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WHAT'S INSIDE: ORIGINAL RESEARCH • CASE REPORT

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TABLE OF CONTENTS

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Collaborating with Culturally Competent Prenatal Education among Hispanic Communities

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ABSTRACT

Introduction. Hispanics represent the largest minority group in the United States. In Kansas, the population of Hispanics has been increasing; unfortunately, their infant mortality rate has increased as well. Baby Talk is a prenatal education program promoting maternal and infant health through risk-reduction strategies and healthy decision-making. The aim of this pilot project was to develop and evaluate a Spanish curriculum for Baby Talk.

Methods. A collaborative partnership between bilingual community members and health professionals from different origins, nationalities, and Spanish dialects was formed to create a culturally and linguistically appropriate Spanish Baby Talk curriculum. This interventional pilot mixed methods research study employed quantitative and qualitative methods to evaluate participant knowledge, intentions, satisfaction, and perceptions of the new curriculum.

Results. Fifteen pregnant women participated in Spanish Baby Talk. Of those, 12 participated in either phone interviews (n = 6) or a focus group (n = 6). All respondents described their experience with the Spanish Baby Talk program as "excellent". Significant increases in knowledge were seen related to topics such as benefits of full-term pregnancy and benefits of breastfeeding. Four themes were identified from the focus group and interviews: 1) lack of accessible community resources; 2) sense of community; 3) Spanish Baby Talk strengths; and 4) areas for improvements.

Conclusions. Findings suggested that the Spanish Baby Talk curriculum was linguistically appropriate and resulted in increases in knowledge and intentions related to health and safety behaviors. Areas for improvement were related to marketing the program and referring to resources that provide material supports (i.e., diapers) to continue the move towards a culturally competent program.

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INTRODUCTION

Hispanics represent the largest minority group in the United States[1] and are expected to increase from 60 million in 2019 to 111 million by 2060.[2,3] Within Hispanic communities, there are many different dialects, cultural practices, and beliefs impacting prenatal and postnatal care. Variations in infant death rates between Central American, South American, Cuban, Puerto Rican, Dominican, and Mexican women are thought to be related to cultural variations between these groups.[4] In Sedgwick County, 15% of the population are Hispanic,[5] with 79% reporting Mexican origin and 67% reporting a language other than English spoken at home.[6] Hispanic infants are nearly twice as likely to die as non-Hispanic white infants in Kansas (infant mortality rates (IMRs) 7.3 and 4.9 deaths per 1,000 live births, respectively). In Sedgwick County, IMRs for Hispanics are higher (8.1) than overall state Hispanic rates.[7]

Making prenatal education available in Spanish and taught by a Spanish-speaking instructor are important steps towards health equity, as cultural and linguistic barriers impact access to care.[8,9] Access to linguistically appropriate educational content may guide parents and caregivers towards evidence-based best practices to care for themselves and their babies. While English-language prenatal education resources existed in Sedgwick County, community partners determined there was an urgent need to offer prenatal education for Spanish-speaking women in their native language which also reflected Hispanic cultural practices, values, and beliefs. In addition, it was critical to recognize the heterogeneity of Hispanic women, including nativity, and develop resources to enhance understanding by offering examples and word options in different dialects as appropriate.

Baby Talk Prenatal Education Program. Baby Talk provides six free, two-hour prenatal education classes[10] promoting maternal and infant health through risk-reduction strategies and healthy decision-making (Table 1). Classes utilize a variety of education formats including lecture, video, demonstration, and hands on activities. Participants who complete all six classes receive an infant health or safety item (i.e., car seat, portable crib). Beginning in November 2015, Baby Talk was offered in English at five locations throughout Sedgwick County. Outcome data suggested significant improvements in knowledge, intentions,[10] and behavior[11] related to self- and infant-care choices.

Table 1. Baby talk curriculum topics.

Session	Title	Key topics*
1	You and your Pregnancy	Importance of early and regular prenatal care, oral health, signs and symptoms of preterm labor, common pregnancy complications, how to communicate with your provider
2	Healthy Pregnancy	Nutrition, physical activity, stress management, tobacco cessation and second-hand smoke exposure, infections and chemical exposures, work safety
3	Labor and Delivery	Benefits of a full-term pregnancy, pain coping strategies, birth plan, skin to skin
4	Feeding your Baby	Breastfeeding and its benefits, community resources for breastfeeding
5	Infant Care	Safe infant sleep, essentials for newborn care, bonding with your baby, vaccination, developmental milestones, school readiness
6	Healthy after Pregnancy	Postpartum depression, birth spacing, physical and emotional changes, healthy habits, postpartum care, healthy relationships

*Some topics, like mental health, are covered in multiple sessions, but only indicated in the primary session on the table.

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Community Collaborative. The Spanish Baby Talk Curriculum Development Committee (henceforth referred to as Committee) was a collaborative partnership between bilingual health professionals from Hispanic communities in Sedgwick County, Kansas. Committee members included doctors, nurses, medical translators, college students, and Baby Talk program staff. The Committee goal was to create culturally competent and linguistically appropriate curriculum. This group represented different origins, nationalities, and Spanish dialects from Mexico, Colombia, and Peru.

Due to the success of the English Baby Talk classes, the committee decided to utilize the framework of six 2-hour sessions, the same instruction techniques when an equivalent Spanish version could be employed (e.g., video, handout); and offer the same infant health and safety items. The Committee translated Baby Talk materials to Spanish, offering word options in different dialects as appropriate. The dialect for Mexico, Colombia, Peru, and most of Central and South America is very similar and sometimes referred to as Latin American Spanish, though there are often different words with the same meaning in English. Additionally, Spanish-speakers in the U.S. may have their own didact in which words may be formed from a mix of Spanish and English words and the meaning will depend on the origin.

The original Baby Talk program content was health focused and evidenced-based, therefore, the Committee's primary goals were to ensure material was translated to Spanish and presented in a way that would be perceived positively by participants. The Committee discussed examples provided within the six sessions and how those might be modified to be culturally appropriate. For example, the nutrition and exercise session provided examples of the importance of caloric balance during pregnancy. The English curriculum used cakes and cupcakes as examples but other countries use the words "pastel", "torta", "tarta", or "bizcocho". The curriculum was modified to reflect the traditions and culture of participants better, with additional suggestions included in the instructor facilