11] In 2019, 4 abortion clinics remained, clustered in the southern quarter of Wisconsin; 3 provided medication abortion (see Figure). Act 217 compounded existing regulations by requiring the same physician be physically present when state-mandated abortion consent forms were signed and to administer abortion medications over 24 hours later. No corollary law existed for physicians providing in-clinic abortions. Act 217 also banned medication abortion provision via telemedicine; in 2020, 17 other states also required a physical clinician to provide medication abortion, although research suggests telemedicine is safe, effective, and often patient-preferred.[3,9,12,13]

No research to date examines how Wisconsin regulations specifically affected medication abortion care and access. Studies documenting the impact of all abortion restrictions are important; our team turned to Act 217 given its relative severity. While many other states impose non–evidence-based restrictions on medication abortion care, Wisconsin's law involved considerable stipulations. Wisconsin legislation created one of the most restrictive medication abortion environments nationwide at the time. Thus, evidence about this law's effects could be useful in the context of changing restrictions about medicine, from telemedicine to abortion. We documented Wisconsin abortion care providers' reports of how Act 217 influenced patient care.

METHODS

Because this study focused on the understudied effects of legislation on abortion provision, we chose a qualitative methodological approach to ask why, how, and under what circumstances.[14] Between May and October 2020, 3 researchers recruited health care professionals who were currently providing or had recently provided abortion care in Wisconsin. Using snowball sampling and professional networks, the team invited providers via phone, email, or text message to participate in an interview. While recruitment focused on physicians since only physicians could provide abortions in Wisconsin in 2020, the team also recruited other abortion health care providers. Many interviewees had abortion care experience in Wisconsin before the implementation of Act 217, providing comparative perspectives.

Our orientations and experiences, as an MD abortion provider, PhD researcher with decades of experience in abortion research, and two health professions students with experience working at abortion clinics, informed research design, analysis, and triangulating findings. This team compiled the interview guide to elicit providers' descriptions of how Act 217 and intertwined legislation in Wisconsin affected abortion provision, particularly of medication abortion. The semistructured interview guide included questions about abortion care, medication abortion, abortion policy, COVID-19 in abortion care, and *Roe v Wade*. A trained interviewer conducted and recorded all interviews over WebEx. She obtained informed consent before every interview, took notes throughout, and prepared 2- to 3-page post-interview memos. Interviews lasted 30 to 60 minutes, and participants received a $75 gift card upon completion. The team ceased recruitment after reaching theoretical saturation.

Each participant received a unique study number and pseudonym. A professional transcription service transcribed interview recordings. Using NVivo 12 (QSR International Pty Ltd, Australia, 2019), 2 independent coders built consensus themes using a combined inductive-deductive approach. To ensure methodological rigor and research integrity, we completed the Standards for Reporting Qualitative Research checklist.[15]

RESULTS

The final sample included 22 abortion care providers: 18 physicians, 2 nurses, and 2 surgical technicians. All providers and staff members worked at freestanding abortion clinics; the majority of providers worked there part time. Interviewees lived across Wisconsin when they provided services. Further identifying information is not provided here for participant anonymity. Interviewees universally expressed that Act 217 and its contingent regulations negatively affected abortion care. The research team identified the following 4 main themes about related but distinct effects of this policy.

1. Providers found the same-physician requirement especially burdensome.

Act 2017 required that the same physician consent the patient and then provide and watch the patient take the medication, 24 or more hours later. Many providers expressed that, at the time of their interview, the same-physician restriction was the most burdensome abortion restriction in Wisconsin. One noted that it

both required patients to base the timing of their care on one provider's availability and was inconsistent with other care:

"To use the pill, the same doctor has to be the same person doing it; whereas if a woman decides to have the surgical, any of the other doctors can do that procedure. So what, where's the consistency in that? And so I would say that it's the [...] single biggest problem."

Another provider highlighted how, instead of protecting pregnant people, the law limited their autonomy. Since different providers could consent and later provide in-clinic abortions, some patients "would be forced" to have in-clinic abortions due to provider timing, despite having originally wanted medication abortions:

"People would come in on the day of counseling, and they would actually wish that they could get a medication abortion, but their schedule wouldn't line up to come back and see me, and so they would be forced to choose an in-clinic […] it really limited their access to medication abortion."

Many providers worked only one full or half day per week at an abortion clinic. The same-physician law meant patients were required to wait until that provider returned to the clinic, a timeline that could vary from one to many weeks. Such delays in care put some patients outside of the gestational age range for medication abortion:

"I saw many times that women were obligated to having [sic] a surgical procedure when they really had hoped to have a medical procedure because there wouldn't be a provider there twice before they became too far in gestational age to qualify for the medication abortion."

Finally, one provider expressed the burden of the same-physician law on physicians and staff:

"We have tried to minimize the impact on the patient. But that's often really at the expense of the physician and the health care staff trying to do whatever they can. I've had days when I'm post-call that then I try to come in to see a patient so they can have their pill."

This provider, among others, described going above and beyond normal duties, including working on days they are not scheduled to ensure that their patients receive care. Ultimately, providers painted a picture of overwork, frustration, and burnout from the same-physician law specifically and Act 217 overall.

2. Providers emphasized the lack of medical evidence or clinical rationale for Wisconsin's abortion restrictions.

Many providers explained that, in addition to causing burden, the same-physician restriction was not evidence-based or best medical practice:

"Two separate visits. Not evidence-based. Not necessary to provide safe care, as evidenced by all the other states that [don't] have it, as evidenced by the state of Wisconsin before that law was enacted."

Interviewees often mentioned the inconsistency of the same-physician requirement in abortion care, as other medical procedures do not require the same physician to both consent for and provide care. One provider expressed how Act 217 and contemporaneous regulations led to longer waits for abortions, undermining safety and quality of care:

"All of these regulations, none of them make sense. None of them are useful or promote a more safe procedure or a healthier procedure. It would clearly be better if the day the woman walked into the clinic, [...] she could have an abortion that day, she would have a safer abortion than if you make her wait."

Finally, one provider explained how Wisconsin abortion restrictions, including Act 217, did not aim to ensure best medical care:

"I think about some of the restrictions on providing that care safely that did not seem to be really about providing the best medical care but were obvious barriers to women and impositions from the legislature into the patient-doctor relationship. The intent was to interfere with the patient-doctor relationship, and it was being hidden under the guise of caring about women."

3. Providers reported that alongside the mandated 24-hour waiting period, Act 217 decreased access to medication abortion, especially for rural and low-income Wisconsinites.

Providers expressed that Act 217 and previously instated restrictions disproportionately affected rural and low-income pregnant people. One stated:

"For women who have to drive sometimes 2, 3, even 4 or 5 hours to a clinic appointment, need to take time off work, need to find childcare, need to explain to family and friends why they need to do these things, it really is a barrier to being able to access a safe form of abortion that I think could be more accessible to women if there weren't legislative barriers."

Providers knew the hours added up for rural Wisconsinites, especially since abortion care in Wisconsin was available only in one corner of the state.

"[Act 217] presents a tremendous, not just inconvenience, but a barrier for women who drive 3 and 4 hours [...]to sign a consent and then come back and take a pill and then [...] have to come back a third time for a follow-up."

Another provider outlined how they saw marginalized people in Wisconsin, including poor people, rural residents, and people of color, struggle the most under abortion restrictions:

"There's so many barriers for poor women. Women of color are disproportionately affected as well, because they make up a disproportionate amount of poor women. In terms of accessing care, paying for care when insurance doesn't cover it, childcare, and work, taking time off work and having to make multiple visits... Rural women [..] are terribly affected."

Some providers mentioned their concern that people who "are pregnant and in dangerous situations," including abuse, also had a more difficult time accessing high-quality care under Act 217:

"They have to balance so many factors, from the legal end of what we're telling that patient, of when she has to return and what she has to do, to when she may be able to leave the house or fit that in or be able to make that happen in a safe way. [Accessing abortion may be] the key for her to be able to get out of the relationship."

4. Providers argued that the telemedicine ban on medication abortion provision should be lifted, especially during the COVID-19 pandemic.

Interviews were conducted before COVID vaccines were available; providers shared that COVID-19 revealed ways that limitations on medication abortion provision harmed both patients and providers, particularly given unnecessary requirements for multiple in-person appointments. One interviewee summarized:

> *"[The impact of Wisconsin abortion restrictions] was especially highlighted during COVID-19. [... I feel] the pressure of gosh, I have a cold. How bad is that cold? Should I just go to work? During COVID-19 [...] you shouldn't go to work. [...] But if I don't go to work, that means the women that I saw a week ago—who are counting on me to be able to have their medication abortion—can't have it. So it's a terrible place to be in as a provider, to feel like I can't not go to work."*

This provider experienced moral distress: abortion legislation shaped their ability to provide medical care. Another interviewee explained that legislators could solve this moral distress by lifting the ban on telemedicine for medication abortion provision. They explained how telemedicine would confer benefits to women's health, amidst COVID and generally:

> *"Providing quality medication abortion services by physicians and other trained providers via a telehealth platform would be something that would be a real positive force in public and population health in Wisconsin... if we really want to take care of women, it would be important to them to work to be able to make these services more accessible."*

Finally, providers argued that the prohibition on telemedicine, in conjunction with other Wisconsin regulations, prevented clinics from providing abortion care in the safest way possible during a pandemic:

> *"Our 24-hour, same physician, our physician only, our ultrasound law, our parental consent—all of these things. Whereas other states have been able to not only protect their patients and their staff and everyone else by working towards less contact during a time of COVID, we haven't been able to do any of that because our laws force us to do what has now become inherently unneeded but unsafe things to continue to abide by medically unnecessary restrictions."*

DISCUSSION

Findings from this study indicate that Act 217, alongside previously instated regulations, limited physicians' ability to provide evidence-based abortion care in Wisconsin. Participants argued that people from racial and ethnic groups who have been historically oppressed, as well as rural and low-income residents, bore the brunt of this legislation, which providers underscored as non–evidence-based. No provider indicated that Act 217 specifically, or Wisconsin's abortion restrictions generally, improved or protected patient care or health. Interviewees also emphasized that Act 217's telemedicine ban caused unnecessary barriers to care.

Wisconsin's Act 217 implemented some of the most restrictive medication abortion regulations in the country at the time. State-level abortion policy is especially important given changing national precedent and subsequent deferral to state law; evidence is needed in judicial responses to changing state laws.[16] Rich research has elucidated effects of state-specific abortion legislation in other states,[1,13,17,18] but few studies have been qualitative[19–21] and none to date studied providers and legislation in Wisconsin. This research contributes empirical details about providing abortion care amidst restrictive legislation, which may help inform research and practice in areas where new or shifting laws affect abortion provision in unexpected ways.

Our findings underscore telemedicine's key role in medication abortion provision, especially considering the ongoing COVID-19 pandemic and dwindling number of abortion clinics. Interviewees emphasized that, when they were interviewed, many Wisconsin residents already traveled 100 miles or more to access abortion.[22] The effect of distance, providers explained, fell disproportionately on disadvantaged Wisconsinites, especially those in rural areas. Telemedicine is widely used for other medical care, yet despite the preponderance of evidence on the safety and efficacy of telemedicine for medication abortion,[3,9,12,17,23] Wisconsin and 17 other states prohibited it.[24] Overturning these non–evidence-based laws would facilitate safe, effective, and equitable telemedicine medication abortion services.

While evidence from our study indicates that one act significantly limited abortion care, results also underscore the cumulative effect of Act 217 and previously existing abortion restrictions, making accessing abortion care difficult for many—especially those oppressed due to race, geography, and socioeconomic status. While for legislative purposes we researched the effects of one unstudied law, further research should focus on legislation's holistic effects.

Results highlight the consequences of abortion restrictions on providers themselves and the health care workforce. Providers often tried to protect patients from antichoice legislative sequelae, but this had emotional and physical tolls. Future researchers should study provider dropout and burnout amid state-based abortion restrictions.

Limitations and Strengths

Limitations of this research include our oversampling physicians, which limited our conclusions about abortion care teams overall. Scholarship suggests that different types of providers have differing relationships to and opinions about abortion care work;[25] researching other providers' perspectives would be beneficial. However, because Wisconsin legislation only permitted physician provision of abortion in 2020, oversampling reflected who provided abortion care in Wisconsin. Data collection timing—during the first 6 months of the COVID pandemic—likely affected providers' perspectives but carried attendant advantages, revealing intersections of the pandemic with abortion restrictions.

Strengths include the timeliness of delineating some of the effects of Wisconsin abortion restrictions, especially Act 217, given pending lawsuits at the time of data collection. We sought

provider perspectives; health care professionals are exposed to day-to-day effects of legislative barriers, and we additionally asked providers how they thought laws affected patients. Finally, while we focused on one specific law, our study narrates what at the time were maximal legislative barriers, which can help researchers and clinicians across the United States plan for abortion provision in changing legal landscapes.

CONCLUSIONS

In this study, Wisconsin abortion providers detailed how Act 217, in conjunction with previous regulations, dramatically limited medication abortion access in the state. Providers described how people who had already struggled to access abortion—like people with low incomes, people of color, and rural Wisconsinites—experienced even more obstacles as a result of this law. This study provides evidence that Act 217 and overlapping legislation, often justified by suggesting they protect the "health and safety of women" but are not based in scientific evidence,[10] worsened patients' abortion access and care. Act 217 prevented Wisconsin physicians from following medical best practice for their patients or following their patients' preferences in abortion modality. Our research, which describes the impact of state-specific legislation on abortion access and provision, is paramount considering recent changes to national precedent and subsequent deferral to state law. The fall of *Roe v Wade* in 2022 means that abortion care has ceased in Wisconsin for the immediate future, but legal challenges will continue. Findings from this study and others can help build a crucial, implementable evidence base as policy change unfolds.

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Naloxone Prescribing in an Academic Emergency Department: Provider Practices and Attitudes

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ABSTRACT

Introduction: Naloxone reverses opioid overdose, but it is not universally prescribed. With increases in opioid-related emergency department visits, emergency medicine providers are in a unique position to identify and treat opioid-related injury, but little is known about their attitudes and practices around naloxone prescribing. We hypothesized that emergency medicine providers would identify multifactorial barriers to naloxone prescribing and report varying levels of naloxone-prescribing behaviors.

Methods: A survey designed to assess attitudes and behaviors regarding naloxone prescribing practices was emailed to all prescribing providers at an urban academic emergency department. Descriptive and summary statistics were performed.

Results: The response rate was 29% (36/124). Nearly all respondents (94%) expressed openness to prescribing naloxone from the emergency department, but only 58% had actually done so. Most (92%) believed that patients would benefit from greater access to naloxone, however 31% also believed that opioid use would increase as access to naloxone increases. Time was the most frequently identified barrier (39%) to prescribing, followed by a perceived inability to properly educate patients on naloxone use (25%).

Conclusions: In this study of emergency medicine providers, the majority of respondents were amendable to prescribing naloxone, yet almost half had not done so and some believed that doing so would increase opioid use. Barriers included time constraints and perceived self-reported knowledge deficits regarding naloxone education. More information is needed to gauge the impact of individual barriers to prescribing naloxone, but these findings may provide information that can be incorporated in provider education and potential clinical pathways designed to increase naloxone prescribing.

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INTRODUCTION

Opioid-related injury and death are major public health problems that result in thousands of deaths per year. Deaths due to opioid overdose have steadily risen in the past 2 decades. In 2018, opioids were involved in 46,802 recorded overdose deaths, 69.5% of all drug overdose deaths.[1] The trend of opioid-related mortality in Wisconsin reflects that of the nation as a whole, as statewide opioid-related deaths have steadily increased over the past decade, from 410 in 2010 to 1226 deaths in 2020.[2]

Naloxone is a competitive opioid antagonist used as an antidote for opioid poisoning that can reverse opioid overdose and save lives. It was approved in 1971, carries virtually no overdose risk or potential for nonmedical use,[3] and has a long (2-year) shelf life. While medical professionals typically deliver naloxone intravenously, prefilled Narcan intranasal naloxone delivery spray devices have made it easier for laypersons with no medical training to administer naloxone effectively.[4] While Narcan may perhaps be more user-friendly, naloxone vial and syringe(s) kits are often the least expensive option for laypersons.[5] Since 1996, a growing number of naloxone distribution programs across the US have provided naloxone kits to laypersons, including those at risk of overdose, their loved ones, and potential bystanders, which have been used successfully to reverse tens of thousands of potentially fatal overdoses.[6] Initiatives to educate and distribute naloxone to populations

at risk of opioid misuse have been shown effective at reducing the risk of death. For example, a program was carried out in Wilkes County in rural northwestern North Carolina, which had some of the highest rates of drug overdose deaths in the country prior to the implementation of Project Lazarus—a program that provides opioid overdose education and naloxone distribution.[7] After project implementation, the overdose death rate dropped from 46.6 per 100,000 in 2009 to 29.0 per 100,000 in 2010.[7] Similarly, opioid-related overdose death rates improved in Massachusetts areas where opioid overdose education and naloxone distribution was implemented compared to those where it was not.[8] Other naloxone education programs across the country have effectively increased laypersons' skills and knowledge regarding naloxone administration.[9] Even brief education sessions have increased at-risk individuals' competence in naloxone administration.[10]

When using opioids to manage patients with chronic pain, the Centers for Disease Control and Prevention recommends that clinicians consider offering naloxone to patients with risk factors for opioid overdose or nonmedical use, including histories of overdose and substance use disorder, higher dosages of opioids (≥50 MME/day), and concurrent use of benzodiazepines with opioids.[11] In response to the increased number in opioid-related deaths, all 50 states and the District of Columbia have passed legislation to increase access to naloxone, including state standing orders for naloxone, ability for prescribers and pharmacists to enter into prescribing agreements, and latitude for pharmacists to prescribe and dispense on their own.[12] Furthermore, because the nature of opioid overdose renders patients unable to administer naloxone to themselves, at least 45 states and the District of Columbia have permitted third-party naloxone prescriptions, making naloxone more accessible to families and acquaintances of overdose victims who may be on scene to administer it.[13]

Despite its well-established effectiveness in reversing opioid poisoning and growing legislation to increase access, naloxone may be underutilized in general and after emergency department (ED) encounters. In a sample of 138,108 individuals, 1 study found that only 1.5% of patients at high risk of opioid overdose were prescribed naloxone following encounters with the health care system broadly.[14] Another found that only 1.1% of patients utilized insurance to fill a prescription for naloxone within 30 days of an opioid-related ED encounter specifically.[15] There is little disagreement about the effectiveness of naloxone as an overdose reverser. For example, Wilson and colleagues[16] found that 86.5% of internal medicine physicians agreed that naloxone is effective in preventing opioid overdose deaths. Acceptance and knowledge of prescribing naloxone has gradually increased in primary care clinicians in the past 2 decades,[17] but acceptance among emergency medicine providers is relatively unknown and there still exists multiple barriers that have prevented it from becoming a universal practice.

Perceived Usefulness, Utilization, and Influences on Patient Behaviors

Academic clinicians (ie, emergency medicine, primary care and internal medicine, and hospital medicine) reported apprehension that increased access to naloxone may enable nonmedical opioid use behavior as a barrier to increased naloxone prescribing,[18,19] despite findings showing that increased naloxone access is not a risk factor for increased nonmedical use behavior and overdoses.[20,21] Additionally, primary care staff have cited the stigma of nonmedical opioid use and wishing to avoid eliciting negative reactions and patient dissatisfaction from those who may not see themselves at risk for overdose.[22]

Moreover, some clinicians are concerned that that laypersons would not be able to properly respond to overdoses.[18,19,22] Unlike most prescription drugs that the patient self-administers, naloxone is typically administered by another individual, which may complicate the utility of naloxone from a practicality standpoint, as not only the at-risk patient would need to be educated on administering naloxone, but ideally the patient also would be teaching that information to people who may be present during an overdose.[19,22] However, it has been shown that even brief education sessions are sufficient to teach proper naloxone administration.[10]

Clinician Perceptions of Their Own Knowledge About Naloxone

One of the most commonly reported barriers to prescribing naloxone is not patient-centric but due to the clinicians themselves not feeling adequately trained to responsibly prescribe take-home naloxone,[16,17,23-25] and some academic clinicians (ie, emergency medicine, primary care and internal medicine, and hospital medicine) would rather defer to clinicians who may be more knowledgeable, such as pain management specialists.[18]

Logistical Barriers to Prescribing Naloxone

Some physicians cite lack of time during a clinical encounter as a barrier to prescribing, as it may be too time-consuming during a patient visit for a proper discussion on using naloxone—not only due to the time needed to explain the use of the naloxone delivery device itself, but also because patients who use opioids often have extensive problem lists that are multifactorial in nature and necessitate prioritization.[22]

Between 2005 and 2014, nationwide ED visits related to opioid misuse and overdose increased 99.4% from 89.1 per population of 100,000 to 177.7.[26] Special considerations need to be taken for patients who present to the ED for treatment of a nonfatal opioid overdose. About 1 in 20 of these patients will die within 1 year of their visit, with two-thirds of these deaths being directly attributed to subsequent opioid-related overdose. Naloxone can be especially life-saving for these patients.[27]

Emergency medicine providers are in a unique position to identify and treat patients with opioid overdoses, opioid misuse and use disorders, and opioid-related injuries. Much of the litera-

Table 1. Sample Demographics

	n (%)
Sex	
Male	25 (69)
Female	11 (31)
Role	
Faculty physician	27 (75)
Resident physician	7 (19)
Physician assistant	2 (6)
Years in practice	
<5	15 (43)
5–9	12 (34)
10–19	4 (11)
20+	4 (11)
Amendable to prescribing naloxone	
Yes	34 (94)
Prescribed naloxone from the emergency department in the past	
Yes	21 (58)

ture on physician attitudes towards naloxone prescribing focuses on primary care and may not be representative of emergency medicine providers or the state of Wisconsin. For this study, we aimed to investigate the attitudes and perceptions of Wisconsin emergency medicine providers regarding naloxone prescribing. We hypothesized that they have varying attitudes and behaviors around naloxone prescribing and that barriers to prescribing naloxone would be multifactorial. We aimed to provide findings that EDs can utilize to address potential underutilization of naloxone in this unique setting.

METHODS

An institutional review board-approved, cross-sectional survey consisting of demographics and 28 multiple choice, 6-point Likert-scale items (eg, highly agree to highly disagree), and a final opened-ended free response item was created using Qualtrics and administered via email to providers (ie, physicians and advanced practice providers [nurse practitioners, physician assistants]) in an academic ED within a large, urban city. The study received a waiver to document informed consent, and the invitation email informed potential respondents that clicking on the email link inferred their consent to participate in the study. Respondents were not offered compensation for participation. They were asked about their behaviors, attitudes, and beliefs around naloxone and prescribing naloxone, as well as barriers to naloxone prescribing in the ED. The 6 response categories were condensed into 2 (agree/disagree), and frequency counts and descriptive statistics were calculated.

RESULTS

Sample Characteristics

The survey was sent to 124 emergency medicine providers, 36 of whom responded (29%). The majority (n = 25; 69%) were male. Participants included 27 (75%) faculty physicians, 7 (19%) residents, and 2 (6%) physician assistants (Table 1). Although the response rate may seem low, 1 study group found that response rates and responsiveness for email surveys may only approximate 25% to 30%, especially without follow-up email and reinforcements.[28,29]

Naloxone Knowledge

All respondents (100%) knew that naloxone is effective in reversing opioid overdoses, and most (89%) knew that it reduces the likelihood of death due to opioid overdose (Table 2). Most respondents knew that there are no considerable health risks associated with naloxone use (69%), but 25% reported they were unsure of the risks. Most (75%) indicated that they could properly educate patients on proper naloxone use. Most (75%) indicated that they could properly educate patients on naloxone use. All thought that bystanders could effectively administer naloxone, but 31% were unsure if bystanders could administer it with little training.

Perceived Usefulness, Utilization, and Influences on Patient Behaviors

The majority of respondents (58%) had previously prescribed naloxone in an ED setting, and the great majority (94%) indicated they were at least open to possibly prescribing naloxone (Table 1) and thought that emergency medicine providers should prescribe naloxone (86%) (Table 2). Most (92%) thought that patients would benefit from greater access to naloxone.

Respondents expressed concern that naloxone would affect patient behaviors around opioid use and contact with first responders. A quarter of respondents agreed that someone who uses opioids nonmedically would increase use if given increased access to naloxone, and 31% reported that increased naloxone access to patients would likely increase opioid use because patients would believe that they have a safety net with naloxone. Finally, 67% reported that an opioid overdose survivor who is subsequently revived with naloxone would be less likely to contact emergency medical services.

Barriers to Prescribing Naloxone

Some respondents (18%) thought that patients get offended by the suggestion of naloxone due to the inference that they may have a drug use problem, while 36% believed that there is not enough time during a clinical encounter to properly discuss naloxone use with a patient.

DISCUSSION

Increased naloxone availability is associated with decreased opioid-related mortality.[6,21] Yet, providers at our urban academic emergency department reported a range of behaviors and opinions about prescribing naloxone. All respondents agreed that naloxone itself is an effective agent in reversing overdose, suggesting that hesitance to prescribing naloxone may not be rooted in

doubt about the effectiveness of naloxone itself.

The majority of gaps and barriers appear to center around knowledge. For example, 25% of respondents indicated that they are not effectively able to educate their patients on proper naloxone administration, suggesting a lack of knowledge among some providers regarding naloxone that may preclude prescribing; and 25% indicated that they were unsure about the health safety profile of naloxone. Further, it has been repeatedly shown in multiple studies that laypersons with minimal training are able to effectively administer naloxone,[10,22] but nearly a third of our respondents indicated that they were unsure about training required for bystanders. Increased education about the virtually nonexistent negative side effects or drug interactions of naloxone, as well as its ease of use among laypersons with even short durations of training, may increase prescribing behavior.

Importantly, some respondents were concerned that increased access to naloxone would increase patients' nonmedical opioid use. It is important to ensure that clinicians are educated on naloxone's apparent ability to save lives short-term, as well as its ability to serve as an entrée for longer-term treatment engagement.[30] Concerns among clinicians that increased naloxone prescription may increase risky opioid use behavior and increased morbidity/mortality is not uncommon. However, growing evidence actually suggests the opposite; the provision of naloxone does not encourage opioid users to increase their drug consumption or harm themselves.[20,21] It is important to educate clinicians on this harm reduction strategy.

Table 2. Survey Results by Domain and Question

Domain/Survey Question	Response	N (%)
Knowledge		
There are considerable health risks to naloxone use (other than failure to overturn overdose)	Yes	2 (6)
	No	25 (69)
	Unsure	9 (25)
I am able to effectively educate patients on how to administer naloxone	Agree	27 (75)
	Disagree	9 (25)
Naloxone is effective in reversing opioid overdoses	Agree	36 (100)
	Disagree	0 (0)
Prescribing naloxone reduces the likelihood of death due to opioid overdose	Agree	32 (89)
	Disagree	4 (11)
Naloxone can be effectively administered by laypersons with very little training	Yes	25 (69)
	No	0 (0)
	Unsure	11 (31)
Bystanders will not be able to effectively administer naloxone	Agree	0 (0)
	Disagree	36 (100)
Perceptions and behaviors		
Overall, patients would benefit from greater access to naloxone	Agree	33 (92)
	Disagree	3 (8)
Someone who abuses opioids, when given increased access to naloxone, will increase his/her opioid usage	Agree	9 (25)
	Disagree	27 (75)
Patients will likely increase opioid usage because they feel as if they have a safety net in naloxone	Agree	11 (31)
	Disagree	25 (69)
It is better for an untrained bystander to attempt to administer naloxone to an unresponsive person than to do nothing at all	Yes	34 (94)
	No	0 (0)
	Unsure	2 (6)
An overdose victim who is revived with naloxone is less likely to call emergency medical services or report to the hospital	Agree	24 (69)
	Disagree	11 (31)
Who should prescribe naloxone? (check all that apply)	Primary care providers	33 (92)
	Emergency providers	31 (86)
	Pain management specialists	33 (92)
Barriers		
Patients are offended by the suggestion of naloxone because it implies that they have opioid-use problems	Agree	6 (18)
	Disagree	28 (82)
There is not enough time during a clinical encounter to properly discuss naloxone use with a patient	Agree	13 (36)
	Disagree	23 (64)

In addition to belief barriers, results also revealed logistical barriers to prescribing naloxone. For example, many respondents acknowledged a lack of the time necessary to educate patients about proper naloxone use during a clinical encounter. In our current clinical work environments where output and efficiency are often prioritized, it can be challenging to find time and resources to dedicate to patient education. This is not uncommon, with more EDs aiming to increase patient "throughput" and shortening patients' total length of stay. Efforts to recognize patients early in the patient encounter via nursing education and posted patient inclusion criteria information materials may integrate workflow without slowing down patient care. Specially designed bundled order sets and templates in the electronic medical record can prevent charting delays. Strategies to streamline patient education can include prewritten discharge instructions for naloxone indications and administration, which can be provided verbally by clinicians, pharmacists, social workers, or nurses and can be made available to take home for further review by patients. EDs can adopt workflows that include patient education provided by multiple types of staff during an encounter (eg, nurses, social workers). Some EDs are fortunate to partner with individuals with lived experience (eg, certified peer support specialists, recovery coaches) who can be consulted to provide additional patient education and support in the ED and beyond.

Although we did not specifically ask about financial barriers—specifically the cost of naloxone—as it related to the willingness of providers to prescribe, it may be useful to do so in the future. One respondent indicated in the free-response portion of the survey a lack of knowledge about the pricing and availability of naloxone. This is a valid point of concern, given the rising cost of naloxone over the past decade. Although there are community-

based organizations that may provide naloxone for free, the cost of a 2-pack of Narcan intranasal devices is in the range of $150.[5] Generic naloxone may be available for a more affordable price, and insurance may cover a substantial part of the cost;[31] however, analyses of insurance claims suggest that many patients do not fill prescriptions—at least with insurance—for naloxone after an opioid-related ED visit.[15] It may be beneficial for clinicians to have a more comprehensive knowledge of naloxone pricing, and it would be impactful to gauge whether naloxone pricing relates to prescribing behaviors.

Lack of knowledge on naloxone and education of their patients suggests that greater incorporation of naloxone information into clinician education may lead to improved knowledge and confidence regarding naloxone usage, patient education, and subsequent prescribing. Consistent with the trend of growing acceptance of prescribing naloxone,[18] most (94%) of the respondents indicated that they are open to prescribing it, but only 58% have actually done so, suggesting that there is room for education regarding when and how to appropriately prescribe naloxone or removal of barriers is indicated.

Future Directions and Limitations

As we are a large academic ED, we have a rich variety of resident physicians, new faculty physicians, and advanced practice providers coming to us from all over the country. We have weekly academic conferences that all are encouraged to attend, and there have been various didactic sessions on opioid use disorder over time that many of our providers have attended. Given the results of this survey, there is certainly opportunity to provide additional evidence-based practice recommendations at our site.

More information is needed to gauge the effect of individual barriers to prescribing naloxone, but our findings may provide opportunity for education about the impact and benefits of greater naloxone availability. Providing prefilled naloxone kits to high-risk patients from the ED may increase comfort with emergency medicine providers and patients and lead to greater naloxone accessibility in the community.

Our study had several limitations. The results are subject to all limitations related to self-report and survey methodology. Our sample was limited to a single ED, and results are not necessarily generalizable to other institutions or departments. The survey was limited in length in attempt to achieve a higher response rate—we plan to resurvey our sample population with more focused surveys to investigate the roles of additional logistical barriers, institutional protocols, and local provider cultures. In addition, we sent a reminder to complete the survey but experienced low response rates commonly reported with email[28,32] and physician samples.[33] Low response rates have raised concerns about nonresponse bias or the likelihood that nonresponding physicians will be systematically different from the population under study.[34] This concern is supported by research showing modest differences between responders and nonresponders and between early and late responders on demographic and/or practice-related characteristics.[35]

CONCLUSIONS

In a cross-sectional survey study of emergency medicine providers at an urban academic ED, the majority of providers were open to prescribing naloxone, yet most had not done so. Self-reported barriers to prescribing naloxone included concerns about patient behavior with increased naloxone access (eg, increased opioid use), lack of one's own knowledge about naloxone, and logistical barriers such as lack of time on clinical shift to adequately educate patients. More information is needed to gauge the impact of individual barriers to prescribing naloxone, but these findings may provide important information to EDs that want to increase patient access to life-saving naloxone. We hope that key information identified in this survey can further guide education efforts for clinicians, as well as inform improvements in naloxone education and discharge planning and ultimately lay foundations for other important harm reduction practices such as ED-based buprenorphine induction. We are currently developing an ED-based buprenorphine induction program that includes dispensing home naloxone as an important harm reduction technique—one of the first of its kind in Wisconsin.

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Ambulatory Intensive, Multidisciplinary Telehealth for High-Risk Discharges: Program Development, Implementation, and Early Impact

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ABSTRACT

Introduction: Creating and implementing programs aimed at reducing readmissions for high-risk patients is critical to demonstrate quality and avoid financial penalties. Intensive, multidisciplinary interventions providing care to high-risk patients utilizing telehealth have not been explored in the literature. This study seeks to explain the quality improvement process, structure, intervention, lessons learned, and early outcomes of such a program.

Methods: Patients were identified prior to discharge with a multicomponent risk score. The enrolled population was managed intensively for 30 days after discharge through a suite of services, including weekly video visits with an advanced practice provider, pharmacist, and home nurse; regular lab monitoring; telemonitoring of vital signs; and intensive home health visits. The process was iterative, including a successful pilot phase followed by an expanded health system-wide intervention analyzing multiple outcomes, including satisfaction with video visits, self-rated improvement in health, and readmissions compared to matched populations.

Results: The expanded program resulted in improvements in self-reported health (68.9% reported health was some or greatly improved) and high satisfaction with video visits (89% rated satisfaction with video visits 8-10 on a scale of 0-10). Thirty-day readmissions were reduced compared to individuals with similar readmission risk scores discharged from the same hospital (18.3% vs26.4%) and individuals who declined to participate in the program (18.3% vs 31.1%).

Conclusions: This novel model using telehealth to provide intensive, multidisciplinary care to high-risk patients has been successfully developed and deployed. Key areas for growth and exploration include developing an intervention that captures a greater percentage of discharged high-risk patients, including non-homebound patients, improving the electronic interface with home health care, and reducing costs while serving more patients. Data show that the intervention results in high patient satisfaction and improvements in self-reported health, with preliminary data showing reductions in readmission rates.

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INTRODUCTION

Reducing the number of readmissions to acute care hospitals within 30 days has been an area of focus nationally since the Patient Protection and Affordable Care Act of 2010, which, through Medicare, penalized excessive readmission rates. After the Patient Protection and Affordable Care Act, many efforts to reduce readmissions have focused on the transition of care from hospital discharge back to the primary care setting. It is known that a small number of individuals account for a disproportionate rate of readmission and of health care spending in the United States.[1] Focusing efforts on this small but frequently readmitted population may be key to sustainable and valuable interventions that improve outcomes and reduce readmissions.

Several effective models to reduce readmissions for hospitalized patients have been developed utilizing a bundle of interventions, including structured handoffs, medication reconciliation, and utilization of discharge coaches/advocates.[2-6] However, the literature is less robust surrounding specific tactics to reduce readmissions for high-risk discharges. Longitudinal intensive management programs have been studied and found to have positive effects on patient access and engagement[7] and experience[8] but variable effects on long-term health care utilization.[9,10] A transitional care program providing intensive in-person management has shown particular success,[11] but in a randomized trial, a care program aimed at utilizing care

plans and intensive interdisciplinary management for high-risk patients did not show benefit.[12]

Programs providing intensive management for high-risk patients through telehealth after discharge have not been described in the literature and may provide a unique ability to serve this population, which often suffers from significant physical limitations to attend office-based visits. In support of this method of care, it has been found that in-person home-based primary care[13] and home-based extender care[14] can have positive benefits on health care utilization. Furthermore, preliminary evidence shows that telehealth can be a useful and effective modality of care in all-risk care transitions[15] and with the elderly.[16,17] However, specifics of programs serving high-risk patients on discharge with telehealth have not been described in the literature.

We aim to describe the piloting and development, feasibility, and observational impact of an intensive management program for high-risk discharges using a multidisciplinary team connecting to patients through telehealth facilitated by a home health registered nurse (RN). This paper describes the details of how this program was developed, structured, implemented, and iterated and the key lessons learned so that others can use the principles identified to develop programming for high-risk discharges. Analysis of outcomes outlined in the Results section aims to support understanding of the program.

METHODS

Population Characteristics

An academic tertiary care hospital and 2 community hospitals with an extensive network of 40 health clinics that employ 1700 physicians comprise our health system. Patients were recruited only from those hospitalized at the academic tertiary care hospital and included those with internal or external primary care clinicians.

Prior to this program implementation, multiple readmission reduction tactics had been deployed, including high-risk discharge huddles, pharmacist medication reconciliation, expedited scheduling in primary care, and transitional care management calls. Despite implementation of these measures, a review of patients readmitted to the academic hospital from primary care practices affiliated with the system revealed that the majority had complex illness with a 36% readmission rate. This population required more effective monitoring, including the ability to rapidly intervene when issues arose.

Population Identification

In order to identify risk to appropriately target the intervention, an internal risk score was developed—the Hospital Admission Readmission Risk Discriminator (HARRD), which used multiple components described in the readmission literature, including polypharmacy, previous readmissions or emergency department (ED) visits, high-risk chronic conditions, and age (Table 1). The components of this score could be obtained directly from the electronic health record on admission and expedited recruitment during the hospital stay. This score had been retrospectively validated on discharges from within our system and found to outperform the LACE index[18] in predicting readmissions with a continuous receiver operating characteristic curve of 0.86 (Table 1). Prior to the start of the program, a HARRD score of 4 or 5 was found to correlate with a readmission rate of up to 36% or above. Individuals with a HARRD score of 4 or 5 and who qualified for home health care were the target population for this program. Patients were excluded if they were receiving chemotherapy, discharged to a nursing facility, part of the advanced heart failure program, within 2 years of any solid organ transplant, in hospice, or were admitted for congestive heart failure, sickle cell disease, or a myocardial infarction, as the health system had existing outreach programs for these patient populations. Patients were recruited in person by a staff member prior to discharge and consented to program participation.

Table 1. Components of the Hospital Admission Readmission Risk Discriminator Score

Component	Weight
ED visits ≥ 3 in past 6 months or ≥ 1 inpatient readmission(s) within the last 90 days	2 points
≥ 2 chronic diseases: diabetes, congestive heart failure, COPD, liver disease, dementia, connective tissue disease, HIV, stroke, peripheral vascular disease, cancer, psychiatric diagnosis (bipolar, schizophrenia, depression)	1 point
Age > 65 years	1 point
>10 medications	1 point

Abbreviations: ED, emergency department; COPD, chronic obstructive pulmonary disease.

Pilot Program

A pilot project was developed to test the hypothesis that the proposed program could reduce readmissions. The project focused on patients admitted from a single internal medicine clinic affiliated with the hospital. Eligible patients were interviewed using a standard tool addressing social, financial, disease knowledge, self-care ability, medication, and transportation issues. The inpatient team contacted a nurse practitioner in the clinic prior to discharge to initiate the handoff process. A home care referral was initiated to one hospital-affiliated home care agency, and the patient was seen at home within 24 hours by an RN and social worker. The patient was scheduled in clinic within 72 hours, evaluated by the primary care clinician or advanced practice nurse prescriber (APNP) and met with a pharmacist to review medications. A weekly huddle was held with the APNP, home health nurse, and RN care coordinator. The patient also received a weekly phone call from the RN care coordinator. After hours, if any problems arose, patients were instructed to call the home care nurse who, in turn, would contact the on-call physician. Analysis demonstrated a reduction in readmissions for patients of the study clinic with a HARRD score of 3,

Table 2. Details of Team Member Roles in the Hospital Discharge Care Program

Team Member	Credentials	Role	FTE
Medical director	MD or DO	Daily patient care huddles with team, after hours oncall coverage, program development and direction	0.2
Advanced practice provider (APP)	APNP, DNP, PA-C	Video visits with patients, monitor lab results and telemonitoring results, coordinate with Home RNs, coordination with ED and inpatient teams when patients admitted, work directly with medical director	1.0
Registered nurse coordinator	BSN	Patient recruitment and initial biopsychosocial screening, triage, coordination with home RNs, durable medical equipment, support to APP or medical director as assigned	1.0
Home RN	BSN	Home-based program intake within 24 hours of discharge, patient assessment vitals, and basic physical exam, facilitate video visits, wound care, medication reconciliation and adherence counseling, home safety evaluation, frequent visits with patient as defined by need and directed by APP	1.0 split among multiple RNs
Pharmacist	PharmD	Initial extensive medication reconciliation, weekly patient video visits, between-visit availability for APP and home RN	0.7
Scheduler	HS degree or more	Assistance with patient recruitment, processing of paperwork, coordinate schedule for home visits, supplies and equipment for the team, and other duties as assigned	1.0

Abbreviations: FTE, full-time equivalent; MD, medical doctor; DO, doctor of osteopathic medicine; APNP, advanced practice nurse prescriber; DNP, doctor of nursing practice; PA-C, physician assisstant, certified; RN, registered nurse; ED, emergency department; BSN, bachelor of science in nursing, PharmD, doctor of pharmacy; HS, high school.

4, or 5 from 34.9% during the 7 months prior to the intervention (January 1-July 31) to 11.9% during the 7 months following the intervention (August 1–February 2) and a decrease in total cost per patient from $6860 to $3839. Total costs factored in costs to the health system, including outpatient, ED, and inpatient visits but did not include program costs; the reduction in costs of care was driven largely by reductions in inpatient care and ED visits versus an increase in outpatient visits. Patients discharged with HARRD scores of 3, 4, or 5 at 2 comparison clinics without intervention were followed in real time, showing respective readmission rates during the study period of 20.5% and 21.6% in one clinic and 34.5% and 27.1% in the other clinic.

Full Program

Based on the positive results of the pilot study, an expanded program called the Hospital Discharge Care Program (HDCP) was developed to manage all discharged patients at very high risk for readmission (HARRD scores 4 or 5), regardless of location of primary care clinician.

New programmatic adjustments relative to the pilot program were the use of video visits with the program's advanced practice provider (APP) and the addition of a pharmacist to each video visit, which was facilitated by the home health nurse. The video visits replaced scheduled clinic visits, allowing patients to recover in the comfort of their home while undergoing intensive monitoring by the team.

Multiple team members were involved in patient care, including a medical director responsible for overall program direction and clinical supervision; an APP responsible for the daily intensive patient care; a clinic-based RN responsible for recruitment, initial assessments, and triage; a home health RN responsible for intake assessments, weekly assessments, facilitating video visits, and many other duties as required in the home; a pharmacist responsible for medication reconciliation and follow-up; and a scheduler responsible for the program's day- to-day operational efficiencies. Details of these roles are listed in Table 2.

Patients were seen within 24 hours by the home health nurse; then video visits facilitated by that nurse with the APP and pharmacist were held within 72 hours of discharge and weekly thereafter for 30 days. All care was provided in the home as feasible, and those with acute issues requiring in-person care were brought to the clinic to be seen by the APP or physician. Telemonitoring, including daily blood pressure, pulse, oxygen saturation, and weight, was deployed for select patients, such as individuals with congestive heart failure, renal disease, or other disease states that would necessitate this monitoring. Telemonitoring data were communicated in real time to the APP for close monitoring of the patients' condition and titration of medications. Labs were completed in the home by the home health agency and transmitted to the APP. Video visits were utilized to assess and communicate with the patient and their caregivers. To minimize work for the patient, maximize enrollment and benefit from the program, and to avoid the known disparities that exist in access to telehealth technology, the home health nurse managed all of the technological aspects of care to connect via video visits. Home palliative care providing home-based visits by an APP frequently was ordered for individuals struggling with end-of-life decisions or symptoms. A discharge document was prepared for the primary care clinician upon completion of the program for continuity of care purposes.

The initial program goal was to care for 20 patients per month; after approximately 1 year of operation, this goal was increased to 40 patients per month. This mark was difficult to obtain given a combination of factors, including the tightening of the home care requirements by the home health organization, loss of active referrals from inpatient case management, and an increasing number of discharges managed by the health system's telephonic-based care coordination programs. Given enrollment difficulties, some patients with HARRD 3 scores were included when requested by inpatient or program staff. Program enrollment was maintained at approximately 20 to 35 patients per month over this time.

Data Analysis

Although the program spanned multiple years, data for fiscal year 2018 were included in the final analysis. Process data were collected as the program was deployed, including enrollment, reasons for decline, and HARRD scores.

A telephone survey was offered to all program participants from fiscal year 2018 asking multiple questions, such as satisfaction with video visits and self-reported health improvement before and after program enrollment.

Thirty-day readmission data were retrospectively analyzed utilizing Vizient data on readmissions. Planned readmissions were excluded from analysis. The readmission rates for those enrolled in the program were compared to those who were eligible for the program but declined to participate or those for whom we were unable to offer enrollment (missed) due to staff shortage or an after-hours discharge. A second comparison population was created analyzing the readmission rates for HARRD scores 3, 4, and 5 versus HDCP patients with similar HARRD scores, as well as a total readmission rate that was weighted to the same population enrolled in HDCP (Table 3).

This project and analysis were approved for institutional review board exemption by the institution's department of medicine quality improvement exemption process.

Table 3. Retrospective Readmission Rates (Excluding Planned Readmissions) for the Hospital Discharge Care Program Compared to Patients Who Declined the Program and Hospital Averages by Risk Score for Fiscal Year 2018

HARRD Score	HDCP Enrolled		HDCP Eligible But Declined/Missed		HDCP Enrolled vs Declined	Overall Hospital[a]	HDCP Enrolled vs Hospital
	n	Readmission Rate (%)	n	Readmission Rate (%)	Variance (%)	Readmission Rate (%)	Variance (%)
0	2	0	0	0			
1	2	0	0	0			
2	7	14.3	0	0	14.3		
3	12	0	3	33.3	-33.3	20.8	-20.8
4	93	19.4	117	35.9	-16.5	30.3	-10.9
5	75	21.3	41	17.1	4.3	24.9	-3.6
Total	191	18.3	161	31.1	-12.7	26.4[b]	-8.1

Abbreviations: HARRD, Hospital Admission Readmission Risk Discriminator; HDCP, Hospital Discharge Care Program.

[a]Excluding advanced heart failure and active oncology.

[b] Weighted to HDCP population distribution.

RESULTS

For fiscal year 2018, 191 patients were enrolled in the program, and 161 were eligible but declined to participate (45.7%). The top 3 reasons cited for declining included the lack of desire to have home health care, not wanting to lose personal care services related to insurance requirements, and perceived lack of need for home health care services. All of the individuals who refused the program also refused home health care. Many of the enrolled patients had a HARRD score of 4 or 5 at the time of discharge. Some patients with lower scores on discharge (n = 23) were enrolled, as the HARRD score changed during admission as medications and problem lists were modified.

Forty-five patients responded to the telephone survey (23.5%). When asked to rate the video visits on a scale of 0 to 10 with 0 being the worst and 10 being the best, 82% of participants responded between 8 and 10 (Figure 1). At the end of the intervention, 68.9% of respondents reported improvement in their overall health (Figure 2).

Of the enrolled individuals, the readmission rate was 18.3%. For those who were eligible but declined or missed program enrollment, the overall readmission rate was 31.1%. Higher differences between the enrolled and declined population's rates were seen at a HARRD score of 3 or 4 compared to 5. Similarly, the weighted "all-hospital" discharge cohort had a readmission rate of 26.4%, with greater differences again seen at HARRD scores of 3 and 4 compared to 5 (Table 3).

DISCUSSION

This novel program managing high-risk patients discharged from an academic health system provided care through intensive telehealth with a multidisciplinary team (APP and pharmacist) in collaboration with a home health RN. Preliminary analysis shows high patient satisfaction and a reduction in the readmission rate for those who were enrolled versus other comparison populations. This effect could be due to the intervention; however, further studies are needed to verify these results.

The literature surrounding readmission reduction programs focused on high-risk patients is limited. A recent manuscript describing the Complex High Admission Management Program (CHAMP) outlining intensive non-telehealth management of high-risk patients has shown no benefit on readmissions or health care utilization.[12] The described intervention was successful in relation to a few key differences from CHAMP, including a virtual platform and telehealth care that was based in the home—two methods of care that have been proven in multiple areas of the literature to be effective in reducing health care utilization.[13-17]

In addition, literature describing the process of implementation, iteration, and structure are limited in the literature. This manuscript provides details necessary for health system leaders to consider when developing programs focused on patients with high risk of readmission.

The study also highlights the high satisfaction of high-risk patients with video visits and telemedicine care after hospital dis-

Figure 1. Hospital Discharge Care Program Patient Satisfaction With Video Visits

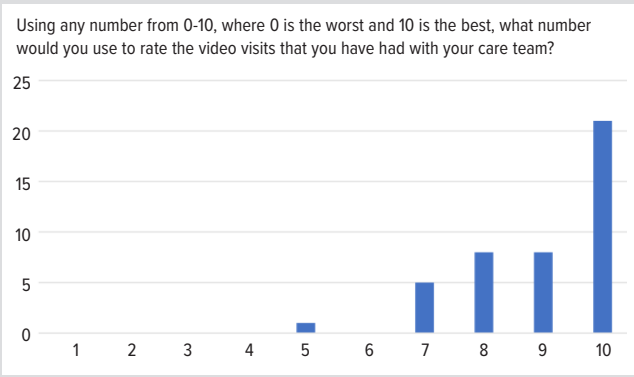
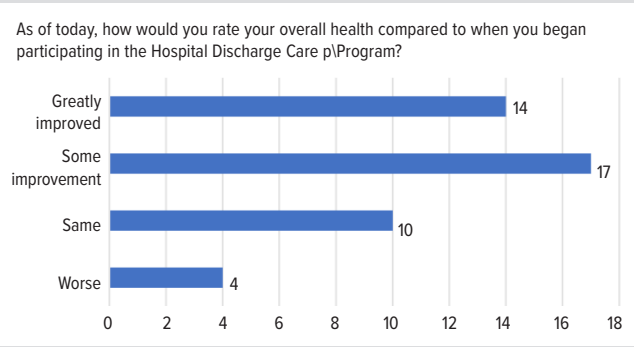


Figure 2. Hospital Discharge Care Program Patient Satisfaction With Video Visits



charge. However, the population is likely self-selected, as those who declined to participate often cited the lack of desire to have individuals in the home or engaging virtually as reasons not to enroll. Regardless, options including telehealth for discharges are useful and effective strategies to reduce readmissions, in conjunction with other strategies to provide multiple options for high-risk patients.

This intervention was more successful in individuals who had lower risk scores. Those with the highest risk score (5) did not experience much benefit from the program with regard to readmission reductions, while those with moderate risk scores (3-4) experienced the most benefit. There is no literature to guide the understanding of this phenomenon. It can be postulated that individuals at very high risk needed different types of services or were too medically complex or ill to respond to even this high level of care. Further studies should be completed to understand this phenomenon.

One of the limitations of the outcomes analysis is that the comparison groups were selected for convenience, but there are potential biases that could affect the interpretation of causality. However, the feasibility and successful deployment of this program has been clearly described. Furthermore, data on demographics of those enrolled, declined and missed, and the matched comparison populations are not available. Further work to understand the true impact of the program on readmissions, which populations the intervention may benefit most, and how this intervention can be scaled to serve non-homebound and moderate-risk patients is underway.

Key Successes

Video visits: This method of intensive video visit care facilitated by a home health RN has not been described in the literature. Compared to traditional telephonic transitional care, this care method allowed the care team to visualize the patient's condition; communicate effectively with the patient, RN, and family members; and form more trusting and therapeutic relationships with patients. Furthermore, patients recovered in the comfort of their home post discharge. Patients were seen rarely in the clinic or required to come to the lab for testing. This intervention may have increased the engagement of a very high-risk patient population with mobility challenges who otherwise may not have been able to engage with office-based primary care after discharge. Our satisfaction and health improvement ratings display that this method of care was well-received by this patient population.

Intensive patient management: Frequent touches and acute availability allowed the care team to catch health changes early before they led to an ED visit or hospitalization. Furthermore, the ability of the home health agency to deploy home vital sign monitoring and laboratory analysis allowed the APP and pharmacist team to closely monitor and treat these patients.

Collaborative care: Collaboration between home health RNs and a campus-based APP and pharmacist was important. This method of care allowed the home health RNs to have the needed support to manage complex patients with a clear connection to the discharging institution to ensure gaps were not missed in the discharge plan of care. Home health RNs emphasized the benefit of real-time communication versus leaving messages to be returned at the end of a clinic day.

Future Directions

Enrollment: The population of eligible patients declined with time due to two factors: (1) home care requirements became stricter; (2) the health system concurrently deployed multiple telephonic care coordination programs over time that excluded more patients from the intervention based on payor. Efforts to recruit more patients or consider other groups of patients who may benefit from this intervention are being explored, including those who are not eligible for home health care and those who would not prefer video visits. In addition, efforts to include the primary care clinician in management are being explored to improve patient trust and engagement.

Non-homebound patients: On average, 16 patients per month are ineligible due to the insurance requirement that patients be homebound to receive home care. Other interventions, including

use of telephonic outreach and community health worker-based programs are being explored to cover this gap. This method of care may not be feasible or effective for non-homebound patients.

Lack of electronic interface: The lack of an electronic interface between the home health agency electronic health record and the hospital electronic health record led to the need for frequent verbal and email-based communication. Furthermore, lab results relied on fax transmittal and often were delayed, leading to delays in care. An interface would facilitate care.

Scalability: The program is resource intensive, serving a small number of patients. Current work is being done to explore how this care can be deployed more cost-effectively and how to properly target the intervention to the population that may benefit from it the most.

CONCLUSIONS

This novel model using telehealth to provide intensive, multidisciplinary care to high-risk patients has been successfully developed and deployed. Key areas for growth and exploration include developing an intervention that captures a greater percentage of discharged high-risk patients, including non-homebound patients, improving the electronic interface with home health care, and reducing costs while serving more patients. Data show that the intervention results in high patient satisfaction and improvements in self-reported health, with preliminary data showing reductions in readmission rates.

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Impacts of Socioeconomic Status on Dentoalveolar Trauma

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ABSTRACT

Introduction: Children sustain dentoalveolar trauma and lose teeth at the same rate regardless of socioeconomic status; however, debate surrounds these rates in adults. It is known socioeconomic status plays a major role in access and treatment in health care. This study aims to clarify the role of socioeconomic status as a risk factor for dentoalveolar trauma in adults.

Methods: A single center retrospective chart review took place from January 2011 through December 2020 for patients requiring oral maxillofacial surgery consultation in the emergency department, due to either dentoalveolar trauma (Group 1) or other dental condition (Group 2). Demographic information including age, sex, race, marital status, employment status, and type of insurance were collected. Odds ratios were calculated by chi-square analysis with significance set at $P < 0.05$.

Results: Over the course of 10 years, 247 patients (53% female) required an oral maxillofacial surgery consultation, with 65 (26%) sustaining dentoalveolar trauma. Within this group, there were significantly more subjects who were Black, single, insured with Medicaid, unemployed, and 18–39 years old. In the nontraumatic control group, there were significantly more subjects who were White, married, insured with Medicare, and 40–59 years old.

Conclusions: Among those seen in the emergency department requiring an oral maxillofacial surgery consultation, those with dentoalveolar trauma have an increased likelihood of being single, Black, insured with Medicaid, unemployed, and 18–39 years old. Further research is needed to determine causality and the most critical/influential socioeconomic status factor in sustaining dentoalveolar trauma. Identifying these factors can assist in developing future community-based prevention and educational programs.

INTRODUCTION

Dentoalveolar trauma (DAT) represents a serious public health problem, with approximately one-third of children and one-fifth of adolescents and adults sustaining a traumatic dental injury in their lifetime.[1,2] Complex risk factors and confounding variables, including one's socioeconomic status (SES), play a large role in these rates of trauma. There is debate surrounding the impact of SES on the rates of DAT in children; however, most studies demonstrate no correlation between DAT rates and SES.[3-6] Current dentoalveolar research has focused on the pediatric population rather than the adult population, thus creating a gap in knowledge surrounding the effects of socioeconomic factors on DAT in the adult population.[2]

While there is a gap in dentoalveolar research in adults, a few studies do address the effects of SES on other types of injuries in the adult population. For example, Zaleckiene et al demonstrated that males sustain traumatic dental injuries at least twice as often as females (ratio ranging from 1.5-2.5: 1.0, males: females).[7] Others have similarly demonstrated that risk factors for oral and maxillofacial trauma include the male sex and a younger age.[5,8-10] While these risk factors are well-known, there is a gap in knowledge regarding other socioeconomic factors in adult trauma, such as relationship status, employment status, and insurance type. One study indicates a higher rate of hospitalization following general trauma in adults of a lower SES versus those in a higher SES; yet there was no significant dif-

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ference between groups when comparing rates of maxillofacial and dental injuries.[11] This brings up another highly debated topic – the definition of low SES.

Low SES can be defined in a variety of ways: annual income, type of insurance, the highest level of educational achievement, and type of employment.[12] Based on average annual income, the most common racial or ethnic group living below the poverty line in Wisconsin (the location in which this study took place) is White, followed by Black and Hispanic, yet the race/ethnicity of the highest paid Wisconsin workers is also White.[12] The largest demographic living in poverty is females aged 18–24 years old, followed by males aged 18–24 years old, and females aged 25–34 years old, respectively.[12,13] Overall, 11.3% of those living in Wisconsin in 2019 were considered living in poverty.[12] For this study, insurance type is the primary determinant of SES; Medicaid insurance and no insurance coverage are indications of a lower SES.[14] As a baseline, in Wisconsin, 5.71% of the population is uninsured, and 13.4% have Medicaid coverage.[12]

While SES is a difficult topic to standardize across research, prior studies demonstrate an influence of SES on the incidence of adult trauma. Until now, however, there has been virtually no investigation that delineates the relationship between SES factors and DAT. Our study analyzed patient demographics and SES factors in adults who sustained DAT through a single-center retrospective review across 10 years to understand prospective disparities related to these injuries.

METHODS

The OTO Clinomics platform and processes for querying the electronic medical record in our health system were approved by the Medical College of Wisconsin/Froedtert Hospital Institutional Review Board (PRO00036649). The Clinical Research Data Warehouse, a component of the Clinical and Translational Science Institute of Southeast Wisconsin (UL1TR001436), maintains a monthly updated mirror of the entire electronic health record system in a Jupyter Hub (jupyter.org).

The Froedtert and the Medical College of Wisconsin health network predominantly serves southeastern Wisconsin and contains over 1.3 million individual patient records. Its academic medical center is the only Level 1 trauma center in the region.

Patient Demographics

Electronic medical records for all adult patients (≥ 18 years) requiring oral maxillofacial surgery (OMFS) consultation after being seen in the emergency department (ED) from January 2011 to December 2020 were selected for data extraction. Data extracted for each patient included diagnosis, age, race, ZIP code of primary residence, marital status, employment status, and insurance status at, or nearest to, the date of encounter.

Regional Demographic and Socioeconomic Data

US Census Bureau data (2010–2014) was accessed to determine the median age, race and/or ethnic distribution, median household income, educational level, and insurance status distribution for adults in each ZIP code from southeast Wisconsin. ZIP codes were stratified by median income into groups of <$42,000, $42,000–$53,100; $53,101–$59,300; $59,301–$67,500; $67,501–$77,800; $77,801–$87,000; and >$87,000. This stratification was used to be consistent with DATAUSA (datausa.io), a publicly accessible database compiling multiple government sources, including the Census Bureau, the Bureau of Labor Statistics, and the Bureau of Economic Analysis.

Statistical Analyses

Patients were divided into 2 groups. Group 1 was composed of patients sustaining DAT, which included International Classification of Diseases 10 (ICD 10) codes S02.5XXA, 5XXB, 5XXD, 5XXG, 5XXK, 5XXS, K08.411-414, K08.419, S03.2XXA, 2XXD, 2XXS, M26.34, M26.33. Group 2 was composed of patients requiring OMFS consultation due to any other etiology (eg, infections, abscesses, temporomandibular joint disorders, or follow-up from previous dental procedure); ICD 10 codes K00-K14 (K04.7, K08.89,K12.2) and M26.60. Group 2 was used as a control group.

Patient characteristics all were obtained through query of the electronic medical record by one researcher. Population-level data were computed from census records. Age between groups was compared using independent 2-group *t* test. Median values and interquartile ranges are reported and $P < 0.05$ represents statistically significant differences. Odds ratios were performed to compare the likelihood of a certain age, sex, race, marital status, employment status, and insurance type in Group 1 versus Group 2. All statistical tests were performed within the Jupyter notebook using R language (3.6.1).

RESULTS

Over the course of 10 years, 247 patients (53% female) required an OMFS consultation in the ED. Of the 65 patients (26%) who sustained DAT (Group 1), the average age was 42 years old, with the majority of patients ages 18–39 years (52%). Additionally, 57% were male, 68% were single, 63% were Black, 54% had Medicaid insurance coverage, and 40% were unemployed (Table, Figure 2).

By comparison, of the 182 (74%) control subjects who required OMFS consultation for a different reason (Group 2), the average age at consultation was 47 years old (18–90 years), with an even distribution across age ranges 18–90 years old. Further, 56% were female, 49% were single, and 55% were White. There were no significant differences in rates of insurance type (33% Medicaid, 37% Medicare, 26% private insurance). A majority (51%) were employed full time (Table, Figure 1).

Table. Comparison of Adult Patient Characteristics Among Those Who Sustained Dentoalveolar Trauma to Those Who Received Oral Surgery Consultation Due to a Different Etiology

	Group 1 DAT (n = 65)		Group 2 No DAT (n = 182)		Odds 1 vs 2	CI for OR	Chi-square Value	*P* value
Race (%)								
White	31%	20	55%	101	0.36	0.19 – 0.65	11.5	< 0.001[b]
Black	63%	41	40%	73	2.55	1.43 – 4.55	9.2	0.002[c]
Asian	0%	0	2%	3			0.2	0.689
American Indian	2%	1	1%	1	2.82	0.17 – 50.0	0.0	1.000
Other[a]	5%	3	2%	4	2.16	0.47 – 10.0	0.3	0.579
Sex								
Male	57%	37	44%	80	1.68	0.95 – 2.94	2.7	0.098
Female	43%	28	56%	102	0.59	0.34 – 1.05	2.7	0.098
Marital status								
Single	68%	44	49%	90	2.14	1.18 – 3.85	5.8	0.010[d]
Married	15%	10	31%	57	0.40	0.19 – 0.84	5.8	0.017[d]
Widowed	9%	6	8%	15	1.13	0.42 – 3.03	0.0	1.000
Divorced	8%	5	8%	14	1.00	0.35 – 2.86	0.0	1.000
Separated	0%	0	1%	2			0.0	0.960
Insurance								
Medicaid	54%	35	33%	60	2.37	1.33 – 4.17	7.8	0.005[c]
Medicare	20%	13	37%	67	0.43	0.22 – 0.85	5.7	0.017[d]
Private	18%	12	26%	47	0.65	0.3 – 1.32	1.1	0.297
Combo	3%	2	2%	4	1.41	0.25 – 7.69	0.0	1.000
None	5%	3	2%	4	2.16	0.47 – 10.0	0.3	0.579
Employment								
Full Time	37%	24	51%	92	0.57	0.32 – 1.01	3.2	0.0732
Part Time	8%	5	6%	11	1.30	0.43 – 3.85	0.03	0.858
Unemployed	40%	26	22%	41	2.31	1.27 – 4.17	6.3674	0.012[d]
Retired	15%	10	18%	33	0.83	0.38 – 1.79	0.0873	0.7676
Self Employed	0%	0	3%	5			0.8376	0.3601
Age group (%)								
<18	0%	0	1%	1			0.0	1.000
18-39	52%	34	36%	66	1.93	1.09 – 3.45	4.4	0.036[d]
40-59	23%	15	38%	70	0.47	0.25 – 0.90	4.9	0.027[d]
≥60	25%	16	25%	45	0.99	0.52 – 1.92	0.0	1.000
Mean	42.25		46.79					
SD	18.44		17.73					

[a]"Other" race encompassed American Indian or Alaska native and multiracial.
Statistically significant values included [b]$P < 0.001$, [c]$0.01 < P < 0.05$, and [d]$P < 0.05$.

Statistically significant differences between the two groups were found for almost all variables tested. There were significantly more subjects with DAT who were Black ($P = 0.002$), single ($P = 0.010$), insured with Medicaid ($P = 0.005$), unemployed ($P = 0.012$), and 18 – 39 years old ($P = 0.036$). Conversely, the nontrauma group had significantly more subjects who were White ($P < 0.001$), married ($P = 0.017$), insured with Medicare ($P = 0.017$), and 40 – 59 years old ($P = 0.027$). While there was no statistically significant difference in number of males between the two groups ($P > 0.597$), a majority of those who sustained DAT were male (57%) (Table).

Overall, there was an increased likelihood that those who sustained DAT were Black (OR 2.55; 95% CI, 1.42-4.55), single (OR 2.14; 95% CI, 1.18-3.85), insured with Medicaid (OR 2.37; 95% CI, 1.33-4.17), unemployed (OR 2.31; 95% CI, 1.27-4.17), and 18 – 39 years old (OR 1.93; 95% CI, 1.09-3.45) (Table).

DISCUSSION

There is a gap in knowledge regarding the influence of race and SES in adult DAT. This study uniquely addresses this gap by demonstrating significant correlations between adult DAT and race, age, insurance, employment status, and marital status. Further, while not statistically significant, our study demonstrates the majority of those who sustained DAT were male, consistent with other reports that males have a higher likelihood of sustaining trauma than females.[5,10,15]

When looking at age at the time of OMFS consultation, results demonstrated that those who sustained DAT were more likely to be younger adults (aged 18 – 39 years). Sbordone et al and Rose et al similarly found a higher percentage of those sustaining maxillofacial trauma to be males aged 19 – 39 years old.[16,17] A comparable trend also was found when looking at emergency hospital admissions due to violence, showing an increased prevalence in young males.[18]

While there is limited research surrounding the incidence of DAT and marital status, a few studies indicate unmarried or single individuals have an increased likelihood of sustaining violence-related or burn injuries, respectively.[19,20] The current study expands these findings to indicate that DAT is more prevalent in those who are single.

Moreover, prior reports suggest Black patients are more likely to sustain maxillofacial and general trauma than those who are White or other races.[15,17] Comparable results were found when researching penetrating trauma as well; penetrating trauma was more likely to occur in patients who identified as Black or Hispanic versus White patients.[21] This study specifically reveals that those seen in the ED for DAT were more likely to be Black. In contrast, there have been reports of facial trauma being more likely to occur in individuals who are White versus those who are Black. Hanba et al analyzed the National Electronic Injury Surveillance System to reveal that both White and Asian individuals (of either sex and across age groups) had significantly greater rates of facial fracture injury than Black individuals.[22]

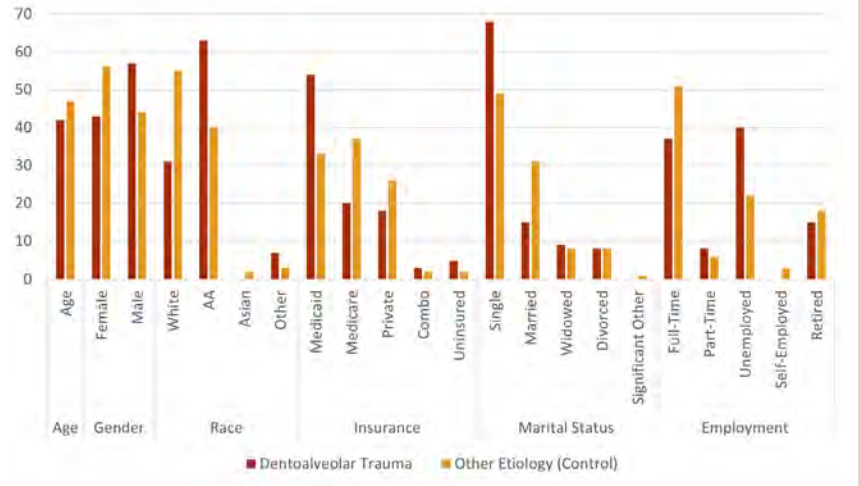
The last statistically significant SES factors correlating with DAT were employment status and insurance type. Individuals who sustained DAT were more likely to be both unemployed and insured by Medicaid. While this study looked at those who

sustained DAT due to a variety of etiologies (eg, assault, fall, motor vehicle accidents), a different study looking at assault by burn injury showed an increased likelihood that victims were female, Black, single, unemployed, and insured by Medicaid.20 Another study looking at recurrent trauma found an increased prevalence of trauma in males, those who are Black, and the uninsured.[20,21,23] Further, penetrating trauma victims were more likely to be either uninsured or receive state or county aid.[24]

While these comparable studies demonstrate significant differences in trauma rates across various socioeconomic factors, prior to this study, none have taken into account rates of DAT, in particular. Most studies on DAT focus on the etiology or type of injury but fail to evaluate risk factors.[9,25,26] Our study explores these socioeconomic risk factors, revealing a significant difference between individuals requiring an OMFS consultation for DAT or for another etiology. Specifically, results showed an increased likelihood of individuals sustaining DAT to be young (18-39 years old), single, unemployed, Black, and insured by Medicaid.

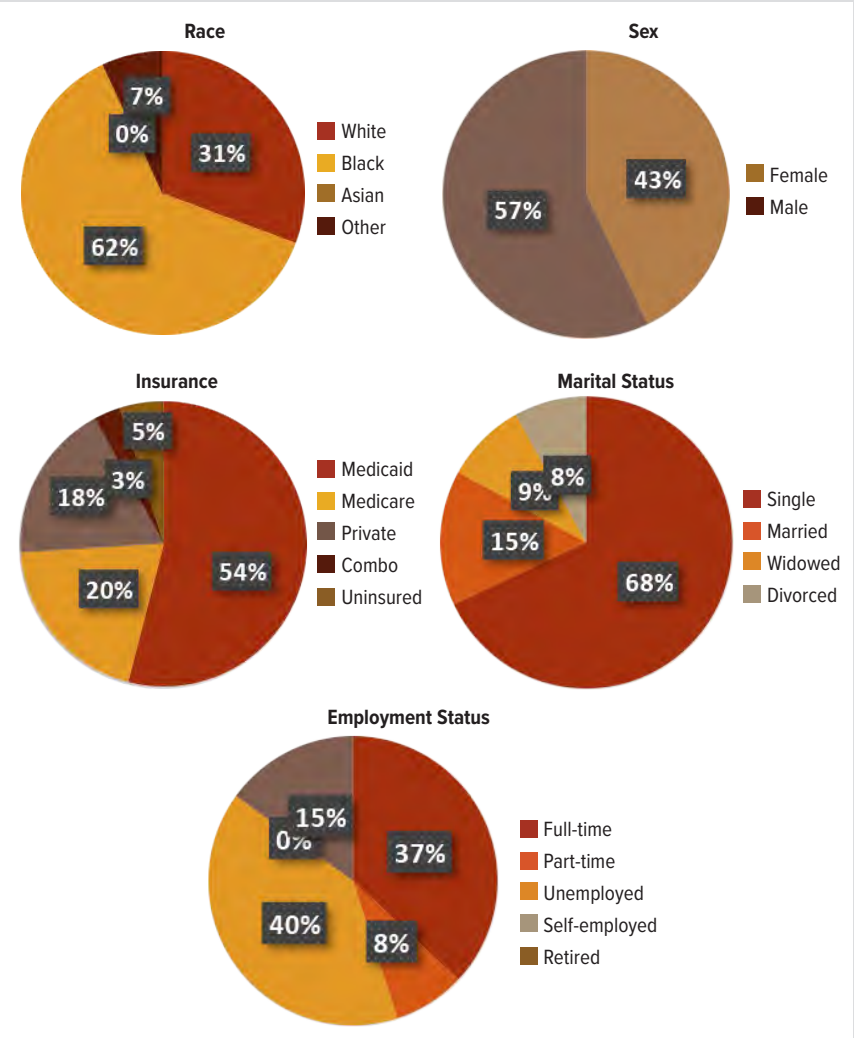
It is interesting to point out that there is an oral health access issue in Wisconsin.[27] The Wisconsin Oral Health Program noted that in a statewide basic screening survey of adults aged 21-74 in 2010 and 2011 (N = 1495), there were disparities for vulnerable populations, although the overall difficulties with dental services were low. They found that Black patients were significantly twice as likely to have untreated decay and were also significantly more likely to report having difficulty gaining access to dental services than White patients. Additionally, adults with an income less than $25,000 had significantly higher percentages of untreated decay, need for dental care, and self-reported oral health problems.[27] These findings would suggest Black patients are more likely to seek dental care at a nontraditional clinic, such as an ED. Yet, in our study, more Whites patients (N = 101)

Figure 1. Demographic Data Between Those Sustaining Dentoalveolar Trauma and Those Requiring Oral Maxillofacial Surgery Consult for a Different Etiology Based on Percentages



Note: "Other" race encompassed American Indian or Alaska native and multiracial. Statistically significant values included [b]$P < 0.001$, [c]$0.01 < P < 0.05$, and [d]$P < 0.05$.

Figure 2. Demographic Breakdown of Those Sustaining Dentoalveolar Trauma



than Black patients (N = 73) went to the ED for a dental issue that was not considered DAT.

A few limitations to our study include its bias as a single-center study; generalizations may not accurately translate to other populations in different areas of the country or world. Regional, cultural, and seasonal differences all affect the incidence of trauma. Furthermore, retrospective data collection is limiting when compared to a prospective, longitudinal data collection. By the same token, this dataset includes only patients actually seen for OMFS in the ED; thus, patients requiring outpatient follow-up only for DAT may skew results. Finally, while variables were analyzed between groups, each variable may have an influence on the other, and confounding variables do exist.

Yet, it is critical these issues are addressed to determine not only the best way to research effects of SES on trauma/injury but also to determine the best way to decrease the risk of injury in specific populations, whether that is through educational and social programs or another methodology. In this study, the likelihood of DAT was more common in Black individuals, which may be, in part, reasoned by racial/ethnic disparities. Non-White populations are more likely to live in socioeconomically disadvantaged areas than White populations, which is the case in Wisconsin.[28] Furthermore, while DAT trauma was more common in individuals who were unemployed and insured by Mediciad, Girasek et al noted that individuals of a lower SES are less likely to believe injury is preventable and, thus, less likely to practice effective injury-prevention measures.[28,29] This highlights that there is need for greater understanding of the reasons certain SES factors lead to a higher likelihood of trauma—whether that be due to environmental, social, behavioral, or perceptual differences—and how to best implement change to decrease trauma risk.

CONCLUSIONS

While there is a gap in knowledge of the effects of socioeconomic and racial inequalities on DAT in adults, this study reveals that those who sustain DAT are more likely to be young adults, Black, insured with Medicaid, single, and unemployed. By highlighting the various social determinants correlating to DAT, it is hoped that this research will aid in establishing social support and educational programs to decrease the disproportionate incidence of dentoalveolar trauma.

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Temporal Artery Biopsy: When Is It Worth the Headache?

Bronson T. Bomkamp, MD; Andrew J. Borgert, PhD; Alec J. Fitzsimmons, MPH; Travis J. Smith, MD; Irina Shakhnovich, MD; Jacob R. Peschman, MD

ABSTRACT

Introduction: Temporal artery biopsy is ordered when clinical symptoms and elevated C-reactive protein values and/or erythrocyte sedimentation rates suggest giant cell arteritis. The percentage of temporal artery biopsies positive for giant cell arteritis is low. The objectives of our study were to analyze the diagnostic yield of temporal artery biopsies at an independent academic medical center and to develop a risk stratification model for triaging patients for possible temporal artery biopsy.

Methods: We retrospectively reviewed the electronic health records of all patients who underwent temporal artery biopsy in our institution from January 2010 through February 2020. We compared clinical symptoms and inflammatory marker (C-reactive protein and erythrocyte sedimentation rate) values of patients whose specimens were positive for giant cell arteritis with those of patients with negative specimens. Statistical analysis included descriptive statistics, chi-square test, and multivariable logistic regression. A risk stratification tool, which included point assignments and measures of performance, was developed.

Results: Of 497 temporal artery biopsies for giant cell arteritis performed, 66 were positive and 431 were negative. Jaw/tongue claudication, elevated inflammatory marker values, and age were associated with a positive result. Using our risk stratification tool, 3.4% of low-risk patients, 14.5% of medium-risk patients, and 43.9% of high-risk patients were positive for giant cell arteritis.

Conclusions: Jaw/tongue claudication, age, and elevated inflammatory markers were associated with positive biopsy results. Our diagnostic yield was much lower when compared with a benchmark yield determined in a published systematic review. A risk stratification tool was developed based on age and the presence of independent risk factors.

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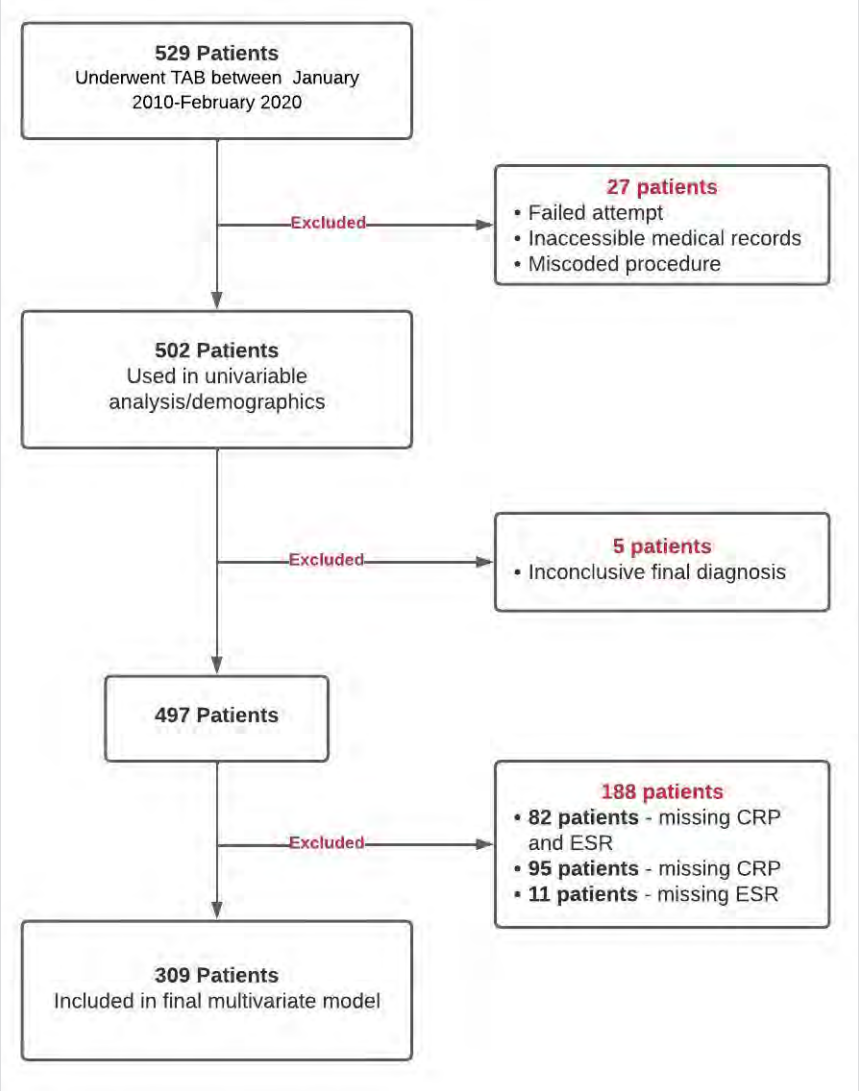
INTRODUCTION

Giant cell arteritis (GCA), also known as temporal arteritis, is an inflammatory vasculopathy that affects large- to medium-sized vessels, most often affecting patients of advanced age.[1] The pathophysiology involves the infiltration of giant cells into the vessel walls. These giant cells are created due to granulomatous changes of CD4+ T lymphocytes and macrophages.[2] A variety of symptoms have been reported in patients with temporal arteritis, including constitutional symptoms (fever, fatigue, and weight loss), headaches, jaw or tongue claudication, visual symptoms (transient vs permanent visual loss, diplopia, hallucinations), and musculoskeletal symptoms. If left untreated, GCA may progress to permanent blindness; therefore, early identification and treatment are paramount to evaluating patients with the potential of having the disease. Yet GCA diagnosis is challenging. Temporal artery biopsy (TAB) is the best confirmatory test, but the false-negative rate of biopsy is estimated to vary between 10% and 61%.[3]

GCA can manifest as extracranial disease, also known as large-vessel GCA. Studies have shown that large-vessel involvement is present in more than 80% of patients with GCA,[4] and patients with GCA are 17 times more likely than age/sex-matched patients without GCA to develop aneurysms of the thoracic aorta.[5] Evaluation for large-vessel GCA is different from that for temporal arteritis and was beyond the scope of this project, which focused on TAB for GCA.

The diagnosis of GCA has several considerations. In 1990, in an effort to standardize its diagnosis, the American College of Rheumatology (ACR) developed 5 criteria to distinguish GCA from other forms of vasculitis, criteria that have subsequently been used to assist with GCA diagnosis: over 50 years of age, new-onset headache, temporal artery tenderness or decreased temporal artery pulse, erythrocyte sedimentation rate (ESR) greater than 50 mm/hour, and arterial biopsy showing necrotizing arteritis characterized by the predominance of mononuclear cell infiltrates or a granulomatous process with multinucleated giant cells. When 3 of 5 criteria were met, their sensitivity and specificity were 93.5% and 91.2%, respectively.[6] ACR criteria do not require TAB to make the diagnosis. A Kaiser Permanente study published in 2013 developed a new protocol for temporal arteritis evaluation that included an enhanced clinical evaluation and the incorporation of color duplex ultrasonography and biopsy when appropriate. Using this protocol, their TAB yield increased from 8.5% to 24%.[7]

Figure 1. Patient Inclusion and Exclusion Flow Diagram



Abbreviations: TAB, temporal artery biopsy; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate.

The presence of "skip lesions" and inadequate specimen length may contribute to the false-negative rate of TAB. A recent 10-year retrospective review with over 1000 specimens published in 2020 suggested an optimal prefixation biopsy specimen length of 1.5 to 2 cm.[8] The studies included in a systematic review of 113 articles about GCA published in 2018 had a high degree of heterogeneity, rendering a meta-analysis unsuitable.[9] However, the median yield of TAB was 25% (95% CI, 0.21-0.27), which the authors concluded would provide a benchmark to determine whether TAB is under- or overutilized.

Most biopsies are performed in the clinic setting within 72 hours of receiving the biopsy request. Timing is crucial to improve diagnostic yield because significant histological findings can resolve after 2 weeks of steroid use.[10]

The primary objective of this study was to evaluate the yield of TAB at our institution and to compare it with the reported benchmark of 25% biopsies positive for GCA. Our secondary objective was to create a risk stratification tool with management recommendations in conjunction with our Department of Rheumatology. Our working group agreed that our tool would be designed to favor a negative predictive value, given the risk of untreated GCA. The intent of this tool and the associated management recommendations were focused on improving care for patients in 2 ways: (1) to identify those patients for whom biopsy results—whether positive or negative—would be unlikely to alter management, thereby obviating the need for the procedure and avoiding its associated risks and costs, and (2) to help limit the prescribing of unnecessary steroids, given their potential for long-term complications.

METHODS

Following Institutional Review Board approval, we reviewed the electronic health records (EHR) of patients who underwent TAB from January 2010 through February 2020 in our medical center. TABs were performed either in the clinic or the operating room by general or vascular surgeons working with general surgery residents. The operative technique employed is consistent within the

Table 1. Preoperative Patient Characteristics and Postoperative Diagnoses of Positive and Negative Temporal Artery Biopsy Cases

Demographic and Clinical Characteristics	Positive (n = 66)	Negative (n = 431)	*P* value
Demographic			
Age, mean (SD), y	74.6 (8.5)	71.8 (11.5)	0.1
Sex, no. (%)			0.6
Men	26 (39.4)	154 (35.7)	
Women	40 (60.6)	277 (64.3)	
BMI, mean (SD), kg/m^2	28.0 (6.1)	31.0 (8.2)	< 0.01
Laboratory values			
CRP (n = 320), mean (SD), mg/L	8.0 (7.7)	4.3 (6.0)	< .001
ESR (n = 404), mean (SD), mm/h	72.9 (29.7)	55.7 (33.8)	< 0.01
TAB setting, no. (%)			0.8
Clinic	63 (95.5)	402 (93.3)	
Operating room	3 (4.6)	29 (6.7)	
Surgical specimen length, mean (SD), mm	1.5 (0.7)	1.5 (0.7)	0.5
Symptoms, no. (%)			
Localized headache	51 (77.3)	330 (76.6)	0.9
Scalp tenderness	3 (4.5)	43 (10.0)	0.2
Jaw or tongue claudication	25 (37.9)	82 (19.0)	< 0.01
Visual abnormalities	30 (45.5)	178 (41.3)	0.5
Biopsies, no. (%)			0.1
Unilateral	55 (83.3)	391 (90.7)	
Bilateral	11 (16.7)	40 (9.3)	

Abbreviations: BMI, body mass index; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; TAB, temporal artery biopsy.
Note: All percentages may not total 100% due to rounding; symptom percentages will not equal 100% because some patients had more than 1 symptom.

practice and is based on the steps outlined in "Bedside Procedures for General Surgeons: Part 2."[11]

Commonly reported symptoms that have been identified as concerning for temporal arteritis in previous studies, including localized headache, scalp tenderness, jaw/tongue claudication, and visual abnormalities, were captured from the EHRs of study patients.[4,7] Symptoms that were not specifically documented in the clinician note were considered absent and coded as not present. Laboratory values obtained included ESR and C-reactive protein (CRP) performed within 2 weeks before or 3 days after the biopsy. Procedural information, including the anatomical location of the biopsy (laterality), the setting where the biopsy was performed (clinic vs operating room), and specimen length, also were included for analysis, as were complications within 30 days, including bleeding and surgical site infection.

Descriptive statistics were used to report biopsy positivity and complication rates. Clinical, demographic, and outcome data were compared using chi-square and Fisher exact tests for categorical data, trend tests for ordinal categorical data, and Wilcoxon rank-sum tests for continuous data. After converting age and laboratory values into ordinal categories, factors showing significant univariate associations with the final clinical diagnosis were included in a multivariate logistic regression model as potential covariates. An iterative cross-validation process was employed to construct the final multivariate model. Candidate models were created by adding potential covariates to a logistic regression model in descending order of the strength of association between the covariate and biopsy status via univariable analysis, starting with the covariate with the strongest association. In each iteration, an additional candidate variable was added to the logistic regression model, and a 4-fold, 25-repetition cross-validation procedure was executed whereby the dataset was split into 4 groups; a model was trained on 3 of the 4 groups and then evaluated against the single remaining group via receiver operating characteristic area under the curve (AUC) analysis. This was repeated 25 times for all 4 possible training group combinations (100 total steps), and the average AUC was calculated for this iteration. The covariates included in the iteration with the highest average AUC were selected as the final model.

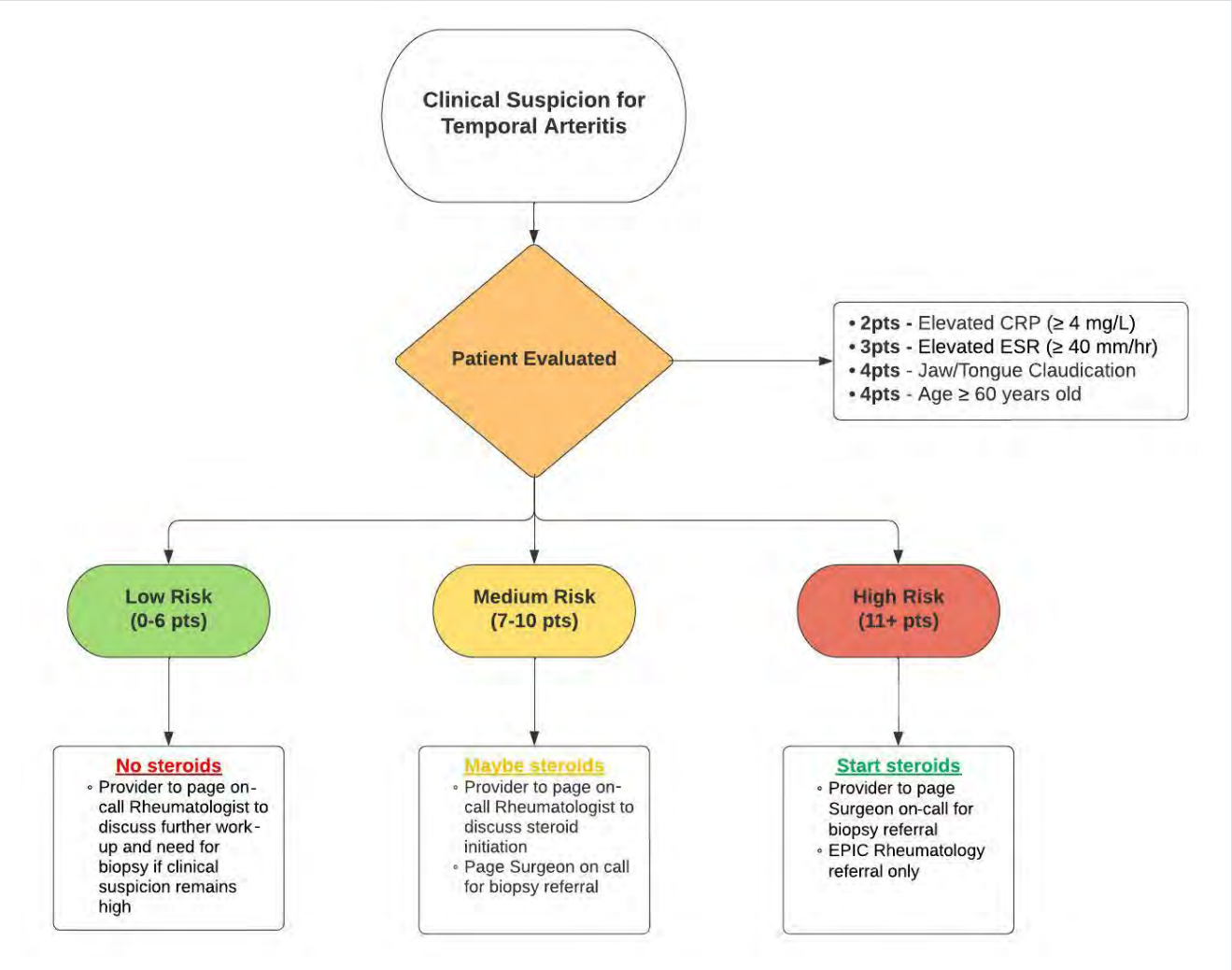
A points-based risk score was created from the final multivariate model by assigning points to a risk factor based on the resulting odds ratio for that factor, rounded to the nearest whole number. Point totals were then categorized as low-, medium-, or high-risk based on the proportion of positive clinical diagnoses associated with those point totals. Final model performance was assessed via receiver operating characteristic analysis and calculation of standard binary classification performance metrics using a simplified low- versus medium/high-risk classification system. All analyses were performed using the SAS 9.4 software suite (Cary, North Carolina).

RESULTS

During the study period, 529 patients underwent biopsy procedures. Twenty-seven were aborted before obtaining a specimen, 3 were inconclusive, 1 had reported evidence of prior arteritis, and 1 vein specimen. Of the 497 remaining biopsy specimens, 66 were positive for GCA and 431 were negative; 188 were excluded from the final multivariate analysis for lack of an ESR and/or CRP result (Figure 1).

Demographic and clinical data are provided in Table 1. Sixty-four percent of study patients were women. The study population's mean age was 72.2 ± 11.2 years. The majority of biopsies were performed in the clinic (465/497; 94.4 %), and the remaining 32 (6.6%) were performed in the operating room. Pathologic positive diagnosis was identified in 66 (13.2%) specimens. Jaw/tongue claudication was significantly associated with a TAB positive for GCA, as were elevated CRP (≥ 4 mg/L) and ESR (≥ 40 mm/hr.).

Figure 2. Current Assessment and Recommendation Workflow Utilizing Risk Stratification Tool



Abbreviations: CRP, C-reactive protein; ESR, ethryocyte sedimentation rate; pts, points.

Ninety-seven percent of biopsies positive for GCA were acquired from patients 60 years of age or older. Subgroup analysis by period (2010-2013, 2014-2016, and 2017-2020) to exclude potential biases of practice pattern change over time revealed no significant differences in positivity rate or exclusion rate from risk stratification development. Although lower body mass index was associated with a positive result, it was no longer significant after our multivariate analysis.

Using a cross-validation model selection procedure, a final multivariate logistic regression model was constructed that included the covariates age, jaw/tongue claudication, ESR, and CRP. From the cross-validation procedure, the average

Table 2. Risk Stratification Tool Development and Performance Assessment

Risk Factor Point Assignment			
Risk factor	**Odds Ratio**	***P* value**	**Points Assigned**
CRP ≥ 4 mg/L	1.98 (0.91-4.28)	0.0837	+2
ESR ≥ 40 mm/h	3.10 (1.14-8.46)	0.0272	+3
Jaw or tongue claudication	3.63 (1.78-7.38)	0.0004	+4
Age ≥ 60 years	3.94 (0.87-17.81)	0.0748	+4
Model Risk Status vs Biopsy Outcome			
	Negative, n	**Positive, n**	**Total, n**
Low risk (≤ 6 points)	112	4	116
Elevated risk (7+ points)	153	40	193
Total	265	44	309
Measures of Model Performance, %			
Negative predictive value	96.6		
Positive predictive value	20.7		
Sensitivity	90.9		
Specificity	42.3		
Accuracy	49.2		

Abbreviations: CRP, C-reactive protein; ESR, erythrocyte sedimentation rate.

AUC for this model was 0.75 ± 0.08. Using these elements, we created our risk stratification tool (Figure 2) using odds ratios, as described above, after excluding patients with incomplete data points. Two points were given for an elevated CRP concentration and 3 points for an elevated ESR. Four points were given for jaw/tongue claudication and 4 points for age 60 years or older. Patients were then divided into low-risk (0-6 points), medium-risk (7-10 points), and high-risk (11+ points) risk groups (Table 2). We placed our patient data into our algorithm to validate our points-based risk scoring system. Of the original 502 patients, 309 were evaluated using our new algorithm. The model's negative predictive value was 96.6%, and its positive predictive value was 20.7% when comparing low-risk patients with any medium- or high-risk patients. When further assigning the 309 patients to low-, medium-, and high-risk categories based upon the points assigned in our algorithm, we found TAB positive for GCA in 3.4% (4/116) of low-risk, 14.5% (22/152) of medium-risk, and 43.9% (18/41) of high-risk patients.

DISCUSSION

GCA is a severe disease potentially leading to permanent blindness. There are no universal protocols available, and diagnosis remains a challenge. Although ACR classification criteria do not require TAB, most rheumatology clinicians favor pathological confirmation of the disease. Our primary goal was to identify our institution's TAB yield, which we determined to be approximately 13%. This study identified specific clinical symptoms, laboratory values, and age values based on data from our EHR system that help categorize patients as at low-, medium-, or high-risk of having a TAB positive for GCA and created a point-based clinical tool to guide patient care (Figure 2). In addition to helping avoid low-yield biopsies, it also helps referring clinicians identify specific laboratory tests and clinical symptoms to include in their workup, with the ultimate score guiding decision-making on steroid use and need for rheumatology collaboration and biopsy referral.

Using the published systematic review with a median yield of 25% as benchmark, we have an opportunity to improve our diagnostic approach, as well as the potential to decrease unnecessary biopsies and their associated comorbidities, reduce the use of steroids, and decrease the cost. Although the overperformance of TABs could be attributable to many factors, one factor we have identified in our health system is the lack of a consistent diagnostic approach. Prior studies have reported that biopsy yield is improved when a referral is made utilizing a multidisciplinary approach.[5] We were unable to identify yield rates by referring clinicians. However, reports from our surgeons suggest that rheumatologists are more likely than those in other specialties to have completed a workup that includes considering all the potential risk factors we have identified in our study. This is evidenced by nearly 40% of the patients who underwent biopsy being excluded from the risk stratification tool due to the lack of a CRP or ESR drawn during the diagnostic workup.

In addition to directing the next steps for the at-risk patient, our algorithm will ensure that patients have the appropriate laboratory workup before undergoing a biopsy. It also elicits direct communication with Rheumatology, which is actively involved in the entire process of diagnosis and treatment. They review every pathology report and clinical context and, ultimately, determine if a patient will come off steroids or if biologic therapy is necessary. Every therapy is individualized, and TAB is an additional clinical tool for them. A high-quality negative biopsy that is not degraded by steroids is the gold standard for a rheumatologist. They can then taper off steroids with clinical confidence while knowing that the patient is unlikely to lose vision. Neither TABs nor steroids are entirely benign. Although TAB is a minor procedure and complications are very low, cost and morbidities, such as discomfort at the biopsy site and bleeding, are associated with the procedure.

We acknowledge that low risk does not equate to no risk, and that the 3.4% of patients so categorized could have serious consequences. Thus, they will be followed closely by the rheumatologist. If their clinical concern remains high, they will be referred for a biopsy and treated at clinician discretion. The on-call rheumatologist is contacted in all cases suggestive of GCA and is involved in the entire course of diagnosis and treatment.

Our future direction will be to institute our risk stratification tool and prospectively track patients to further refine this protocol. This will include the addition of other adjunct diagnostic tools currently not employed by our institution. The first is color duplex ultrasonography.[12] For example, low-risk patients with normal ultrasonographic findings will not need a confirmatory test with TAB to rule out GCA, while high-risk patients with abnormal ultrasonographic findings will have a GCA diagnosis and avoid TAB. Patients with medium risk will undergo TAB. Ultrasonography can provide further guidance when clinical suspicion and biopsy results do not correlate—for example, when skip lesions or disease phenotype spares cranial branches but can be seen in axillary arteries. In addition, eye examinations are not currently a routine referral at our institution for patients with symptoms suggestive of GCA and, therefore, could not be included in our analysis but may be helpful in future models. Finally, we will also need to better follow all patients with a TAB negative for GCA result to understand which may continue treatment with steroids due to high clinical suspicion and which go on to potentially have worsening symptoms and need a repeat biopsy or steroids due to presumed false-negative initial biopsy results.

This study is not without limitations. First, we started with 529 patients, 27 of whom were excluded due to failed biopsy attempts, incomplete or inaccessible medical records, or miscoded procedures. Five patients were excluded owing to inconclusive diagnoses, and 188 patients were excluded from the final multivariate

analysis and risk stratification tool owing to incomplete laboratory workup. Year of diagnosis and TAB exclusion rate were not significantly associated. Some studies have found that bilateral TAB has an increased yield compared with unilateral.[13] In our study, the difference in yield of bilateral biopsies versus unilateral biopsies was approaching significance. As mentioned previously, we did not capture the percentage of patients who continued to undergo treatment despite a negative biopsy result.

Several patients included in this study likely were not evaluated for all the investigated symptoms. Therefore, our consistent approach was to count the absence of a reported symptom as negative. However, if a patient had a particular symptom—jaw claudication, for example—but was not questioned by their clinician, that symptom would have been incorrectly categorized as not present. Additionally, we evaluated biopsies only as positive or negative. In working with our rheumatologists, we found that they typically treat GCA in settings where there is loss of the internal elastic lamina, sometimes referenced as healed arteritis. This may mean that other arterial segments could have active disease. Loss of the internal elastic lamina was not consistently reported in our pathology results. Therefore, biopsies considered negative for GCA in our study may have existed in patients who had or were still treated for presumed GCA. These other features, which were present but not documented in the formal report, were relayed during any pathologist and clinician follow-up discussions.

CONCLUSIONS

Jaw/tongue claudication, elevated inflammatory markers, and older age were associated with positive biopsy results. Therefore, we developed a risk stratification tool that might increase our positive TAB yield from 13% to 20% (nearer to the proposed 25% benchmark) by avoiding biopsies and the potential morbidity of steroid use in most low-risk patients. This change should reduce unnecessary procedures and reduce health care spending. After implementing this tool, we plan to prospectively evaluate our changes and their effect on patient care.

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One Hospital–Five Doors: A Model for Critical Access Hospital Sustainability

Henry J. Simpson, MD; Dean B. Eide; Richard A. Helmers, MD; Jason E. Craig; Bailey G. Salimes

ABSTRACT

Background: We wanted to assess whether a regional approach to bed management and staffing could improve financial sustainability without reducing services in rural communities.

Methods: Regional approaches to patient placement, hospital throughput, and staffing were coupled with enhanced services at 1 hub hospital and 4 critical access hospitals.

Results: We improved the use of patient beds in the 4 critical access hospitals, increased hub hospital capacity, and improved the health system's financial performance while maintaining or enhancing services at the critical access hospitals.

Discussion: Sustainability of critical access hospitals can be attained without a decrease in services for rural patients and communities. One way to achieve this result is to invest in and enhance care at the rural site.

INTRODUCTION

The rural United States population is about 60 million people,[1] making the sustainability of rural hospitals vital. However, from 2005 through 2019, at least 162 rural hospitals closed, and 700 more were at risk of closing.[1] In 2019, when 19 rural hospitals closed, at least 40% of all rural hospitals had negative operating margins.[2] By January 2022, nearly 900 rural hospitals (> 40% of all rural US hospitals) were at immediate or high risk of closure.[3] The primary reason for closure is an inability to remain profitable.[1]

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Historically, rural hospitals that affiliated with a larger health system decreased their risk of closure by 50%.[2] This affiliation may improve the financial performance of rural hospitals, but it also may decrease access to services for rural patients and contribute to worse health outcomes in rural communities, through either a reduction in service lines or a transition into an outpatient-only or skilled nursing facility.[4]

The disparities between rural and urban populations in access to health care, life expectancy, and mortality have been exacerbated by the decrease in rural hospital services and the loss of more than 100 rural hospitals since 2010.[4] Indeed, people living in rural communities have disproportionately adverse outcomes, including poorer health, greater disability, and higher age-adjusted mortality, and they face additional challenges accessing health care.[2] Hospital closure, which both is driven by and fuels the departure of rural clinicians, further erodes access.[5] In addition, the disparities in recruitment, training, and retention of hospital staff may require unique solutions for rural hospitals. For example, Smith et al[6] discuss how nurses in rural locations must put more effort into obtaining continuing education courses.

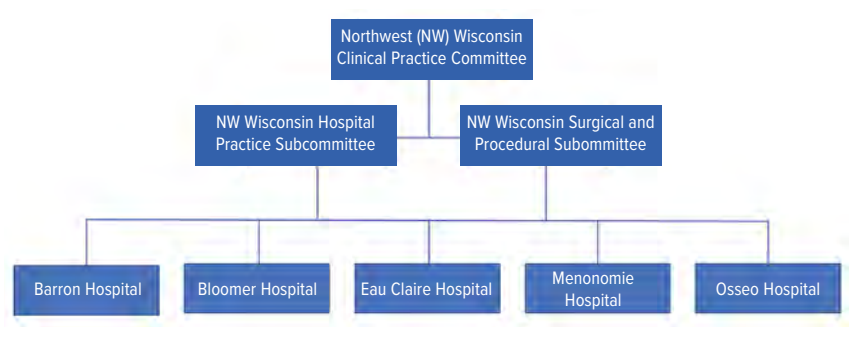
Our work sought to answer two questions: (1) what is the path to sustainability for rural hospitals that are already affiliated and still facing financial challenges; and (2) can sustainability be achieved without a major decrease in services at a critical access hospital (CAH).

METHODS

In 2019, our regional health system (Appendix) undertook an effort called "One Hospital–Five Doors" to improve use and

service at our hub hospital and 4 CAHs, with the intent to manage bed capacity at all 5 hospitals as if they were one. Our hub hospital has 185 staffed beds and an array of medical and surgical subspecialties, while our CAHs range in size from 16 to 25 staffed beds with a staff of primary care physicians and a limited number of local specialty services. Our regional health system includes one of the regions of a larger health system. Over the previous 5 years, the number of inpatients had increased at the hub hospital, while the inpatient census and the number of patients undergoing surgical and other procedures had decreased at the 4 CAHs, leading to variable financial performance.

Figure. Organizational Leadership for the 5 Hospitals in the Mayo Clinic Health System – Northwest Wisconsin Region



The regional Clinical Practice Committee provided direction and clarified the scope of the Hospital Practice and Surgical and Procedural subcommittees, giving them authority over all 5 hospitals (Figure) and their use of beds and surgical capacity. Each CAH also had a physician leader, a nurse leader, and an administrative leader who worked with CAH leaders and staff to assess and manage needed changes.

Improving the use of CAHs involved adopting the perspective that all 5 hospitals belonged to a coordinated system. The focus at the CAHs was to decrease the number of medical patients transferred to the hub hospital, increase the number of admissions from the hub hospital for swing beds (ie, beds for patients needing skilled nursing care), and decrease average length of stay in the hospital. Specific tactics to support the care of more patients at our CAHs included the following: (1) enhance the skill set of existing staff (including nurses) at the CAHs to retain and appropriately care for more medically complex patients who were clinically appropriate for the CAHs; (2) add staff with new skill sets to the CAHs by developing a regional staffing model that included hospitalists, hospital advanced practice providers, and ancillary staff (eg, respiratory therapists) to support complex patient care at CAHs (eg, with use of ventilators or left ventricular assist devices); (3) improve telemedicine support of local clinicians; and (4) enhance local physician specialty presence and outreach.

Efforts to improve use of the hub hospital focused on decreasing the average length of stay, enhancing appropriate patient placement within the hospital, decreasing patient wait times for transitions between different levels of care in the hospital, and decreasing the number of patients transferred to the hub hospital.

Regional hospital teams worked on new initiatives to improve use, including the creation of a Patient Flow Action Team and a CAH centralized referral center. The Patient Flow Action Team—a multidisciplinary team with representatives from all 5 hospitals—

Table. Annual Hospital Data for 2018 and 2019

Metric	Year 2018	2019	Difference
4 Critical Access Hospitals (CAH)			
Average daily census (medical and surgical patients)	171	187	9%
Average length of stay (medical and surgical patients)	155	132	–15%
Net operating income	NA	NA	1.6%
Net revenue	NA	NA	7.6%
Likelihood to recommend for 4 CAHs and 1 hub hospital			
Quarter 1, %	79.1	80.8	1.7
Quarter 2, %	81.1	80.2	–0.9
Quarter 3, %	78.4	81.2	2.8
Quarter 4, %	79.3	84.0	4.7

Abbreviations: NA, data not available for publication.

met daily to discuss barriers and opportunities for placing patients in the correct facility, including skilled nursing facilities, according to the patient's needs and level of care. After the Patient Flow Action Team was operational, a CAH centralized referral center was developed and launched to review referrals to all regional CAHs. This process replaced the need for each CAH to review each referral. Patient satisfaction, represented by likelihood to recommend, was intended to be a countermeasure as patients were placed in clinically appropriate locations, including CAHs with enhanced clinical capability.

We also worked to optimize use of surgical and procedural capabilities in the region to accommodate needed surgical growth in the hub hospital, enhance CAH service availability, and increase CAH financial sustainability. The initial focus was on ophthalmology and gastroenterology outpatient procedures. This work was planned before the COVID-19 pandemic and was successfully accelerated during the pandemic.

A cost report analysis also helped to identify opportunities to attain financial sustainability. CAH reimbursement permits allowable costs (ie, costs that are reasonable and related to patient care) to be reimbursed as part of the cost report. While ongoing cost report analysis is part of normal operations, an in-depth review helped highlight opportunities to improve CAH financial sustain-

ability. A practical example included the divestiture of on-campus skilled nursing facilities, which were successfully transferred to community partners.

RESULTS

When data were compared for 2018 and 2019, the average daily census at the CAHs increased by 9%, and the average length of stay decreased by 15%. The combined net revenue increased 7.6%, the net operating income for the 4 CAHs increased by 1.6%, and all CAHs had positive operating margins. Moreover, the hub hospital also had an increase in the average daily census, in surgical and procedural cases, and in net operating income. Responses in 3 of 4 quarters showed an improvement in likelihood to recommend (Table). Attempts to track these data in 2020 and 2021 were disrupted because of the COVID-19 pandemic.

DISCUSSION

Our experience suggests that (1) rural hospitals that continue to face financial challenges after affiliation can improve their financial performance by investing in and enhancing care at their site, and (2) sustainability can be achieved without a decrease in services at a CAH.

Further, when patients receive care close to home, patients and their communities benefit. Patients benefit when access to services is maintained, as health outcomes are improved.[4] Communities benefit when rural hospitals are financially stable, because community economic vitality is preserved. The estimated annual economic benefit for our 4 CAHs ranged from $36 million to $155 million.[7] Hospitals—often the primary employer in a rural community—provide direct and indirect economic benefits, and they attract other businesses, which create additional jobs.

In addition to patients and their communities benefiting, the health system benefited as resources at the 4 CAHs were used more effectively, which, in turn, provided more bed capacity at the hub hospital. The improved financial performance of the CAHs, without service reductions, provided sustainability. Opportunities may exist for other large prospective payment system hospitals and rural hospitals, including CAHs, to partner to decrease the risk of closure and to maintain patient services. As value-based reimbursement grows, the preservation of rural access and the associated improved outcomes will be an important cost-avoidance strategy. In addition, the ability to care for patients in a clinically appropriate, lower-cost setting may help systems use their resources more effectively.

Keys to success included clarifying the lines of authority and accountability and using regional governance structures more effectively in tandem with CAH site leaders and managers of the affected disciplines. Although other strategies, such as increasing swing bed use, decreasing the number of beds for long-term care, and increasing clinical volume are common financial improvement strategies at CAHs,[8] the importance of governance structures may be overlooked.

This work strengthened cultural and operational foundations and allowed us to successfully meet the pandemic challenges encountered in 2020 and 2021. Specifically, the coordination of patient placement and census management has helped us work with record numbers of inpatients at the hub hospital and an increase in the average daily census by as much as 30% at the CAHs.

Several cultural barriers and challenges encountered in this work needed to be addressed. Staff members were concerned about changes in clinical expectations and the increased acuity of patients as more medically complex patients were retained at or transferred to CAHs. This was addressed through upskilling of existing staff, bringing new staff resources on site, and expanding telemedicine support and specialty outreach. Staff members also were concerned about work schedules and the use of nursing and other support services across sites within the region. In response, nurse leaders developed a culture of "taking the care to the patient" to help address this. Further, even with a preexisting regional management structure, scope and governance clarifications were required, along with active engagement of affected disciplines by CAH site leaders. Some patients had concerns related to prior impressions that being sent to the hub hospital would mean that they would receive better care, even if their condition could be treated appropriately at a CAH, or that being transferred from the hub hospital to a CAH transitional care bed would mean that they would receive less advanced care. Continued conversations with patients about the appropriate placement helped preserve patient satisfaction.

Future Direction

As the work with "One Hospital–Five Doors" continues to be refined, a virtual home hospital option, called Advanced Care at Home, has been introduced. This virtual sixth door expands the ability to care for patients in the location most appropriate for their clinical need and has benefited from the groundwork already laid for regional governance, institutional culture, and clinical processes.

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The Effect of a Mock Medical Visit on Refugee Health Self-Efficacy and Medical Trainee Communication Apprehension

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ABSTRACT

Background: As refugees adjust to a new country, their health care can take a toll. Refugees may have difficulty navigating a new health care system and experience low health self-efficacy. Another potential contributor is inadequate medical trainee curriculum addressing refugee health.

Methods: We devised simulated clinic experiences called mock medical visits. Surveys were utilized before and after the mock medical visits to assess the Health Self-Efficacy Scale for refugees and the Personal Report of Intercultural Communication Apprehension for trainees.

Results: Health Self-Efficacy Scale scores increased from 13.67 to 15.47 ($P = 0.08$, n = 15). Personal Report of Intercultural Communication Apprehension scores decreased from 27.1 to 25.4 ($P = 0.40$, n = 10).

Discussion: While our study did not reach statistical significance, the overall trends suggest mock medical visits can be a valuable tool to increase health self-efficacy in refugee community members and decrease intercultural communication apprehension in medical trainees.

BACKGROUND

Refugees experience a decline in health status after settling in the United States.[1] There are manifold reasons for this decline, including limited knowledge about the country's health care system.[2] Refugees are eager to seek services, learn to navigate health care, and achieve self-sufficiency.[3]

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Meanwhile, self-efficacy, which has been defined as "what you believe you can do with what you have under a variety of circumstances,"[4] has been associated with lower psychological stress and higher subjective well-being.[5] Relatedly, medical providers' interactions with refugees may influence refugees' health self-efficacy. Medical trainees are expected to work cross-culturally and serve a diverse population,[6] yet many are not comfortable with their knowledge of immigrant and refugee health.[7] Medical education and local-global health experiences can enhance physician awareness of challenges refugees face, provide trainees with opportunities to interact with and serve this vulnerable population, and increase cultural humility.

One possible barrier for medical learners providing care for refugees is intercultural communication apprehension, defined as the fear or anxiety associated with interaction with people of different groups.[8] Currently, there are no studies to our knowledge that explore approaches to decrease intercultural communication apprehension in medical trainees or the feasibility of a mock medical visit to potentially achieve this aim.

Community Partner

The International Learning Program (ILP) in Milwaukee, Wisconsin provides secondary English, literacy, adult basic education, and citizenship classes to refugees in the area. ILP educators noted that the refugee learners may benefit from becoming more familiar with the US health care system and having more opportunities to positively interact with health care professionals. With this in mind, faculty and medical trainees at the Medical College of Wisconsin partnered with ILP to provide a health literacy cur-

riculum to refugee learners that consisted of didactic sessions on basic health topics and periodic mock medical visits (MMV). Through the series of educational sessions and MMVs, we sought to build partnership and trust with both refugees and clinic staff. This study explores the impact of a pilot simulated clinic experience—MMVs—on refugee learners and medical trainees. Specifically, our goals were to test the feasibility and possible effect of MMVs, with the hope that they can then be replicated to increase health self-efficacy in refugee community members and decrease intercultural communication apprehension in medical trainees.

METHODS

Two MMVs were held at the ILP in April 2019 and November 2019. On the day of the MMV, the refugee learners present at the community center were given the option to participate in the MMV after their classes. Prior to the visit, an introductory video in both Karen and Burmese languages was shown to refugee learners to demonstrate what a typical new patient adult visit at a physician's office might look like. During the MMV, 2 medical interpreters were present to help obtain informed consent, translate surveys, and serve as interpreters. The learners also had the option to participate in the MMV without participating in the survey and without the use of medical interpreters.

Trainees were volunteers from the Medical College of Wisconsin residency training in pediatrics and medicine-pediatrics programs, as well as 3 medical students. Of note, all trainees who participated were interested in global health and had prior exposure to health literacy work among refugees at this community center. Each trainee was assigned a role during the MMV (ie, receptionist, physician, nurse, or answering questions before and after the MMV), provided consent, and completed pre- and postsimulation surveys.

After consent was obtained and the presurvey completed, learners were instructed to check in at the reception desk to fill out mock paperwork mirroring typical adult intake forms, then wait for their name to be called by the trainee acting as a nurse. This trainee then escorted the learner and interpreter into an exam room and took vital signs. The trainee acting as a physician then entered the exam room and completed a medical, social, and family history, along with a physical exam. Afterwards, the learners were instructed to check back in at the front desk and complete the postsurvey.

Refugee Learner and Trainee Surveys

The refugee learner presurvey included 5 questions from the Health Self-Efficacy Scale (HSES), which consists of 5 items rated on an agreement Likert scale from 0 to 4, with higher scores representing higher health self-efficacy.[9] (See Appendix) The HSES was tested previously with cancer patients and showed adequate internal consistency ($\alpha > 0.75$). We chose the scale based on its health relevance and accessibility for participants who do not read English as a primary language, although it has not been used previously with refugees. Examples of HSES items include "I am confident I can have a positive effect on my health" and "I feel that I am in control of how and what I learn about my health." The postsurvey included a repeat of the HSES questions, 3 questions assessing the visit using a Likert scale, and 1 question regarding perceptions of future comfort at a clinic or hospital visit.

Table. Demographics of Refugee Learners and Medical Trainee Volunteers

Demographic	Refugee Learners (n = 15)	% of Total
Female	9	60.0
Male	6	40.0
Identified Karen as native language	14	93.3
Identified Rohingya as native language	1	6.7
Identified Burma as native country	15	100
Has been in the US for 2 to 4 years	8	53.3
Has been in the US for 5 to 6 years	5	33.3
Has been in US for > 6 years	2	1.3
Demographic	**Trainees (n = 10)**	**% of Total**
Female	8	80.0
Male	2	20.0
Medical student	3	30.0
First-year resident	1	10.0
Second-year resident	3	30.0
Third-year resident	3	30.0

The trainee presurvey included the Personal Report of Intercultural Communication Apprehension (PRICA), a 14-item Likert-type scale with each question ranked from 0 = strongly disagree to 4 = strongly agree, with sum scores ranging from 14 to 70.[8,10] (See Appendix.) The PRICA has high reliability ($\alpha > 0.9$) and content, construct, and predictive validity evidence among undergraduate learners.[8,10] Communication apprehension scores are interpreted as low (14-31), moderate (32-51), or high (52-70). Examples of PRICA items include, "Communicating with people from different cultures makes me uncomfortable," "I am afraid to speak up in conversations with a person from a different culture," and reverse-scored items such as, "I face the prospect of interacting with people from different cultures with confidence." The postsurvey included a repeat of the PRICA questions and an open-ended question to gather qualitative responses on how the trainees perceived the MMV added to their education.

A paired sample *t* test was used to compare presurvey and postsurvey HSES and PRICA scores.

This study was approved by the Medical College of Wisconsin Institutional Review Board.

RESULTS

A total of 15 refugee learners and 10 medical trainees participated in the two MMV sessions. The Table shows demographics of the study participants. Figure 1 shows the trend in HSES following

Figure 1. Effect of the Mock Medical Visit (MMV) on Refugee Health Self-Efficacy Scale

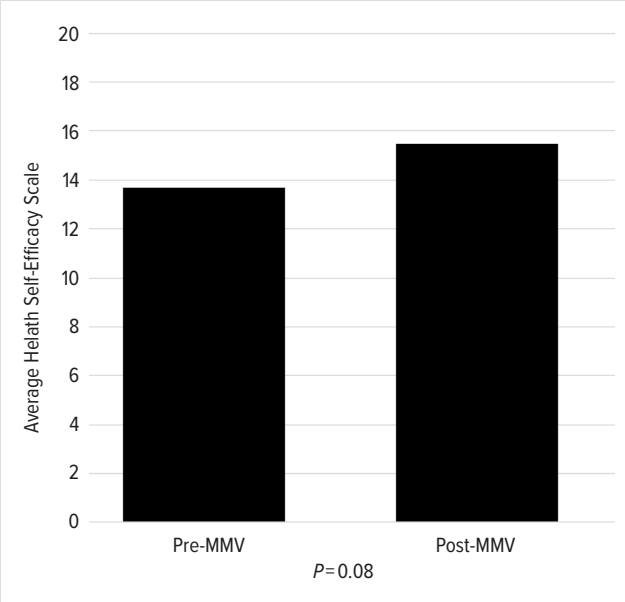
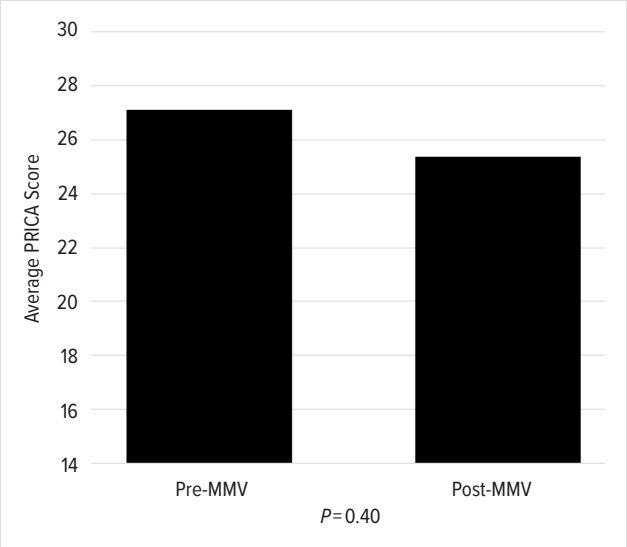


Figure 2. Effect of the Mock Medical Visit (MMV) on Trainee Communication Apprehension



Abbreviation: PRICA, Personal Report of Intercultural Communication Apprehension.

the MMV. Average HSES among refugee learners increased from 13.67 to 15.47 ($P=0.08$, n = 15). Cronbach's alpha across items on the HSES was 0.892 in this sample. Of the 15 participants who responded, 11 reported that after the MMV, they would feel comfortable when seeing a doctor in a clinic or hospital. Four participants reported that they would feel neutral.

Figure 2 shows the trend in PRICA following the MMV. Average PRICA scores among trainees decreased from 27.1 to 25.4 ($P=0.40$, n = 10). Internal consistency for the PRICA in this sample was $\alpha = 0.899$. Trainee responses regarding how the MMV added to their education included the following: "helped me realize how much language barriers can impact interactions with patients/individuals from different cultures," "increased cultural humility," "practice communicating through a translator," and "it allowed me to see what parts of the medical visit are confusing."

DISCUSSION

Figure 1 shows an overall positive trend in HSES following the MMV. Refugee learners also reported that they would feel either neutral or more comfortable when seeing a doctor after the MMV. Figure 2 provides data to suggest that the MMV may improve communication apprehension in medical trainees. In addition, the open-ended responses from trainees indicate they thought the MMV experience was valuable to their education. Though not statistically significant in this limited sample, a trend toward score improvement and overall positive experiences by both refugees and trainees suggest the MMW is a worthwhile educational tool to explore further.

Regarding limitations to this study, participation in basic health didactic sessions in addition to the MMV was not tracked as a potential confounder. Additionally, this study did not assess if the effect of participating in the MMV may differ based on the role the trainee is assigned (ie, receptionist, nurse, doctor). For future studies, tracking the role(s) trainees are assigned may help determine if this is a significant contributor to the trend in PRICA scores. Further, this pilot program cannot be generalized because participants who volunteered may be more interested or motivated than the general population; PRICA scores were low at baseline among these trainees, so future studies could test its impact as part of a randomized curriculum to limit convenience sampling bias.

Future steps also may include engaging and incorporating refugee feedback for more targeted MMV interventions, refining our measurement tools, expanding to other community partners, and engaging trainees beyond those with a specific interest in refugee health care.

This study introduces the MMV as a tool that may potentially improve self-efficacy and comfort with the US health care system in refugees; it also may decrease communication apprehension in medical trainees. To our knowledge, this is the first study describing the implementation of a MMV in a community setting with participation of both refugees and medical trainees. It is also novel in that it addresses a potential approach to improving communication apprehension in medical trainees and health self-efficacy among refugees. The MMV may be a valuable and intriguing tool to introduce in communities and medical curricula and could be used broadly with a variety of populations to develop self-efficacy.

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Pediatric Orbital Cellulitis/Abscess: Microbiology and Pattern of Antibiotic Prescribing

Alina G. Burek, MD; Geanina Tregoning, DO; Amy Pan, PhD; Melodee Liegl, MA; Gerald J. Harris, MD; Peter L. Havens, MD, MS

ABSTRACT

Background: The treatment for pediatric orbital cellulitis/abscess is trending towards intravenous antibiotic management alone in appropriate cases. Without cultures to guide therapy, knowing the local microbiology is of utmost importance in managing these patients.

Methods: We conducted a retrospective case series for patients age 2 months to 17 years, who were hospitalized between January 1, 2013, and December 31, 2019, to evaluate the local microbiology and pattern of antibiotic prescribing in pediatric orbital cellulitis.

Results and Discussion: Of 95 total patients, 69 (73%) received intravenous antibiotics only and 26 (27%) received intravenous antibiotics plus surgery. The most common organism cultured was *Streptococcus anginosus*, followed by *Staphylococcus aureus*, and group A streptococcus. Methicillin-resistant *Staphylococcus aureus* (MRSA) prevalence was 9%. MRSA-active antibiotics remain the most frequently used antibiotics.

BACKGROUND

Orbital cellulitis/abscess (OC) is a rare complication of acute rhinosinusitis that affects the periocular tissues posterior to the orbital septum. It can cause significant morbidities, such as vision loss, cavernous sinus thrombosis, and intracranial infection.[1] Although OC can happen at any age, it is more prevalent in the pediatric population.[2] Common clinical findings include orbital and periorbital edema and erythema, fever, pain with eye movement, diplopia, ophthalmoplegia, and proptosis. OC can be classified using groups 2 through 4 of the Chandler system, based on the extent and severity of infection: group 2 (orbital cellulitis), group 3 (subperiosteal abscess), and group 4 (intraorbital abscess).[3] Chandler group 1 (preseptal cellulitis) does not involve the orbital space and, therefore, generally does not cause intraorbital complications.

Children with OC require hospitalization for treatment and monitoring, with a multispecialty team of pediatricians, ophthalmologists, and otolaryngologists.[4] Intraorbital abscesses (Chandler group 4) represent less than 3% of total cases[5] and are typically treated surgically. With a less than 5% risk of intracranial complications for patients with orbital cellulitis (Chandler group 2) and subperiosteal abscess (Chandler group 3),[1] successful management with intravenous (IV) antimicrobials alone has been reported for many cases.[5,6] However, in the absence of surgical drainage and culture of the affected area, antibiotic selection cannot be targeted to specific pathogens, leading to variation in antibiotic selection within and between hospitals.[7] Data on the microbiology of orbital cellulitis in pediatrics are needed to guide selection of targeted antibiotics. In general, unnecessarily broad antibiotic exposure contributes to development of resistance, side effects, cost, and noncompliance after discharge. Since regional differences are reported for the bacterial causes of OC,[8] we aimed to report the local microbiology of OC to guide better empiric antimicrobial selection and decrease antibiotic overuse.[9]

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METHODS

Study Design and Participants

We conducted a retrospective case series of all pediatric patients, age 60 days to 17 years, admitted to a tertiary children's hospital with the diagnosis of OC between January 1, 2013, and December

31, 2019. The cohort was identified using the electronic medical record (EMR) system and the following diagnostic codes: ICD 9 - 376.01, 376.03 and ICD 10 - H05.011, H05.012, H05.013, H05.019, H05.021, H05.022, H05.023, H05.029, H05.121, H05.122, H05.123. Eligibility criteria included Chandler group 2, 3, or 4 OC confirmed by computed tomography obtained on admission. Exclusion criteria included patients with only preseptal cellulitis (Chandler group 1), those who were immunocompromised, and those with orbital infections secondary to trauma, orbital prostheses, or recent orbital/sinus surgery. The sample was divided in 2 groups for comparison based on therapeutic management: IV antibiotics alone (medical group) and IV antibiotics plus surgical intervention (surgical group).

Table 1. Patient Characteristics

	All Patients n = 95	Medical Group n = 69	Surgical Group n = 26	
	N (%) or Median IQR	N (%) Median IQR	N (%) Median IQR	*P* value
Age, years	8.1 (4.6-11.4)	7.0 (4.3-10.3)	10.7 (5.9-12.2)	0.009
Gender, male	64 (67)	45 (65)	19 (73)	0.62
Race[a]				0.72
White	53 (61)	40 (62)	13 (57)	
African American	33 (38)	23 (36)	10 (43)	
Native Hawaiian/Pacific Islander	1 (1)	1 (2)	—	
Ethnicity				0.34
Not Hispanic/Latino	74 (83)	54 (81)	20 (91)	
Hispanic/Latino	15 (17)	13 (19)	2 (9)	
Length of stay, days	3.8 (2.9-4.8)	3.6 (2.7-4.6)	4.7 (3.8-5.2)	≤ 0.001
Chandler group				≤ 0.001
Group 2 (orbital cellulitis)	33 (35)	33 (48)	0 (0)	
Group 3 (subperiosteal abscess)	62 (65)	36 (52)	26 (100)	
Signs of retinal or optic nerve compromise[b]	1 (1)	0 (0)	1 (4)	0.27
Frontal sinusitis or intracranial extension	24 (25)	14 (20)	10 (39)	0.11
Repeat CT scan or MRI	18 (19)	10 (15)	8 (31)	0.08
Worsening of disease on repeat image	4 (22)	0 (0)	4 (50)	0.023
Readmission within 7 days[c]	1 (1)	0 (0)	1 (4)	0.28
Readmission within 30 days	2 (2)	1 (2)	1 (4)	0.48
Recurrence (> 30 days)	3 (3)	2 (3)	1 (4)	> 0.99

Abbreviations: IQR, interquartile range; CT, computed tomography; MRI, magnetic resonance imaging.
[a]Excludes those who refused to answer or did not answer/declined.
[b]One patient with unknown data was excluded from this analysis.
[c]Three patients with unknown data were excluded from this analysis.

Outcome Measures and Other Variables

The primary aim of the study was to describe the microbiology of OC. Intraoperative cultures from the abscess and/or sinus were recorded, including the patterns of resistance to commonly used antibiotics (eg, clindamycin, methicillin). Nasal, conjunctival, or other surface cultures were not included. Blood culture results were recorded when available. Antibiotics started on admission, and antibiotics prescribed at time of discharge were recorded with associated length of therapy. Other variables collected include demographic data, clinical indicators of disease severity (signs of retinal or optic nerve compromise, frontal sinusitis, or intracranial extension), length of hospital stay, Chandler groups, and signs of possible treatment failure (repeat imaging, readmission).

Statistical Analysis

Data are reported as median and interquartile range (IQR) or n (%). We compared differences between the medical and the surgical groups using Fisher exact test for categorical variables and the Mann-Whitney-Wilcoxon test for continuous variables. A *P* value < 0.05 was considered significant. Statistical analyses were conducted by using SPSS version 26.0 (IBM Corp, Armonk, New York) and SAS version 9.4 (SAS Institute Inc, Cary, North Carolina).

RESULTS

Cohort Characteristics

We reviewed the medical records of 99 patients with OC and excluded 4 due to immunocompromised state (n = 1), trauma (n = 1), or wrong diagnosis (n = 2). Ninety-five patients with pediatric OC were included: 33 with orbital cellulitis (Chandler group 2) and 62 with subperiosteal abscess (Chandler group 3). No cases of intraorbital abscess (Chandler group 4) were identified. The median age (years) was 8.1 (IQR 4.6-11.4); 67% were male (n = 64). (Table 1) Twenty-six (42%) patients with subperiosteal abscess underwent orbital surgery, sinus surgery, or both. Most surgeries were completed within the first day following admission. Thirty-six (58%) patients with subperiosteal abscess were managed with IV antibiotics alone. All 33 patients with orbital cellulitis without subperiosteal abscess were managed medically. Of the total cohort of 95 patients, 69 (73%) did not have surgery. Median length of stay for all patients was 3.8 days (IQR 2.9-4.8), 4.7 days (IQR 3.8-5.2) for patients who underwent surgery, and 3.6 days (IQR 2.7-4.6) for those treated medically with IV antibiotics alone.

Microbiology of Orbital Cellulitis/Abscess

Of 95 total patients, orbital and/or sinus cultures were obtained for all 26 surgical group patients but none of the 69 medical group patients. The organisms identified from blood, orbit, and sinus cultures are listed in Table 2. Eighteen of 22 (82%) orbital cultures, 14 of 18 (78%) sinus cultures, and 2 of 39 (5%) blood cultures were positive. When the same organism grew in more than 1 cul-

Table 2. Microbiology of Orbital Cellulitis/Abscess at Local Institution Between January 2013 and December 2019

Organism	Orbital Culture (18/22 Positive Cultures)	Sinus Culture (14/18 Positive Cultures)	Blood Cultures (2/39 Positive Cultures)	No. of Patients With at Least 1 Positive Culture
Strep anginosus group	10	6	1	13
Group A streptococcus	3	1	-	4
Strep pneumoniae	1	1	-	2
Streptococcus viridans	0	2	-	2
MRSA	1	2	-	2
MSSA	1	1	1	2
Hemophilus influenzae	2	2	-	3
Peptostreptococcus	1	-	-	1
Rotha mucialginosa	1	-	-	1
Parvimonas micra	2	-	-	2
Fusibacterium necrophorum	1	-	-	1
Eikenella corrodens	1	1	-	2
Corynebacterium sp	-	1	-	1
Moraxella catarrhalis	-	1	-	1
Neisseria sp	-	1	-	1
Polymicrobial cultures (n, %)	4 (18)	3 (17)	0 (0)	6 (23)
Anaerobic cultures (n, %)	4 (18)	1 (6)	0 (0)	4 (15)

Abbreviations: MRSA, methicillin-resistant *Staphylococcus aureus;* MSSA, methicillin-susceptible *Staphylococcus aureus.*

Table 3. Antibiotics in the Medical and Surgical Groups

	Medical Group		Surgical Group		
	N	N (%) or Median (IQR)	N	N (%) or Median (IQR)	*P* value
Received antibiotics before presentation	69	35 (51)	26	11 (42)	0.50
Antibiotics started at time of admission[a]					
IV clindamycin	69	68 (99)	26	21 (81)	0.005
Ampicillin/sulbactam	69	64 (93)	26	20 (77)	0.065
Vancomycin	69	1 (1)	26	5 (19)	0.005
Ceftriaxone	69	5 (7)	26	3 (12)	0.68
Other	60	0 (0)	26	4 (15)	0.005
≥2 antibiotics at admission	69	68 (99)	26	26 (100)	>0.99
Antibiotic combination at admission	69		26		0.008
IV clindamycin + ampicillin/sulbactam		62 (90)		17 (65)	
Clindamycin + ceftriaxone		4 (6)		2 (8)	
Vancomycin + ampicillin/sulbactam		1 (1)		2 (8)	
Other		2 (3)		5 (19)	
Antibiotics at discharge[a]					
Amoxicillin/clavulanate	69	63 (91)	26	19 (73)	0.040
Oral clindamycin	69	53 (77)	26	11 (42)	0.003
Other	69	4 (6)	26	4 (15)	0.21
Antibiotic combination at discharge	69		26		≤0.001
Amoxicillin/clavulanate alone		12 (17)		11 (43)	
Amoxicillin/clavulanate + oral clindamycin		47 (68)		7 (27)	
Oral clindamycin alone		6 (9)		3 (11)	
Amoxicillin/clavulanate + other (no clindamycin)		4 (6)		1 (4)	
None		0 (0)		1 (4)	
Other		0 (0)		3 (11)	
Length of oral antibiotics at discharge, days	68	18 (14-21)	25	21 (14-21)	0.37
≥2 antibiotics at discharge	69	51 (74)	26	9 (35)	0.001
MRSA antibiotic at discharge	69	55 (80)	26	10 (39)	≤0.001

[a]May have more than one type of antibiotic prescribed (at time of admission or discharge)
Abbreviation: IV, intravenous; MRSA, methicillin-resistant *Staphylococcus aureus.*

ture from the same patient, the organism was counted as 1 (see column "Number of patients with at least 1 positive culture"). The most common organism cultured was *Streptococcus anginosus* group, a subset of the viridans group streptococci (n = 13), followed by *Staphylococcus aureus* (n = 544) and group A streptococcus (n = 4). Of the 4 *Staphylococcus aureus* organisms recovered, 2 were methicillin-resistant *Staphylococcus aureus* (MRSA) and clindamycin-susceptible, and 2 were methicillin-susceptible. The MRSA prevalence of patients with a pathogen recovered was 9% (2/23). Two of 39 blood cultures obtained were positive and, in both cases, organisms from blood cultures were concordant with the surgical cultures (*Streptococcus anginosus* group and methicillin-susceptible). Nine patients had simultaneous positive orbital and sinus cultures, and these cultures were concordant in only 5 cases (55%). (See Appendix: Supplemental Table.)

Antimicrobial Therapy

Ninety-four patients (99%) were started on dual antibacterial therapy on admission. The most common IV antibiotic combination used was clindamycin plus ampicillin/sulbactam. At the time of discharge, 74% of patients treated with IV antibiotics only (medical group) and 35% of patients treated with surgery plus IV antibiotics (surgical group) were transitioned to dual oral antibiotic therapy ($P = 0.001$). MRSA-active antibiotics were prescribed at discharge in 80% of patients in the medical group and 39% of patients in the surgical group ($P \leq 0.001$). The most common oral antibiotic combination used was clindamycin plus amoxicillin/clavulanate. Dual therapy was prescribed at discharge for a duration of 14 to 21 days (IQR) in both medically and surgically managed patients (Table 3).

DISCUSSION

Since almost 80% of patients with OC and over 50% with subperiosteal abscess are treated without surgery,[5] operative cultures to guide antimicrobial therapy are lacking

in the majority of patients. Therefore, antimicrobial choice for these "antibiotics only" patients demands extrapolation from the local microbiology and antimicrobial resistance patterns identified from surgical cases. In our study cohort, the most common organism isolated from orbital, sinus, and blood cultures of patients with OC who underwent surgery was *Streptococcus anginosus* group, followed by *Staphylococcus aureus* and group A streptococcus, consistent with other midwestern US reports,[6,8] while our low rate of MRSA differs from some other reports.[8]

Although the MRSA prevalence in surgical cases in our study was low (9% of positive cultures), 80% of the patients managed medically—without a culture to guide antibiotic selection—were discharged on MRSA-active antibiotics (clindamycin or trimethoprim-sulfamethoxazole). In our hospital, MRSA prevalence has been low for the past 2 decades: 11% of all positive cultures during the years 2002-2012[6] and 9% of all positive cultures during 2013-2019, the period of the current study. Of the 2 patients with MRSA OC identified in this study, 1 had a known recent exposure to a family member with MRSA cellulitis.

Lack of culture results from the patients managed medically make firm recommendations on antimicrobial management difficult. While nasal swabs showing the absence of MRSA colonization have a high negative predictive value for exclusion of MRSA as a cause of community-acquired pneumonia in adults,[10] this has not been studied in patients with OC. Given the lack of concordance we found between sinus and orbital culture results, further study would be needed before one could use the negative result of a MRSA nasal swab to confidently stop coverage for MRSA in a pediatric patient with OC. Until such data are available, antimicrobials to cover the predominant local pathogens—streptococci and anaerobes—might be supplemented by antibiotics directed toward MRSA, depending on local prevalence and patient history.[7]

CONCLUSIONS

Our single-center retrospective case series showed that the most common organism cultured in surgical patients with OC was *Streptococcus anginosus*, followed by *Staphylococcus aureus* and group A streptococcus. Prevalence of MRSA was low in our population, but therapy with MRSA-active antibiotics was still used in the majority of pediatric patients with OC.

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Lessons Learned From the COVID-19 Pandemic: Factors Affecting Decreased Incidence of Influenza

Hamza Mirza; Mansoor Mirza, MD

ABSTRACT

Introduction: Our goal was to identify if the cases of influenza declined in the state of Wisconsin during the COVID-19 pandemic and, if so, what factors may have been responsible for this decline.

Methods: Influenza rates during the 2018-2019 and 2020-2021 seasons were compared using data from Respiratory Virus Surveillance Reports from the Wisconsin Department of Health Services and the Centers for Disease Control and Prevention.

Results: The number of cases and hospitalizations due to influenza decreased significantly during the 2020-2021 influenza season compared to the 2018-2019 season, although mortality rates increased during 2020-2021.

Discussion: Reducing the burden of illnesses, hospitalizations, and deaths due to influenza on the health care system is imperative. Taking the same preventive measures used during the COVID-19 pandemic, such as wearing masks, physical distancing, and frequent handwashing, should be advised, especially for the most vulnerable patient populations.

INTRODUCTION

In late December 2019, mysterious cases of respiratory illness pneumonia were reported in China. Within a few weeks, the World Health Organization (WHO) had named this illness coronavirus disease (COVID-19).[1] COVID-19 is a highly contagious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Following the initial outbreak, COVID-19 continued to spread rapidly, resulting in a global pandemic that has since led to more than 271 million cases and over 5 million deaths worldwide.[2]

COVID-19 spreads through both direct and indirect contact. Direct contact may occur when one is close to an infected individual who coughs, sneezes, or even talks less than 6 feet from the uninfected individual. Indirect contact may occur when an individual touches a contaminated surface.[3] The most common symptoms associated with COVID-19 are fever, cough, weakness, taste disorder, and myalgia. Other symptoms include anosmia, dyspnea, headache, and the presence of sputum.[4-5]

Another acute viral infection—influenza—causes significant morbidity and mortality. It spreads quickly during the autumn and winter months, infecting both children and adults and resulting in millions of cases and thousands of deaths annually.[6] Although many elderly patients receive influenza vaccinations, they remain at a high risk of contracting and dying from influenza due to changes in the immune system as they age and other underlying medical conditions.[7]

There are 3 different types of influenza, the most common being influenza A and B,[8] and its transmission is very similar to that of COVID-19, including coughing, talking, and touching contaminated objects. Symptoms associated with influenza—fevers, cough, sore throat, runny nose, headaches, fatigue, and myalgia—are similar to COVID-19 symptoms as well.[9]

To identify if the incidence of influenza in Wisconsin declined during the pandemic, we evaluated the respiratory virus surveillance reports and data from the Wisconsin Department of Health Services (DHS) and the Centers for Disease Control and

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Table 1. Wisconsin Influenza Data, 2018-2019

Month	Week Ending Date	No. of Cases	Hospitalizations	Mortality Due to Pneumonia and Influenza
November	11/3/2018	39	5	57
November	11/10/2018	56	4	51
November	11/17/2018	29	7	41
November	11/24/2018	55	4	47
November Total		179	20	196
December	12/1/2018	45	2	55
December	12/8/2018	67	9	48
December	12/15/2018	87	13	59
December	12/22/2018	177	26	59
December	12/29/2018	231	51	64
December Total		607	101	285
January	1/5/2019	214	72	66
January	1/12/2019	-	-	71
January	1/19/2019	491	-	65
January	1/26/2019	784	72	65
January/February	2/2/2019	839	106	55
January Total		2328	250	322
3 Month Total		3114	371	803

Data for week ending Jan 12, 2019 was not reported from the Wisconsin Department of Health Services.

Table 2. Wisconsin Influenza Data, 2020-2021

Month	Week Ending Date	No. of Cases	Hospitalizations	Mortality Due to Pneumonia and Influenza
November	11/7/2020	3	0	478
November	11/14/2020	5	0	586
November	11/21/2020	5	0	608
November	11/28/2020	8	0	545
November Total:		21	0	2217
December	12/5/2020	0	0	544
December	12/12/2020	-	-	489
December	12/19/2020	4	4	428
December	12/26/2020	3	0	386
December Total		7	4	1847
January	1/2/2021	3	1	359
January	1/9/2021	0	0	317
January	1/16/2021	-	-	293
January	1/23/2021	3	1	272
January	1/30/2021	1	1	244
January Total		7	3	1485
3 Month Total		35	7	5549

Data for week ending Dec 12, 2020 and Jan 16, 2021 was not reported from the Wisconsin Department of Health Services.

Table 3. Wisconsin Influenza Data by Month, 2018-2019 vs 2020-2021

Month	Week Ending Date	No. of Cases	Hospitalizations	Mortality Due to Pneumonia and Influenza
November 2018	179	20	196	0
December 2018	607	101	285	0
January 2019	2328	250	322	0
November 2020	21	0	0	2217
December 2020	7	4	0	1847
January 2021	7	3	0	1485

Prevention (CDC). We hypothesized a reduction of influenza cases, hospitalizations, and mortality rates throughout the state and sought to determine contributing factors.

METHODS

To compare morbidity, hospitalization, and mortality rates for influenza in Wisconsin during the 2018-2019 and 2020-2021 seasons, we conducted a cross-sectional study using retrospective data from the Wisconsin Department of Health Services and the Centers for Disease Control and Prevention respiratory virus surveillance reports, as well as secondary data from various health care facilities.

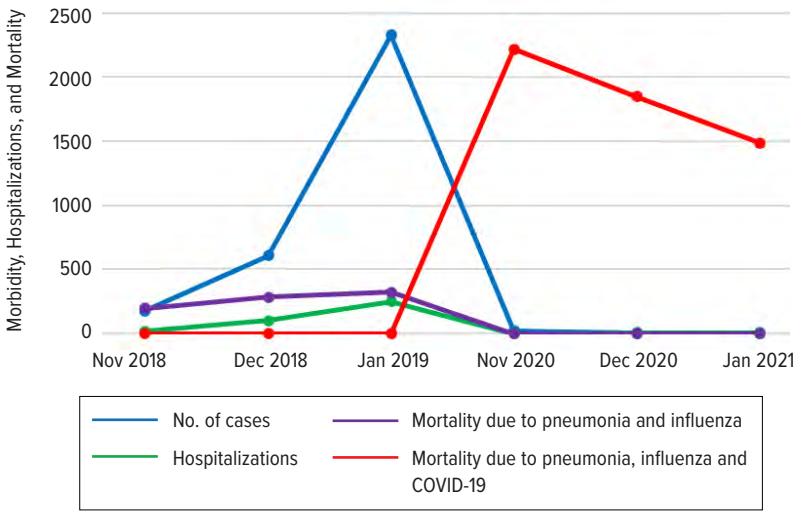
We combined and analyzed data for the months of November, December, and January 2018-2019 and 2020-2021. We focused on these months—the middle of influenza season—because many cases are reported each year during this timeframe, which includes holidays when lots of people spend time together, thereby increasing the chance of spreading influenza through direct contact.

To aid comparison, simple aggregation of data variables column-wise was utilized to determine the sum totals. The weekly cases of influenza were calculated by adding the positive cases of influenza A and B and parainfluenza and the positive results of influenza from rapid antigen tests. Data in the respiratory virus surveillance report included hospitalization rates from September to the current week. Hospitalization rates were determined by subtracting the number of hospitalizations in the current week from the previous week. Finally, we calculated mortality rates by selecting the week and year on the CDC's Pneumonia and Influenza Mortality Surveillance map.

RESULTS

Comparison data show that the number of influenza cases and hospitalizations decreased significantly during 2020-2021 compared to 2018-2019. During the 2018-2019 influenza season, there were a total of 3114 reported cases of influenza and 371 hospitalizations. In comparison, during the 2020-2021 season, there were 35 reported cases of influenza and 7 hospitalizations. However, the mortality rate during the 2020-2021 season was significantly higher than the 2018-2019 season due to the COVID-19 pandemic: 5549 deaths vs 803, respectively.[10-12] (See Tables 1-3 and Figure 1 for detailed comparisons.)

Figure. Influenza Season Data, 2018-2019 vs 2020-2021



DISCUSSION

Both influenza and COVID-19 are acute viral infections that bear similar symptoms and cause considerable illness and death. However, influenza is a seasonal epidemic that results in substantial preventable illness each year, while in 2020, the World Health Organization declared coronavirus a global pandemic that has resulted in over 271 million cases and 5 million deaths worldwide.[4,5]

To curb the spread of COVID-19, preventive measures such as mask mandates and physical distancing were implemented, and individuals were urged to stay home, get vaccinated, practice frequent handwashing, and clean high-touch surfaces. Several retrospective studies have shown that these measures were incidental to reducing the occurrence of COVID-19.[13,14]

Our findings show that during the 2018-2019 influenza season, there were a total of 3,114 cases of influenza and 371 hospitalizations. In contrast, during the 2020-2021 influenza season (during the pandemic), there were 35 cases of influenza reported and 7 hospitalizations. Mortality totals due to pneumonia and influenza rose from 803 pre-COVID to 5549, respectively, during the pandemic.

Adherent use of masks, physical distancing, staying home, handwashing, and frequent cleaning of high-touch surfaces during the peak of influenza season are factors that likely contributed to the reduction of influenza infections and subsequent hospitalizations. Table 3 shows the variation in cases between the two seasons. The same preventive measures used to curb the spread of COVID-19 in 2020-2021 appear to have contributed to the reduction in influenza cases and hospitalizations, thus inferring that more lives were saved, health care costs related to influenza were reduced, and the risk of spread was curbed. We suggest that these preventive measures should be embraced from November through February to reduce the impact of influenza. In the long run, it will spare health care dollars and reduce mortality rates.

Limitations

This study is limited in that it focused primarily on the state of Wisconsin, and generalizations were drawn regarding possible factors that contributed to the decline in influenza. The study may yield different results if a larger geographic region was covered. Further, the preventive measures mentioned proved to be effective only in the control of influenza and pneumonia, but their efficacy in controlling other airborne and viral infections was beyond the scope of this study.

Looking Ahead

More data on influenza cases, hospitalizations, and mortality should be collected and analyzed for the 9-month periods not included in this study. Additionally, further studies should focus on a larger geographic region (ie, other states) to affirm the accuracy of the generalizations made regarding the efficacy of the preventive measures mentioned for influenza control. Similarly, future studies could include more comprehensive data to improve the accuracy of findings. Larger sample sizes reduce incidences of inherent errors and mistakes associated with small samples.

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Financial Disclosures: None declared.

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Atypical Warfarin-Induced Calciphylaxis Outside a Typical Presentation of End-Stage Renal Disease on Hemodialysis

Thomas Licata, DO; Jacob Elliot; Ross Trecartin, MD; Adam Clements, DO

ABSTRACT

We present a case report highlighting a 47-year-old woman who developed warfarin-induced calciphylaxis. She initially developed bilateral leg wounds secondary to restraint straps from helicopter transportation to a higher level of care for treatment of critical aortic stenosis. She was started on warfarin following surgical implantation of a mechanical aortic valve. After her wounds failed to heal, a punch biopsy of the wounds demonstrated ulceration, altered vasculature, and soft tissue calcification. The pathology confirmed the clinical concern for calciphylaxis, which is most often diagnosed in patients with a history of end-stage renal disease on hemodialysis. However, our patient did not demonstrate evidence of renal disease prior to the onset of calciphylaxis. Her wounds began to heal after treatment with sodium thiosulfate and changing her anticoagulation from warfarin to rivaroxaban.

INTRODUCTION

Calciphylaxis is a rare ischemic skin lesion caused by calcium-mediated obstruction of dermal and subcutaneous microvasculature. Its pathogenesis is not well-known but is hypothesized to be due to an imbalance between mineral and bone transcription factors within vascular endothelial cells.[1] It is most commonly observed in patients with end-stage kidney disease, diabetes mellitus type 2, hypoalbuminemia, autoimmune disease, liver diseases, or malignancies. It also has been associated with medications, including warfarin, corticosteroids, calcium-based phosphate binders, or activated vitamin D.[2] While assessing dermatologic lesions during warfarin administration, histological analysis via punch biopsy is essential, as warfarin-induced skin necrosis can commonly present similarly to calciphylaxis. Warfarin-associated calciphylaxis is more common in female patients and usually occurs below the knee. The time between initiating warfarin therapy and the onset of calciphylaxis is, on average, 32 months. Furthermore, survival rates among patients with warfarin-associated calciphylaxis are distinctly improved from patients with comorbidities, specifically end-stage kidney disease.[3]

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CASE REPORT

A 47-year-old woman presenting with dyspnea, bilateral lower extremity edema, pulmonary vascular congestion, and a right-sided pleural effusion was admitted with suspected acute heart failure. A transthoracic echocardiogram demonstrated a mildly dilated right ventricle, a reduced ejection fraction of 20% to 25%, mild thickening of the mitral valve, and a normal tricuspid valve. Most concerning was a severely calcified and stenotic aortic valve with severely restricted movement. She was diagnosed with symptomatic critical aortic stenosis and was admitted to a critical access facility without cardiothoracic surgery capacity. Given the urgency of her clinical condition, she was airlifted to an appropriate facility. During air transport, she suffered bilateral pressure wounds from safety straps. She subsequently underwent a surgical aortic valve replacement with a metal valve. Warfarin was started after surgery as is the standard of care with mechanical heart valves.

Approximately 1 month after her aortic valve replacement and initiation of warfarin therapy, the patient presented to the emergency department concerned about nonhealing wounds on her legs. The pressure wounds from her helicopter transport had worsened since discharge. They were dark purple, increasingly tender, and growing larger in diameter. One spot appeared ulcerated with surrounding erythema, while other smaller locations appeared flat without ulceration. She did not endorse any sys temic symptoms.

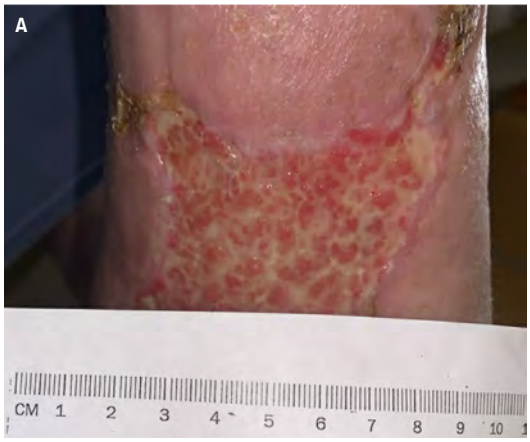
She was diagnosed with bilateral leg cellulitis and started on oral antibiotics.

Over the next month, more lower leg lesions developed, and her original wounds worsened, despite the antibiotics. A vascular workup found a normal ankle-brachial index and no evidence of vascular insufficiency. Further workup for endocrine pathologies, liver disease, and malignancy was negative. She was not using exogenous corticosteroids and did not demonstrate adrenal insufficiency.

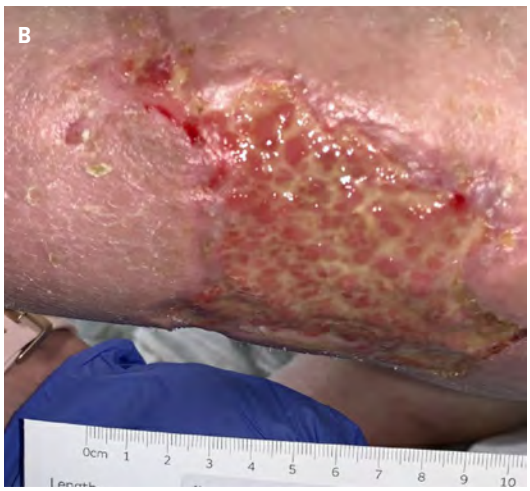
The wound clinic provider performed a punch biopsy of one of the patient's most tender areas of ulceration. The biopsy demonstrated altered vasculature and soft tissue calcification consistent with calciphylaxis. She was referred to dermatology for a second evaluation, and they agreed with the diagnosis of calciphylaxis. Given she had normal kidney function and had never required kidney replacement therapy, warfarin was the most likely cause, despite the low incidence of that complication. Dermatology recommended that she be started on sodium thiosulfate 25 grams intravenously 3 times a week.

The patient's cardiologist recommended discontinuation of warfarin and switching to rivaroxaban. Direct-acting oral anticoagulants (DOACs) typically are not recommended in the setting of mechanical heart valves; however, it was deemed appropriate given her diagnosis of calciphylaxis secondary to warfarin use. In her situation, off-label use of DOACs was necessary despite the mechanical valve. Without discontinuation of warfarin, the lesions were likely to progress. Wounds did appear to show clinical stability without progression once warfarin was discontinued. After starting treatment with sodium thiosulfate and discontinuation of warfarin, her wounds began to heal slowly. Healing only after discontinuing warfarin and starting treatment confirmed the diagnosis. The images included in this report were taken 2 months after she was started on treatment and changed to rivaroxaban (Figure). She continues to be seen by her wound clinic and the prognosis for complete healing is thought to be very good.

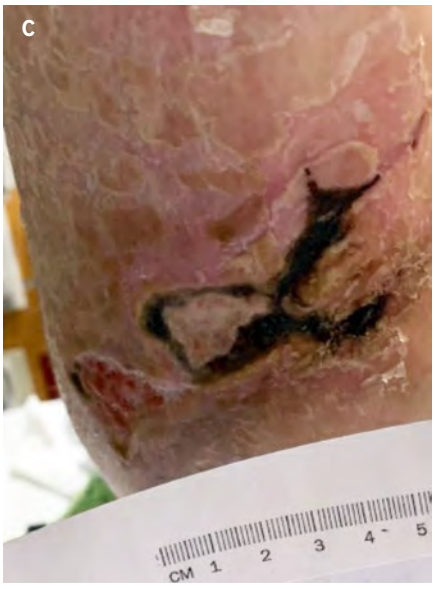
Figure. Clinical Images of Lesions at Presentation



A. Right Posterior Lower Extremity Wound



B. Left Lateral Lower Extremity Wound



C. Right Posterior Lower Extremity Wound

DISCUSSION

Diagnosis of Calciphylaxis

Our patient demonstrated nonhealing leg wounds bilaterally (Figure). She had punch biopsies from both legs that revealed ulcerations with alteration of vasculature, fat necrosis, and soft tissue calcification within medium and large vessels in a mockingbird-like fashion. Inflammatory changes were not noted to be consistent with infectious etiology. Other thrombotic vasculopathies associated with trauma could have a similar appearance, although a nearly symmetric demonstration in the bilateral lower extremities is highly unlikely.

Our patient demonstrated evidence of calciphylaxis within 3 months of starting warfarin therapy, which is remarkably different from the typical 32-month onset. It is also worth highlighting that calciphylaxis in our patient developed on the site of preexisting

wounds rather than spontaneous calciphylaxis. Traditional non-warfarin-induced calciphylaxis is typically irreversible and carries a poor prognosis. It is important to note that warfarin-induced calciphylaxis can be treated effectively with the discontinuation of warfarin and the initiation of sodium thiosulfate.

Use of Warfarin

Warfarin is the anticoagulant of choice in the setting of mechanical heart valves, and for many people, it is well tolerated. Patient adherence and monitoring can be difficult as they require frequent lab monitoring and dietary changes. Warfarin is metabolized by the cytochrome P450 system; medications and foods that interact with the P450 system can interfere with warfarin anticoagulation. For this reason, there is a growing trend to begin using DOACs, such as rivaroxaban and apixaban when possible.

In our patient's case, the initial gold standard of care was administered with the use of warfarin in the setting of mechanical heart valves. Also, given her medical presentation, other diagnoses outside of warfarin-induced calciphylaxis were considered, and warfarin-induced skin necrosis, vasculitis, and infection were excluded as likely causes. This case does raise the question of using DOACs in the setting of a mechanical heart valve. Currently, their use is considered off-label with mechanical valves.[4] Further investigation and research could be appropriate to compare long-term outcomes using DOACs in patients unable to tolerate warfarin therapy. Given the lack of clinical evidence and no Food and Drug Administration approval, it should not be considered standard of care to start a patient first-line on DOACs over warfarin therapy in the setting of mechanical heart valves.

CONCLUSIONS

Calciphylaxis is a rare condition in patients with end-stage kidney disease on hemodialysis and even rarer as a complication of warfarin use. The case described here had several unique aspects that add to the medical literature. The patient's skin lesions appeared to start at the site of existing trauma—a phenomenon not described in the literature to our knowledge. The biopsy showing calciphylaxis was obtained after only 2 months of initiating warfarin therapy, which is sooner than the typical 32-month onset. She appeared effectively anticoagulated on a DOAC in the setting of a metal heart valve, which is not well-described in the literature. This case report suggests that clinicians should always consider calciphylaxis as a complication in people taking warfarin. Further studies are needed to evaluate the efficacy of DOACs for mechanical heart valves.

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Scurvy Presenting as Blood Loss Anemia in the United States

Samantha Rivera, MD; Adam Clements, DO; Joshua Hess, MD; Nicolai Gerhartz, PA-C; Aleksander Downs, MD; Linnea Kruit, MD

ABSTRACT

Introduction: Scurvy is a deadly disease caused by a lack of vitamin C in the diet. Although frequently considered a disease from the past, it still occurs in modern-day society, including in developed countries.

Case Presentation: We report a case of an 18-year-old male who was admitted with bleeding into his legs, prolonged prothrombin time and partial thromboplastin time, and anemia requiring a blood transfusion. His history included congenital deafness and a restrictive eating pattern primarily consisting of fast food. He was deficient in folic acid, vitamin K, and vitamin C. Scurvy best explained the bleeding, and he improved with vitamin supplementation.

Discussion: Scurvy is a collagen production disorder that can cause bleeding on the skin and mucous membranes. Although rare in industrialized nations, scurvy is typically the result of a restrictive diet or malnutrition. Those who are at a particularly high risk are the elderly, alcohol abusers, and those with eating disorders.

Conclusions: Scurvy is easily treatable but can be missed; therefore, a high level of suspicion should be present in patients at risk for malnutrition. Those diagnosed with scurvy should be screened for concomitant nutritional deficiencies.

INTRODUCTION

Scurvy is caused by a lack of vitamin C (ascorbic acid) in the diet. The earliest known mention of scurvy occurs in the Ebers Papyrus, a 20-meter-long collection of magico-medical prescriptions that dates to 1550 BC.[1] Scurvy has caused the death and suffering of European sailors, Irish potato farmers, American Civil War soldiers, and Arctic adventurers.[2] Despite significant morbidity and mortality from scurvy, there was little written about it until James Lind's Treatise of the Scurvy was published in 1753. Lind, a British Naval surgeon, conducted trials for a potential scurvy treatment. During those trials, seamen who received supplementary oranges and lemons quickly recovered. However, this seemingly monumental discovery was not implemented for another 42 years because Lind himself believed scurvy was a disease of faulty digestion and excretion and not a direct consequence of dietary insufficiency.[3]

In 1928, a Hungarian biochemist Albert Szent-Gyorgyi isolated an organic acid from adrenal glands, which he called "hexuronic acid." The structure of this acid was identified and chemically synthesized by 1933 and was renamed L-ascorbic acid for its antiscorbutic (ie, against scurvy) properties.[4,5]

Vitamin fortification and the widespread availability of fresh produce in developed countries have made scurvy primarily a disease of the past. However, rare cases still occur in people with severe malnutrition or restrictive eating habits. Such patients often suffer from substance use disorders or psychiatric diseases. Although the incidence of true scurvy is low, it is estimated that up to 7.1% of the US population has some degree of vitamin C deficiency.[6]

CASE PRESENTATION

An 18-year-old White male, whose only known past medical history was congenital deafness, presented with bilateral lower leg swelling and pain. He communicated through writing and was accompanied by his mother, who provided supplemental infor-

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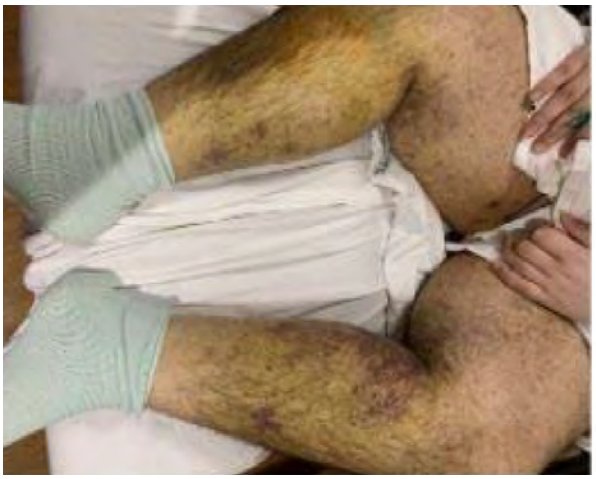
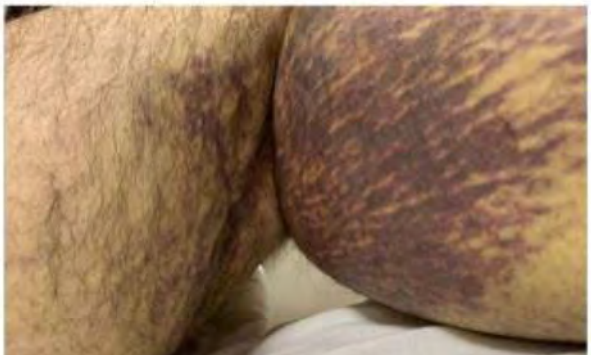
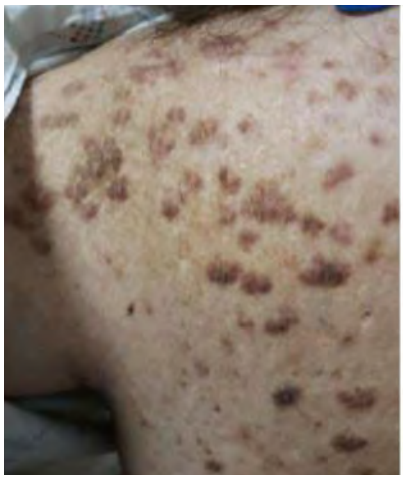
Figure 1. Physical Exam Findings







mation to his history. He had a two-and-a-half-week history of increasing lower leg swelling with pain that gradually worsened to the point that he was unable to walk the day before admission. There was also diffuse ecchymosis to his bilateral lower extremities (Figure 1), specifically near the popliteal fossa and over the gastrocnemius, that was worsening before admission. He also had shortness of breath increasing over the 2 weeks prior to admission. He was not short of breath at rest. He denied any recent trauma to his legs and had no personal or family history of bleeding or clotting disorders. He had no abdominal pain, chest pain, or palpitations and no recent illnesses, ill contacts, or fevers. There was no recent weight gain or loss, no nausea, vomiting, changes in urinary or bowel habits, and no headaches or changes in vision.

The cause of the patient's deafness is unknown, according to his mother. He takes no daily medications, vitamins, or supplements and reported no illicit drug, alcohol, or tobacco use.

She said he was a "picky eater" and "had difficulty with textures." For years, his diet had been limited to plain hamburgers, hotdogs, grilled cheese, and chicken tenders. He also led a sedentary lifestyle and spent most of his days sitting in his room playing video games.

Physical Exam

Exam showed an unkempt, morbidly obese deaf male who was alert and oriented and communicated with writing. He did not have any bruising or bleeding in his mouth, but his gums appeared mildly swollen. Skin exam was significant for follicular hyperkeratosis and perifollicular hemorrhage with petechiae and coiled hairs. He also had extensive bruising noted in his bilateral lower extremities. Heart, lung, and abdominal exams were unremarkable.

Labs

The patient's lab workup demonstrated microcytic anemia with a hemoglobin of 7.1. He was also notably low on folic acid. The coagulation panel revealed an international normalized ratio (INR) of 1.2, partial thromboplastin time (PTT) elevated at 42 seconds (reference 23-36 sec), normal fibrinogen, and normal inflammatory markers. Reticulocyte count was appropriately elevated at 5.5% (0.5%-1.5%). Hemolytic anemia was ruled out with negative direct Coombs, normal lactate dehydrogenase, and elevated haptoglobin 300 mg/dL (30-200). The peripheral blood smear was consistent with a reactive process given neutrophilia, hypochromic-normocytic anemia, and thrombocytosis.

After obtaining the additional history from his mother regarding his restrictive diet, we were concerned about 1 or more nutritional deficiencies. Copper, lead, and zinc were within normal limits. Vitamin K levels were falsely elevated due to supplemental administration before obtaining a sample for testing. His vitamin D level was decreased at 23 (reference 30-80). Ascorbic acid levels resulted on day 4 of hospitalization at <5 umol/L (reference 23-114 umol/L).

Hospital Course

Our patient had bilateral calf pain and was unable to walk. He was admitted to the hospital for acute blood loss anemia. The source of the bleeding appeared to be his bilateral calves, with 1.5 cm hematomas superficial and deep to the gastrocnemius on computed tomography (CT) bilaterally. He was tachycardic, and his blood pressure was normal. He presented with microcytic hypochromic anemia with reactive thrombocytosis. He required a total of 3 units of packed red blood cells during the hospitalization.

Due to his spontaneous bleeding, coagulopathy secondary to factor deficiencies or factor inhibitors were high on the differential. He had normal iron studies. His prothrombin time (PT) and PTT were mildly elevated with thrombin time at the upper limit of normal. This is unexpected in a patient with coagulopathy due to factor deficiency or factor inhibitor. Hematology was consulted, and an extensive workup was started. The patient's mixing studies corrected, again indicating a possible factor deficiency, but his factor activity levels were normal and there was no indication for a factor inhibitor either.

On admission, his history of poor diet combined with his severe anemia prompted a nutritional workup, including vitamins C, D, and B12 and folate levels. His vitamin C, vitamin D, and folate levels were low. Based on his elevated PT, PTT, high/normal thrombin time, low folate, and undetectable levels of vitamin C, we diagnosed him with scurvy. We also suspected vitamin K deficiency leading to an acquired clotting factor deficiency was contributing to his bleeding. Unfortunately, the vitamin K level was drawn after he was supplemented with intravenous (IV) vitamin K. His physical exam was consistent with vitamin C deficiency (scurvy). He had follicular hyperkeratosis, perifollicular hemorrhage with petechiae, and coiled hairs, in addition to his bilateral lower extremity extensive bruising. His gums seemed mildly swollen, but there was no hemorrhage noted. He was supplemented with IV vitamin K for 3 days and oral vitamin C, in addition to a multivitamin. He was educated on the cause of his bleeding and referred to an outpatient dietitian.

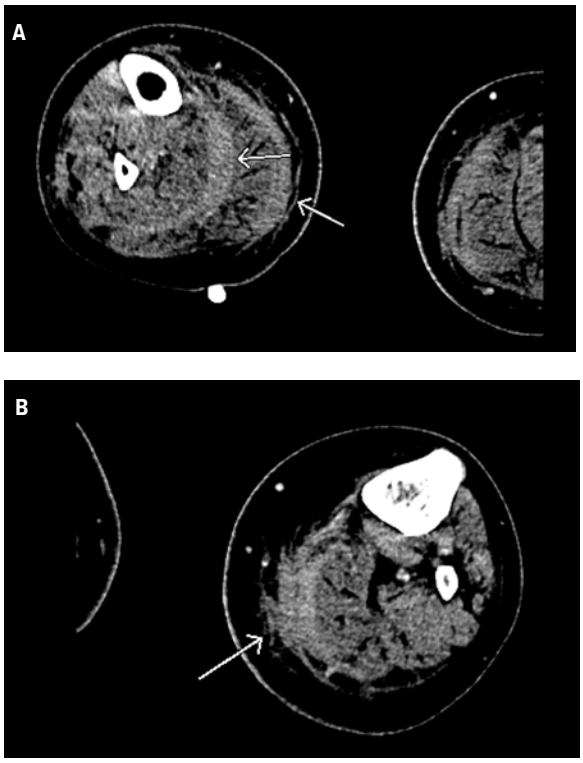
Follow-Up

Approximately 1 month after the patient's hospitalization and adhering to oral vitamin supplementation, his anemia completely resolved, with a hemoglobin at 14.4 g/dL. Chart review showed his bilateral lower leg bruising had resolved after about 4 to 6 weeks. He continues to have a poor diet and has elected to take the necessary supplementation orally.

DISCUSSION

Scurvy is a disease that is more common in history textbooks than in the modern medical literature in developed countries. The illness was prevalent in the 1700s and was a frequent ailment to explorers and sailors who were at sea for long periods without access to adequate nutrition. Humans lack gluconolactone oxidase, an enzyme necessary for the synthesis of ascorbic acid, making dietary intake the only source of this essential nutrient.[7] Vitamin C is generally considered an antioxidant and a reducing agent that is required for many cellular processes, particularly for the hydroxylation of proline. This is necessary for the cross-linking and stabilization of collagen, which provides the structural integrity of many tissues in the body. This protein composes about 30% of cellular protein mass and is frail in the absence of ascorbic acid due to lack of stabilization.

Figure 2. Computed Tomography Scan Images



A. Hematoma of the right lower leg with components that are both deep and superficial to the gastrocnemius muscle.

B. Hematoma of the left lower leg superficial to the left gastrocnemius muscle measuring up to 1.5 cm in thickness with adjacent fat stranding.

Table. Initial Lab Results

Lab Name	Value	Reference Value
Hemoglobin	7.1 g/dL	13.4 - 17.6 g/dL
Mean corpuscular volume	81.7 fL	82 - 96 fL
Platelet count	569 K/uL	140 - 390 K/uL
D-dimer	2.72 ug/mL FEU	0.0 - 0.50 ug/mL FEU
Prothrombin time	14.7 sec	2.0 - 14.6 sec
Partial thromboplastin time	42 sec	23 - 36 sec
Reticulocyte	5.5 %	0.5 - 1.5 %
Folate	2.6 ng/mL	>4.8 ng/mL
Vitamin C, ascorbic acid	< 5 umol/L	23 - 114 umol/L
Vitamin K1	8.17 nmol/L	0.22 - 4.88 nmol/L
Vitamin D 25 hydroxy	23 ng/mL	30-80 ng/mL

Vitamin C deficiency can begin to manifest when plasma levels fall below 0.2 mg/dL,[8] or within 1 to 3 months without dietary consumption. Common symptoms include weakness, malaise, arthralgias, and anorexia. Unstable collagen will result in structurally weak capillary walls that cause bleeding. Patients commonly have purpura in the lower limbs, petechiae, gingival bleeding, and epistaxis. Perifollicular hemorrhages occur in the lower extremities, first due to capillary fragility unable to withstand hydrostatic

pressure.[9] Other common findings include perifollicular hemorrhage, irregularly shaped hair follicles with hyperkeratosis, and corkscrew hair.[8] Ascorbic acid also plays a role in iron absorption,[8] with 54% of adults with scurvy also having iron deficiency anemia.[9] The diagnosis of scurvy is generally considered clinical, established most significantly on the clinical history and physical exam findings. Perifollicular purpura is thought to be specific to this disease.[8]

Though different treatment regimens have been proposed, there are currently no established, evidence-based guidelines for the workup, management, or treatment of scurvy.[9] Both oral and parenteral ascorbic acid supplementation can be given, though it is unclear which, if either, is superior.[9] Generally, adults require 60 mg/day of ascorbic acid to cure or to prevent scurvy.[10] However, other literature describes that as little as 10 mg/day of vitamin C can prevent it.[9] Adequate supplementation can begin to yield symptomatic improvement within 3 to 5 days, while physical exam findings may resolve over a few weeks.[10] Additional laboratory evaluations confirmed low serum folate and vitamin D, though it was assumed that our patient likely had numerous other nutritional deficiencies. In the end, he received dietary counseling from physicians and dietitians and was supplemented with vitamin C, vitamin D, vitamin K, folate, iron, and a multivitamin.

It is important to note that there has been an increase in case reports of scurvy, indicating that this disease is not just a disease of the past but one that occurs today, including in developed countries. The prevalence of vitamin C deficiency varies across the world, being as high as 73.9% in northern India and 7.1% in the United States. It is found more commonly in areas of low socioeconomic status in developed countries. Those who are at a particularly high risk are the elderly, alcohol abusers, and those with eating disorders.[11] It is a disease that can be missed but is easily treated. Therefore, a high level of suspicion should be present in those at risk for malnutrition.

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Kwashiorkor in an 8-Month-Old Infant Due to Homemade Formula Use

James J. McCarthy, MD; Sarah C. Yale, MD

ABSTRACT

Introduction: Kwashiorkor is a malnutrition syndrome most commonly seen in the United States among patients with malabsorptive conditions. While it is rare in otherwise healthy individuals, cases can develop where low nutritional literacy or unorthodox diets are a factor.

Case Presentation: We present the case of an 8-month-old infant who developed kwashiorkor after transitioning to homemade infant formula.

Discussion: This patient developed severe malnutrition due to consumption of homemade formula that did not meet nutritional standards. The recipe was promoted by an alternative health organization as a healthy option, and the difficulty in identifying reliable health information online also played a significant role.

Conclusion: Families of young children face many challenges, particularly during the recent infant formula shortage. Maintaining strong relationships and open communication with trusted health care professionals is vital to combating health misinformation and helping patients and families navigate these challenges safely.

INTRODUCTION

Kwashiorkor is a syndrome of malnutrition that is generally rare in the United States and is most often associated with malabsorptive conditions. Cases in healthy patients are most often associated with low nutritional literacy or unorthodox diets.[1] Feeding is frequently a high-stress area for parents of infants—especially with recent formula shortages—and the difficulty of identifying reliable sources on the internet can put both children and parents at risk. We present a case of kwashiorkor due to homemade formula use in a previously healthy infant.

CASE PRESENTATION

A previously healthy 8-month-old infant presented with poor weight gain, edema, and hypotonia. Vital signs were notable for heart rate 126, blood pressure 58/32, respiratory rate 32, and temperature 36.1°C. His mucous membranes were dry with capillary refill of 3 to 4 seconds and edema of all 4 extremities. He had decreased global muscle tone, minimal spontaneous movement, and was breathing irregularly with subcostal retractions and periods of apnea. Initial labs showed a blood glucose of 47 mg/dL, albumin 2.3 g/dL, total protein 3.9 g/dL, and anion gap metabolic acidosis with bicarbonate 16 mEq/L and lactate 21 mg/dL. Weight at admission was 5.996 kg, down from 6.492 kg 4 months previously; his linear growth had plateaued, and his head circumference growth velocity had slowed, consistent with prolonged malnutrition (Figure). He was placed on high flow nasal cannula for respiratory support and received intravenous fluids and dextrose for resuscitation. His respiratory status and lethargy improved with rehydration and resolution of hypoglycemia. He remained hypotonic with low muscle bulk and head lag and was unable to sit unsupported. Based on his edema, hypoalbuminemia, and clinical signs of severe malnutrition, he was diagnosed with kwashiorkor.

His parents reported that at around 6 weeks of age, he began to show signs of constipation and abdominal pain associated with formula feeds. His symptoms did not improve, despite trying multiple different commercially available formulas, includ-

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Figure. Patient World Health Organization Child Growth Charts for Weight, Length, and Head Circumference

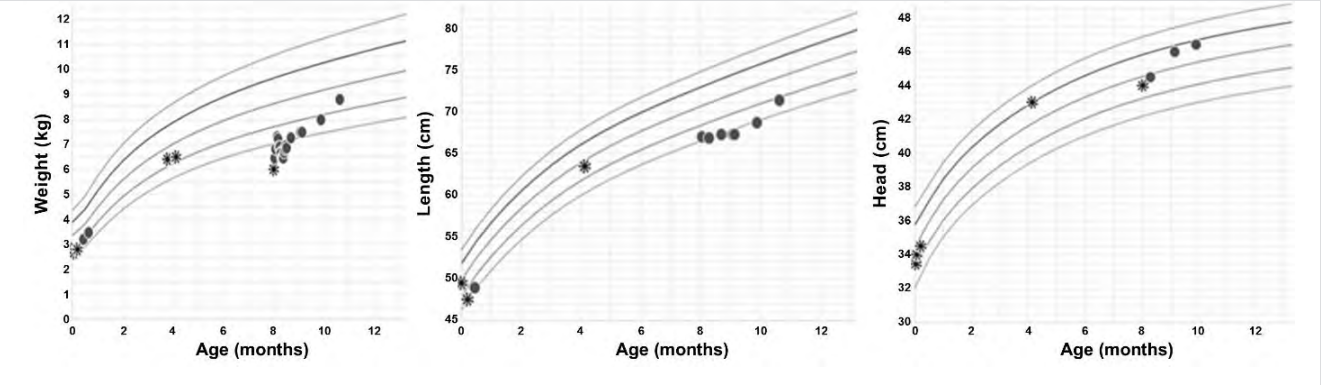

Table. Comparison of Formula Nutritional Content Per Ounce

	FDA Standard	Patient's Formula
Kilocalories	20	9.48
Protein (g)	0.36–0.90	0.05
Fat (g)	0.66–1.20	0.70
Vitamin A (IU)	50–150	486.3
Vitamin D (IU)	8–20	16.37
Vitamin E (IU)	≥0.14	0
Vitamin K (mcg)	≥0.8	0.33
Vitamin B1 (mg)	≥8	0
Vitamin B2 (mg)	≥12	0
Vitamin B6 (mg)	≥7	0
Vitamin B12 (mcg)	≥0.03	0.33
Niacin (mg)	≥50	0
Folate (mcg)	≥0.8	0.06
Biotin (mcg)	≥0.3	0
Vitamin C (mg)	≥1.6	0.38
Calcium (mg)	≥12	23.28
Iodine (mcg)	1–15	0
Iron (mg)	0.03–0.6	0.05
Sodium (mg)	4–12	3.77
Potassium (mg)	16–40	6.59

Abbreviation: FDA, Food and Drug Administration.

ing those recommended by their pediatrician. Although they did not have any difficulty in finding or affording formula, due to their frustration with the lack of improvement after following their pediatrician's suggestions, they transitioned to a homemade, coconut milk-based formula promoted online by an alternative health organization shortly after his 4-month well-child check. After the change in formula, his abdominal discomfort and fussiness improved, and he continued to take 240 mL feeds every 3 to 4 hours. Over the next few months, he remained exclusively formula-fed, but his oral intake slowly decreased and his family noticed slower weight gain. His parents reported they missed his 6-month well-child check and did not reschedule because they had no concerns at that time. He later stopped reaching to grasp objects, and his head control regressed from his previously achieved milestones. He did not see a health care provider until the day of presentation when his parents became concerned about his lethargy and irritability.

Nutritional analysis of the homemade formula recipe showed that it contained 9.5 kcal and 0.05 grams of protein per ounce and fell below US Food and Drug Administration (FDA) standards for multiple other nutrients (Table).[2] The patient tolerated nasogastric feeds with standard infant formula without signs of refeeding syndrome. He became edematous and showed rapid weight gain following fluid resuscitation, which was expected given his hypoalbuminemia, but spontaneously diuresed the excess fluid and showed appropriate weight gain thereafter. He was discharged home with the nasogastric tube in place due to an aversion to taking formula. He has since transitioned to full oral feedings and has made good progress in regaining motor skills.

DISCUSSION

Kwashiorkor is characterized by the presence of dependent edema secondary to hypoalbuminemia, and patients also may present with a listless affect, bradycardia, hypotension, and hypothermia. In this case, the formula's low caloric density and negligible protein content deprived the patient of the nutrients necessary for protein synthesis, leading to his development of kwashiorkor. Initial treatment of kwashiorkor is focused on stabilizing the patient through treatment and prevention of hypocalcemia, hypothermia, dehydration, and electrolyte imbalances. After the acute phase has passed, treatment shifts to resuming feeding with the goal of restoring appropriate growth and development.[3]

The internet continues to grow as a source of health information for parents, but the quality of information can vary widely. The immediate availability of health information online has many potential benefits for patients and families, but studies have shown that while large majorities of parents search online for information about their children's health, fewer than 60% check the reliability of the source or verify the information with a physician.[4,5] Although parents are aware that search engines may not provide

safe and reliable information, 80% reported using search engines as their first step in answering health questions.[4] With no enforceable standards for the quality of health information online, it is ultimately up to patients and families to determine the reliability of what they find.

The difficulty in finding reliable information is evident when researching homemade infant formula. The FDA, American Academy of Pediatrics (AAP), and other professional societies and pediatric health organizations all explicitly recommend against homemade formula use, citing potential problems ranging from excess free water content to nutritional deficiencies and unsafe ingredients. Despite this consensus, prior to the recent infant formula shortage, a Google search for "homemade baby formula" returned over 10 million results, with formula recipes displayed on the first page of results, intermixed with sites that highlight the health risks. Furthermore, while all commercially available formulas must meet FDA standards, the standards are not applied to homemade formula.[6] Most recently, the formula shortage has been further exacerbated by extensive recalls, leaving families in difficult situations on how to feed their babies. Whereas advice from the AAP provides families with guidance on how to navigate this formula shortage, alternative advice with recipes for "emergency use formula" are just as readily available on the internet.[7]

CONCLUSIONS

This case illustrates the potential for serious harm when parents turn to the internet for health information. The patient became critically ill after 4 months of feeding with a formula that was promoted as safer and healthier than commercial formulas. The formula was the direct cause of his kwashiorkor, as illustrated by its nutritional content and his rapid improvement when being fed standard infant formula. With myriad social, economic, and environmental factors often putting patients and parents in near-impossible situations—especially during the recent infant formula shortage—the importance of the guidance offered by health care professionals cannot be understated. Whether through phone or text reminders, outreach after missed appointments, or regular checkins between appointments, it is vital for clinicians to maintain open communication with families to ensure the health and safety of all involved. Preventive care is the foundation of health care and is the most important tool for avoiding adverse outcomes. As this case illustrates, the combination of missed visits and unverified information can lead to disastrous results.

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Acute Hypoxia From Different Clinical Entities Can Potentially Break the Heart: Takotsubo Cardiomyopathy

Muhammad Shoaib Khan, MD; Somto Nwaedozie, MD; Sophie L. Shogren, MD; Rhianna Malovrh, RDCS; Sreerag Surendran, MD

ABSTRACT

Takotsubo syndrome is characterized by transient regional left ventricular wall motion abnormalities and elevated troponin levels like those seen in classic myocardial infarction but without evidence of obstructive coronary artery disease. We present two uncommon cases of Takotsubo syndrome. In Case 1, a 64-year-old man presented with chronic obstructive pulmonary disease exacerbation who later developed chest pain and acute hypoxic respiratory failure. In Case 2, a 77-year-old woman with myasthenia gravis was admitted for acute hypoxic hypercapnic respiratory failure requiring mechanical ventilation following a myasthenic crisis. In both cases, serum high sensitivity troponin was elevated, electrocardiograph showed findings suggestive of infarction, and coronary angiogram did not show evidence of obstructive coronary artery disease. Echocardiogram in both patients revealed abnormal left ventricular wall motion, likely secondary to Takotsubo syndrome.

Takotsubo syndrome is uncommon in the setting of chronic obstructive pulmonary disease exacerbation or myasthenic crisis, and proposed mechanisms for the disease include catecholamine surge, vasospasm of coronary arteries, and microvascular dysfunction. Takotsubo syndrome is reversible; thus, it is important to remove any trigger leading to catecholamine surge. Identification of such triggers and early diagnosis could help optimize pharmacotherapy.

INTRODUCTION

Takotsubo syndrome (TTS) also is known as stress-induced cardiomyopathy and "broken-heart syndrome." It is characterized by transient left ventricular (LV) systolic dysfunction with apical ballooning that presents similar to myocardial infarction but does not show angiographic evidence of coronary artery disease or atherosclerotic plaque rupture.[1] The pathophysiological mechanism of the disease remains mostly unknown; however, triggers for TTS typically include intense emotional or physical stress, and it is proposed that catecholamine excess, coronary artery vasospasm, and microvascular dysfunction are the main contributors.[2] In fact, patients with TTS were found to have 10 to 20 times higher levels of circulating catecholamines when compared to normal, as well as higher catecholamine levels than a matched cohort of ST-elevated myocardial infarction patients.[3] Specific precipitating triggers that have been noted include exercise and dobutamine stress tests, electroconvulsive therapy, surgery, respiratory failure, seizures, central nervous system disorders, acute critical illness, or profound mental stress.[4] It has also been suggested that those with psychiatric or neurologic disorders may be predisposed to TTS.[5,6] Considering the catecholamine surge and activation of excessive adrenergic drive that can characterize many of these disorders, it logically follows that their presence could predispose to TTS. However, literature documenting TTS is sparse.

In this case series, we report two incidences of TTS in the milieu of two different hospital admitting pathologies that led to acute hypoxic respiratory failure – one in a patient admitted for a chronic obstructive pulmonary disease (COPD) exacerbation and the other for myasthenic crisis (MC).

CASE PRESENTATIONS

Case 1

A 64-year-old man with a past medical history of 31 pack-years of cigarette smoking and COPD presented with acute shortness

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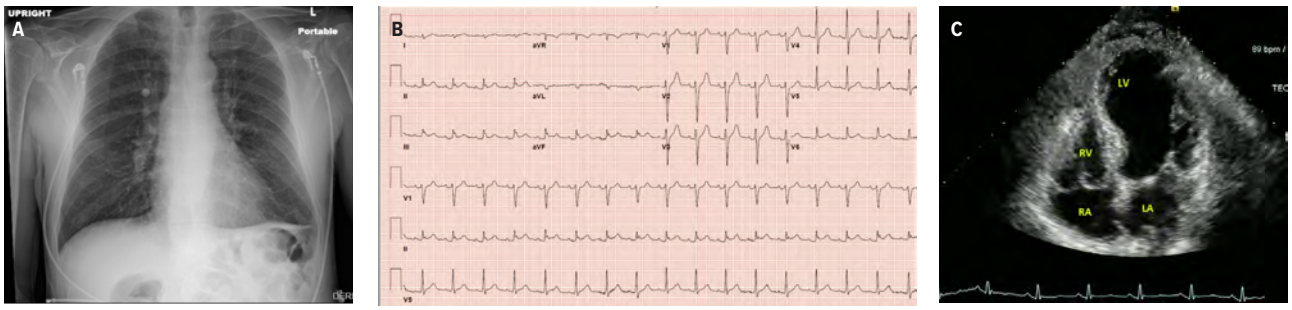
Figure 1. Case 1 Patient's (A) Chest X-Ray, (B) Electrocardiogram, and (C) Echocardiogram



of breath. He had chills and cough that started a few days prior. On lung auscultation, he had decreased air entry in the lung bases bilaterally. Laboratory investigation revealed elevated inflammatory markers (Table 1). Initial chest x-ray did not reveal evidence of acute cardiopulmonary pathology (Figure 1A).

In the emergency department, the patient was started on nebulized albuterol-ipratropium, azithromycin, and prednisone for his COPD exacerbation. Approximately 1 hour after starting nebulization, he began having chest pain and worsening shortness of breath. He became hypoxic, and arterial blood gas suggested acute hypoxic respiratory failure with PaO_2 being 79 mmHg on 2 liters of oxygen. Due to a continuous increase in supplemental oxygen demand and worsening respiratory distress, he was initiated on bilevel positive airway pressure (BiPAP). Labs drawn immediately after the onset of chest pain revealed elevated high-sensitivity troponin (TnI-HS) levels of 236 ng/L, followed by 2033 ng/L obtained 2 hours later (normal reference values = 0-57 ng/L). Electrocardiogram (ECG) revealed minimal ST elevation in leads II, III, and aVF (Figure 1B).

The patient was taken for immediate coronary angiogram, which did not show evidence of occlusive coronary artery disease (Appendix 1). He was intubated during the angiogram due to worsening hypoxia secondary to supination in the setting of COPD exacerbation; however, after the angiogram, he was extubated, reinitiated on BiPAP, and remained hemodynamically stable throughout hospitalization. Subsequent echocardiogram revealed abnormal LV wall motion indicative of TTS (Figure 1B and Appendix 2), with a left ventricle ejection fraction (LVEF) of 25%. LV global longitudinal strain was not measured. The patient's previous echocardiogram, which was obtained 14 months prior, showed normal LV function with LVEF of 62%. He was initiated on metoprolol and lisinopril, which were continued at discharge with the suggestion to start spironolactone as an outpatient. After approximately 1 month, a follow-up echocardiogram revealed no obvious regional wall motion abnormalities and an LVEF that had improved to 60%.

Case 2

A 77-year-old woman with a past medical history of myasthenia

Table 1. Lab Results for Patients 1 and 2

	Patient 1	Patient 2
Complete blood cell count		
White blood cell	12.4	16.8
Hemoglobin	13.9	11.9
Hematocrit	40.9	35
Platelets	252	228
Coagulation tests		
International normalized ratio	1.1	—
Partial thromboplastin time	25.7	—
Basic metabolic panel		
Sodium	134	140
Potassium	4.9	3.7
Chloride	102	109
Bicarbonate	23	22
Blood urea nitrogen	21	8
Creatinine	1.5	0.6
eGFR	47.1	>90
Glucose	137	180
Calcium	8.5	8.7
Total calcium	4.9	5.2
Magnesium	2.3	2.0
Phosphorus	4.4	5.7
Lipid Panel		
Cholesterol	214	58
High-density lipoprotein	51	21
Low-density lipoprotein	151	26
Triglycerides	58	56
Cardiac Markers		
TnI-HS (T_0)	236	6060
TnI-HS (T_0 + 2)	2033	—
B-type natriuretic peptide	25	25
Inflammatory Markers		
C-reactive protein	2.1	—
Procalcitonin	0.11	—
Lactate	1.4	1.9
Arterial blood gas		
pH	7.23	7.16
pCO_2	45	76
pO_2	129	115
Bicarbonate	19	27
Micro		
Urine analysis	Neg	—
Respiratory Viral Panel	Neg	—
COVID	—	Neg

Abbreviations: eGFR, estimated glomerular filtration rate; TnI-HS, high-sensitivity troponin.

Figure 2. Case 2 Patient's (A) Chest X-Ray, (B) Electrocardiogram, and (C) Echocardiogram

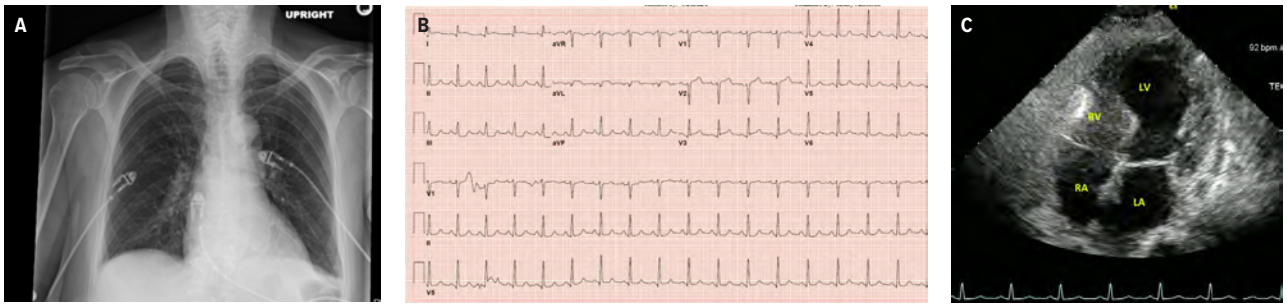


Table 2. Mayo Clinic Diagnostic Criteria for Takotsubo Syndrome

A	Transient left ventricular mid-segment hypokinesis, akinesis, or dyskinesis with or without apical involvement which are typically regional and extend beyond a single epicardial coronary distribution.
B	Absence of obstructive coronary artery disease or angiographic evidence of acute plaque rupture.
C	New electrocardiographic abnormalities (either ST-segment elevation and/or T wave inversion) or modest elevation in cardiac troponin.
D	Absence of pheochromocytoma or myocarditis.

gravis (MG), hypertension, and dyslipidemia was admitted to the medical intensive care unit with sudden onset shortness of breath, hypoxia with fingertip pulse oximeter revealing oxygen saturation of 81%, dysphagia, and dysphonia requiring emergency endotracheal intubation and mechanical ventilation. Her chest x-ray was unremarkable for evidence of acute cardiopulmonary disease (Figure 2A), and her initial arterial blood gas was suggestive of hypercapnia with $PaCO_2$ of 76 mmHg, and TnI-HS was 6060 (Appendix 3). ECG demonstrated lateral injury pattern (Figure 2B). Coronary angiogram did not show significant obstructive coronary artery stenosis (Appendix 3). Echocardiogram revealed abnormal LV wall motion with LVEF of 23% (Figure 2B and Appendix 4). LV global longitudinal strain was not measured. She had no previous echocardiograms for comparison and had no history of exertional symptoms to suggest heart failure. Thus, the findings of elevated TnI-HS, combined with the lack of obstructive disease and decreased LVEF, were suggestive of TTS.

The patient was initiated on metoprolol and lisinopril. Since her presenting symptoms were thought to be the consequence of hypoxia from MC, she underwent plasmapheresis and received pyridostigmine, azathioprine, and prednisone. With this therapy, she was able to be successfully extubated, and her shortness of breath, dysphagia, and dysphonia resolved during hospitalization. Prior to discharge, her guideline-directed medical therapy of lisinopril and aspirin were discontinued due to clinical improvement and no further indication for the medications. Her follow-up echocardiogram after a week of hospital admission revealed an improvement in LVEF to 54%.

Of note, we excluded other possible clinical conditions with similar cardiac presentation, such as drug- or cocaine-related acute coronary syndrome, myocarditis, and pheochromocytoma. These etiologies were all unlikely, as neither patient had history of drug exposure; the preceding classic symptoms of fever, episodic headache, diaphoresis, and tachycardia were not present; and they had unremarkable urine drug screenings during their respective hospitalizations.

DISCUSSION

TTS is a transient cardiac syndrome seen in 1% to 2% of troponin-positive patients that mimics acute coronary syndrome at the time of presentation. It is characterized by regional LV systolic dysfunction extending beyond a coronary territory, without any or minimal evidence of obstructive coronary artery disease or plaque complication following invasive angiography.[1,7,8] Though the exact pathogenesis of this clinical condition remains unclear, some of the proposed pathophysiological mechanisms include catecholamine surge, coronary artery vasospasm, or microvascular dysfunction.[2,7,9] Predisposing factors reported in the international Takotsubo registry study include severe emotional and physical stress in 36% and 27.7% of patients, respectively, while in about 28.5% there were no evident triggers.[5]

Diagnosis of TTS requires fulfillment of the Mayo Clinic diagnostic criteria (Table 2).[1,9] It is important to rule out similar cardiac presentation, such as drug- or cocaine-related acute coronary syndrome, myocarditis, and pheochromocytoma, which could be indicated by a history of drug exposure or a positive urine drug screening, as well as symptoms of fever, episodic headache, diaphoresis, and tachycardia. The case study patients fulfilled all these criteria and, as a result, had definitive diagnoses of TTS.

As noted in the cases, the clinically observed pathophysiology of events triggering acute LV dysfunction included acute hypoxia resulting from ventilation-perfusion mismatch and hypoventilation from acute COPD exacerbation and MC, respectively. TTS, in the setting of acute hypoxic respiratory failure due to COPD exacerbation and MC, is uncommon, and cases have been more commonly described in patients with subarachnoid hemorrhage[7] or epilepsy.[8] These separate clinical entities cause

hypoxia via ventilation-perfusion mismatch and hypoventilation, respectively, which triggers compensatory processes of tachypnea, tachycardia, increased work of breathing, and catecholamine surge. Significant physical, psychological and neurohumoral stress leads to catecholamine-induced microvascular spasm, which may result in myocardial stunning or have a direct catecholamine-associated myocardial toxicity, leading to reversible LV ballooning seen in TTS.[3,7,10,11]

Acute hypoxia has diverse organ-system manifestations – aside from activation of several cardiovascular autonomic processes, it also exerts a stunning effect at the myocardium, which has been demonstrated in patients with ECG changes, elevated TnI-HS levels, and LV motion abnormalities seen on echocardiogram.[7,12,13] Post ischemic dysfunction – or myocardial stunning – is the mechanical dysfunction that persists after reperfusion, despite the absence of irreversible damage. It is a relatively mild, sublethal injury that must be kept quite distinct from myocardial infarction.

While the myocardial stunning effect resembles that described in acute coronary ischemia, there are no obstructive or complicated coronary lesions demonstrated on invasive angiogram in TTS patients, as in the case study patients. The complete reversal of LV dysfunction following management and resolution of each acute hypoxic episode—demonstrated by normalization of both patients' LVEFs within 1 month—supports these cardiomyopathic episodes as transient myocardial hypoxic responses.[7,9]

Additionally, COPD management with administration of albuterol can increase physiological stress on the myocardium through other mechanisms, including beta-2 vasodilatory effects on blood vessels with resultant reflex tachycardia and mild inotropic effects on the heart.[14] These effects can further increase myocardial oxygen demand.

The LV dysfunction and wall motion abnormalities seen in TTS are usually reversible with supportive management aimed at resolution of physical psychological stress, close hemodynamic monitoring, and prevention of acute complications like cardiogenic shock, acute heart failure, and thromboembolism – which, if present, require evidenced-based guideline-directed therapies.[7,9]

Clinical presentation, as in the case study patients, often resembles acute coronary events and, as a result, requires initial management with aspirin, heparin, and beta-blockers, as indicated. With definitive diagnosis of TTS, some of these therapies, like aspirin, should be deescalated, unless there are other indications. Though conservative management usually leads to positive outcomes and spontaneous recovery of LV function within a few weeks, prognosis may be worsened in patients with physical stressors or concomitant illness.[9]

Though TTS is typically reversible, it can result in severe LV systolic dysfunction, which can worsen outcomes in the setting of hospitalization for a preexisting condition, such as a COPD exacerbation or MC. As a result, a high index of suspicion is required to identify TTS and reduce predisposing triggers, as well as initiate prompt management to optimize patient outcomes.

CONCLUSIONS

Though TTS in the setting of acute hypoxic respiratory failure and MC is an uncommon occurrence – and only a handful of cases have been reported – it remains a potentially life-threatening complication of which the medical community must be aware. Since TTS is reversible, it is important to remove any underlying trigger. Thus, identification of COPD exacerbation and/or MC should prompt the clinician to screen for features of TTS, as the early diagnosis could help optimize pharmacotherapy.

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Achenbach Syndrome in Primary Care: A Case Report

Paula Aguirre-Bejarano, MD; Eduardo Tuta-Quintero, MD; Claudia Mora-Karam, MD; Sergio Quiroga-Segura, MD; Juan Pimentel, MD

ABSTRACT

Paroxysmal hematoma of the fingers, or Achenbach syndrome, is a rare vascular disorder of benign course and unknown etiology. The clinical manifestations are sudden onset, paroxysmal spontaneous subcutaneous hematomas, and edema and pain in the fingers and hands. The clinical course is self-limited and does not leave permanent sequela. The diagnosis is clinical, and complementary studies are often unnecessary. We present the clinical case of a 69-year-old woman diagnosed with Achenbach syndrome in a primary care center in Colombia.

INTRODUCTION

The German physician Walter Achenbach first described a rare condition that he called "paroxysmal hand hematoma" or "finger apoplexy" in 1958.[1] Achenbach syndrome or paroxysmal finger hematoma is a female-dominant disease of unknown etiology with a median age at presentation of 50 years.[2] The clinical manifestations are characterized by a paroxysmal, spontaneous subcutaneous hematoma on the palmar aspect of the proximal phalanges. Diagnosis is based on the clinical features, and there is no need for supplementary investigations.[3] The median time to resolution of symptoms is 1 week (2 to 14 days) without treatment.[1,4]

Although Achenbach syndrome is a benign, self-limited disease, primary care physicians are not usually trained to recognize and manage it. In this paper, we describe a case of Achenbach syndrome in a 69-year-old woman who presented to the emergency department with swelling, hematoma, and paresthesia in the third finger of the right hand. We aim to provide evidence to improve the diagnosis and management of this disease in primary care settings.

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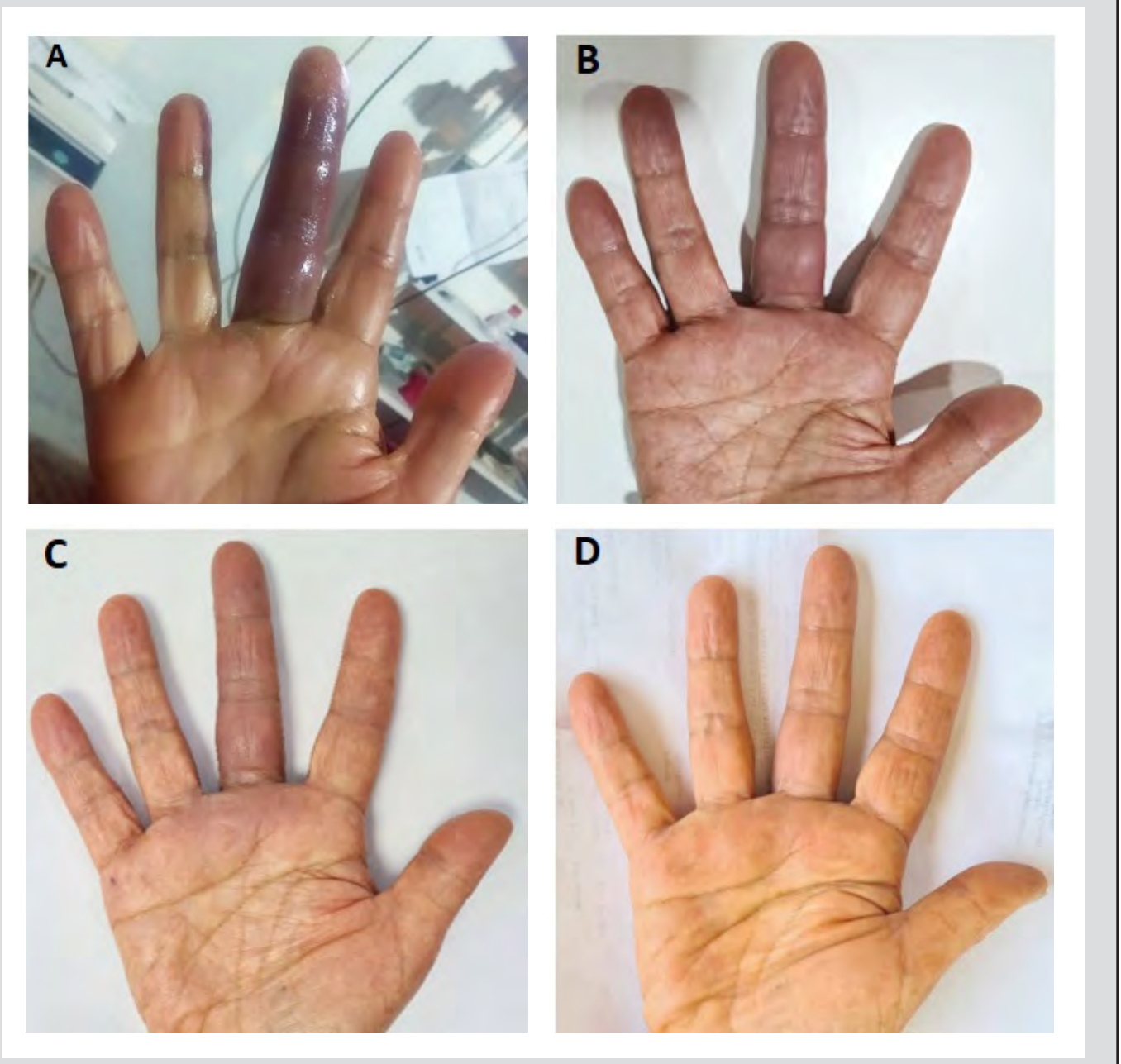
CASE REPORT

A 69-year-old woman presented to the emergency department with an 8-hour history of a sudden inflammation of the third finger of the right hand, associated with mild pain, intense change of color, and paresthesia. She reported no history of causative triggers, such as preceding trauma, cold exposure, stress, or medication; however, she did report a similar episode 7 months prior, which was self-limited after 5 days, without requiring medical management or investigations. Additionally, she reported dyslipidemia on treatment with atorvastatin 20 mg per day. She had a negative toxic-allergic history and did not mention any personal or family history of thrombosis.

The patient had a tachycardia of 105 beats per minute and other vital signs were within physiological limits. Clinical examination revealed edema and change in skin color in the third finger of her right hand, predominantly in the palmar region of the proximal phalanges. On palpation, the area was not painful and had a normal capillary filling and no distal coldness. The brachial, radial, and ulnar artery pulses were palpable and symmetric, with preserved mobility of hands (Figure 1A).

Laboratory results (hemoglobin, leukocytes, hematocrit, platelets) were normal, and a diagnosis of Achenbach syndrome was made. Anti-inflammatory management and physical means were indicated. She had a favorable clinical course, with a total resolution of the symptoms on the third day, which is evidenced in Figure 1. We did not request doppler ultrasonography, angiography, or any additional investigation. The patient signed informed

Figure. Features of Achenbach Syndrome



A. Day 0: Edema and discoloration of the third finger of the right hand, respecting the distal end; B. Day 1: Decrease in edema, evident discoloration; C. Day 2: Resolution of edema, a slight color change; D. Day 3: Full resolution.

consent to be able to use data from the medical history and photographs.

DISCUSSION

Achenbach syndrome is a rare and self-limited vascular condition of unknown etiology that causes paroxysmal bruising of the fingers. In actuality, it is a neglected disease in primary care, mainly because it does not cause mortality or morbidity and there is low prevalence worldwide.[4,5] We report this case of Achenbach syndrome to increase awareness and provide information regarding the diagnosis, clinical course, and outcome of the disease. The diagnosis is essentially based on history and clinical examination; there is no need for additional investigations, especially if they are invasive.[1,4,5] Primary care physicians can use this information to optimize the clinical approach to patients with Achenbach syndrome.

Clinical manifestations of Achenbach syndrome are characterized by a paroxysmal, spontaneous subcutaneous hematoma on the palmar aspect of the proximal phalanges proximal, middle, and distal phalanges (primarily in the middle and ring fin-

gers), episodic pain (58%), and swelling (58%) without a history of prior coagulopathy or trauma.[3,4] Clinical examination should rule out absence of pulse, pallor, pruritus, ulceration, and necrosis that suggests acute limb ischemia, acrocyanosis, and chilblains. It is important to rule out clinical presentations that may manifest with cold and blue-to-white colored fingers, such as Raynaud's phenomenon.[2,6] In this case, clinical manifestations included a paroxysmal spontaneous subcutaneous hematoma on the palmar aspect of the proximal phalanges in 1 or more fingers and episodic pain. The clinical examination revealed pulses present without skin lesions.

Achenbach syndrome is a condition of unknown etiology.[7,8] However, the pathophysiology may be related to the presence of capillary fragility with extravasation of red blood cells, hyperkeratosis, and generalized ectatic capillaries within the dermis.[7-9] The F3 and F2 genes have been associated with capillary fragility and Achenbach syndrome; these genes code for the coagulation factor II and III, respectively.[9]

In some cases, bleeding can occur due to venous rather than arterial hemorrhage, and infiltration and compression affect the extravasated blood.[5] Paradoxically, the lesions disappear without going through the typical stages of ecchymosis reabsorption, and the hand always has a normal temperature.[7] The signs and symptoms are alarming to most patients, who may be referred to vascular surgeons and exposed to unnecessary diagnostic images, such as doppler and angiography, which should be used to rule out stenosis and thrombosis. Skin biopsy can confirm or rule out vasculitis and may demonstrate nonspecific signs such as minor bleeding and inflammation.[7,10] In this case, we did not request image-based investigations or biopsies due to unavailability at the health center.

The painful discoloration resolves on its own, and treatment consists of reassuring the patient to avoid increased pain due to anxiety.[5,11] In our case, no specific treatment was proposed initially due to the high suspicion of Achenbach syndrome on history and clinical examination. Without any treatment, the median time to resolution of signs and symptoms is 1 week (2 to 14 days).[2] Recurrent episodes may occur in months or years without any apparent sequelae.[3,7]

CONCLUSIONS

The acute clinical presentation of Achenbach syndrome often generates concern among primary care physicians due to the fear of a pathology that could permanently damage the fingers. It is important to recognize this condition to reassure the patient and avoid unnecessary investigations. Diagnosis in this case was based on clinical findings as investigations are completely normal. This report will assist with rapid diagnosis and proper management of Achenbach syndrome in primary care, avoiding unnecessary referrals and invasive exams. The prognosis of Achenbach syndrome did not leave apparent sequelae in the patient.

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Primary Malignant Melanoma of the Gastroesophageal Junction Treated With Immunotherapy: A Case Report

Nabil Attlassy, BS; Abiye Agbeh, BS; Rohan Patnaik, BS; James Miller, MD, MPH; James McCarthy, MD

ABSTRACT

Introduction: Primary malignant melanoma of the esophagus constitutes 0.1% to 0.5% of all primary malignant esophageal neoplasms. Melanocytes are present within the squamous epithelium of the esophagus in the stratum basale layer with melanocytosis rare within the esophagus. Primary esophageal melanoma is aggressive and has a poor survival rate; 80% of patients have metastatic disease at diagnosis. Resection surgery is usually first-line treatment for localized primary malignant esophageal melanoma, but recurrence rates remain high. Tumor-specific immunotherapy has shown promising results. We report a case of primary malignant esophageal melanoma with metastasis to the liver treated with immunotherapy.

Case Presentation: A 66-year-old woman presented with 2 months of progressive dysphagia and 3 episodes of hematemesis the previous night. Endoscopic examination showed a hypervascular distal esophageal mass. Biopsy was positive for S-100, SOX-10, and HMB-45 and showed rare mitotic figures with scattered pigment, consistent with melanoma. She was scheduled for esophagectomy initially, but instead pursued immunotherapy after liver metastasis was diagnosed during preop magnetic resonance imaging. Immunotherapy consisted of 8 cycles of pembrolizumab, followed by 4 months nivolumab and ipilimumab. The patient remains in remission 3 years after completing immunotherapy.

Discussion/Conclusions: Our patient was diagnosed with primary malignant esophageal melanoma of the distal esophagus with metastasis to the liver, a presentation that typically has a poor prognosis. Despite this, remission was achieved with immunotherapy without surgical intervention. Only a small number of cases of primary esophageal melanoma treated with immunotherapy have been reported—one showcasing tumor stabilization following several cycles of therapy with eventual metastasis, while our patient had a stable response to treatment. Further exploration of medical management with immunotherapy should be conducted, as it represents an alternative treatment for patients who do not have the option of surgical management.

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INTRODUCTION

Primary malignant melanoma of the esophagus (PMME) is a rare cancer that constitutes 0.1% to 0.5% of all primary malignant esophageal neoplasms.[1] The primary nature of melanoma within the esophagus had long been debated in the 20th century, but 2 findings have clarified its origin. First, melanocytes are typically not found within the esophagus. Aberrant migration during embryogenesis, however, can allow for translocation of melanocytes to the stratum basale within the squamous epithelium of the esophagus. This is seen on pathologic biopsy as increased numbers of dendritic melanocytes and increased deposition of the melanin pigment within the squamous epithelium of the esophagus. Second, esophageal melanocytosis is rare, occurring at rates between 0.07% to 2.1% and can only be seen endoscopically once significant concentrations of melanocytes are present to allow for gross observation.[1]

PMME is highly malignant and confers a poor survival rate. Median survival is typically 8 to 34.5 months following diagnosis, with an overall 5-year survival rate of less than 20%.[2] Hematogenous and lymphatic metastasis of PMME is common, with liver metastasis being the most common at 31%, followed by the mediastinum, lungs, brain, and pancreas.[3] Treatment for PMME is not yet standardized but regimens include surgery, chemotherapy, and immunotherapy.[4] First-line therapy typically includes en blocresection, but this has been associated with high rates of recurrence. Adjuvant chemotherapy

Figure 1. Esophagogastroduodenoscopy Showing 2 cm Lobulated Mass at Squamocolumnar Junction From Esophageal View (left) and Gastric View (right)

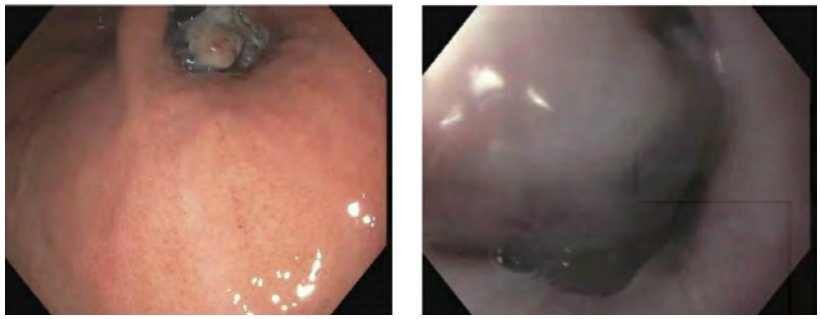
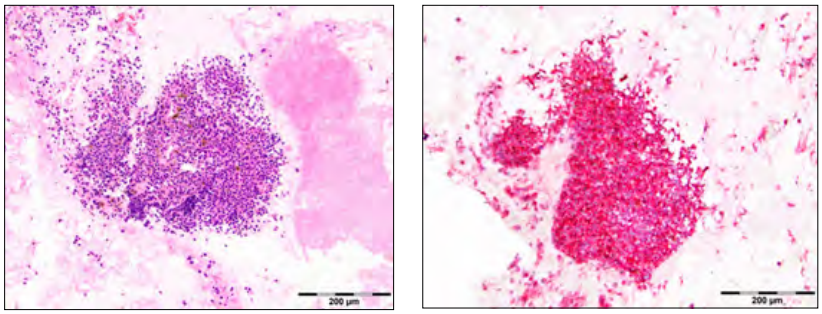


Figure 2. Esophageal Biopsy Hematoxylin and Eosin Stain (left) and Immunostain (right) at 200 x Magnification



Immunostaining was done with a melanoma cocktail consisting of HMB-45, MART-1/Melan-A, and tyrosinase.

and tumor-specific immunotherapy also have shown promise for patients; however, the low prevalence of PMME makes it difficult to provide comprehensive evidence-based therapies.[5]

CASE REPORT

A 66-year-old White woman with a history of hypertension, anemia, and hyperlipidemia was admitted with 2 months of progressive dysphagia, 2 days of fatigue, and 3 episodes of hematemesis the previous night. Endoscopy and computed tomography scan showed a 2 cm mass in the distal esophagus (Figure 1).

Repeat endoscopy confirmed the 2 cm mass at the esophageal squamocolumnar junction without ulceration or bleeding, and endoscopic ultrasound further characterized the mass as submucosal and hypervascular. Fine needle aspiration biopsy revealed sheets of malignant cells consisting of epithelioid cells with amphiphlic cytoplasm, prominent nucleoli, mild nuclear atypia, and occasional melanin pigment with no obvious lymphoid infiltrate. Immunostaining was positive for S-100, Sox-10, and HMB-45, which confirmed diagnosis of esophageal melanoma (Figure 2). Molecular analysis was negative for pathologic mutations, including BRAF and CKIT. Brain magnetic resonance imaging (MRI) showed no evidence of acute intracranial abnormality and positron emission tomography (PET) scan was negative for evidence of distant metastasis consistent with a diagnosis of primary melanoma. The patient had no prior history of melanoma—cutaneous or otherwise.

Cardiothoracic surgery initially recommended an esophagectomy with adjuvant chemotherapy as the lesion appeared primary and localized. However, a preoperative outpatient abdominal MRI revealed a 1 cm hepatic right lobe lesion (Figure 3), with biopsy confirming metastatic melanoma negative for PD-L1 (Figure 4). Surgery was canceled and treatment options were discussed.

Initially, the patient received microwave ablation therapy for the liver metastasis. She then underwent 8 cycles of pembrolizumab followed by 4 months of combined therapy of nivolumab and ipilimumab. She developed allergic interstitial nephritis due to the checkpoint inhibitors and was given a 6-month steroid taper. As of 2019, she continued to be seen for her chronic kidney disease secondary to therapy, but her PET scans were reassuring for no new or progressing melanoma.

DISCUSSION

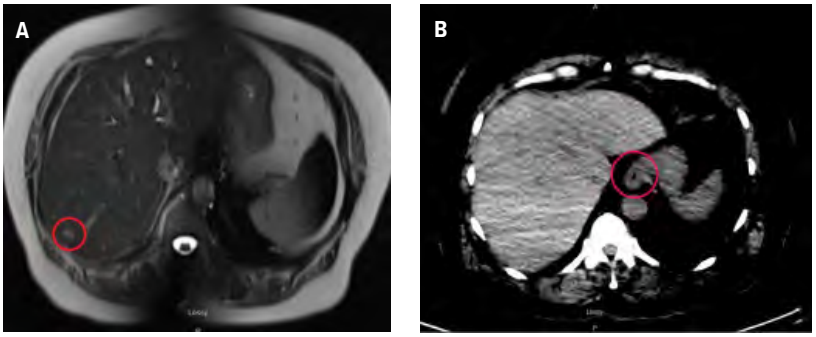
PMME is a rare tumor that accounts for less than 0.2% of esophageal malignancies.[6] Prognosis for these tumors is poor, with past literature reporting 5-year survival rates between 4% and 37%.[7] It mainly arises in the distal esophagus during the sixth or seventh decade of life, as with the patient described in this report.[8] PMME is found around the world but has an increased incidence in Asian populations—especially Japan—with a rate of mucosal melanomas 21.7% to 33.5% of total melanomas compared to 2% in the western world.[9] PMME generally presents late in its course with symptoms of dysphagia, odynophagia, and weight loss similar to other malignancies of the esophagus.[8] However, even with presumptive diagnosis of PMME following positive immunohistochemistry staining, it is important to rule out other potential primary sites, as well as assess the patient for distant metastasis. As was the case for our patient, this includes a full body PET scan, brain MRI, and a dermatologic exam.

For newly diagnosed PMME, surgical resection is currently the most common treatment method.[10] In an analysis of surgical outcomes among 17 patients with PMME, Gao et al showed an overall complication rate of 35.3% among patients who under-

went subtotal esophagectomy and esophagogastrostomy with dissection of mediastinal and abdominal lymph nodes. The median survival time was 18.1 months, with 1-year and 5-year survival rates being 51% and 10%, respectively.[7] Although surgical resection is the most common first-line treatment, the rarity of PMME combined with lack of data has meant a lack of true standardized treatment regimen. For our patient, surgery was not an option due to liver metastasis. She instead started therapy with pembrolizumab, in addition to microwave ablation of 4 hepatic metastases. Her therapy then continued with combination of nivolumab and ipilimumab for 4 months and was complicated by interstitial nephritis. PET scans 4 year after completing treatment were reassuring for no new or progressing melanoma.

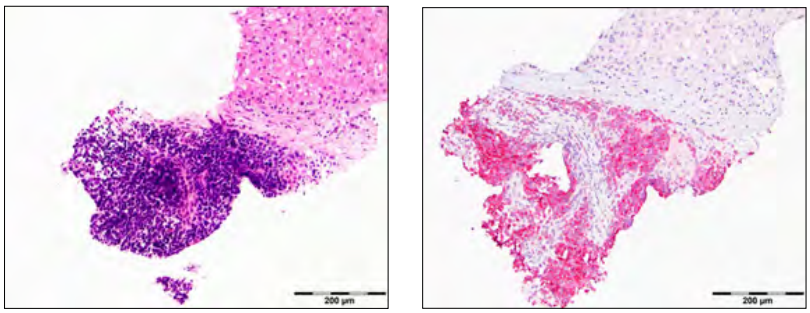
To our knowledge, this is one of the first gastroesophageal junction PMME cases documented in the United States. A minority of cases of PMME treated with immunotherapy have been reported, and our patient has had a remarkable response to treatment. Many treatments in case series in the literature, including Gao et al, involved surgical resection as the primary treatment, with very few involving neoadjuvant therapy. In the case described by Rochefort et al, PMME was treated with nivolumab, with the team reporting knowledge of only 1 other case using checkpoint inhibitor therapy in which the patient passed away 7 months after initiation of treatment.[11] The lack of data on this treatment method should encourage further investigation of PMME in order to develop a better perspective on standardizing treatment. We hope that the rarity of PMME combined with our patient's successful treatment with novel immunotherapy will spur further literature into immunotherapy treatment of PMME.

Figure 3. Magnetic Resonance Imaging Abdomen and Positron Emission Tomography Scan



A. Magnetic resonance imaging abdomen showing lesion suspicious for liver metastases.
B. Positron emission tomography scan showing distal esophageal mucosal thickening consistent with esophagogastroduodenoscopy.

Figure 4. Liver Biopsy Hematoxylin and Eosin Stain (left) and Immunostain (right) at 200 x Magnification Confirming Metastatic Melanoma



CONCLUSIONS

PMME is an extremely rare and aggressive tumor consisting of less than 1% of all primary esophageal neoplasms, especially at the gastroesophageal junction. Surgical resection via esophagectomy with the addition of chemotherapy or immunotherapy remains the most common method of management, although evidence is limited due to the rarity of PMME. Our patient's PMME with minimal metastases provides a data point for the timeline of PMME treated with immunotherapy. Although prognosis remains poor and risk factors poorly understood, further investigation into optimal treatments combined with early diagnosis can elicit better outcomes for patients.

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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.

Learn more at:
DoseOfRealityWI.gov
A message from Wisconsin Department of Justice, and the Wisconsin Department of Health Services

Wisconsin Department of Health Services

University of Wisconsin
School of Medicine and Public Health
Health Sciences Learning Center
750 Highland Ave • Madison, WI 53705

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to our Reviewers

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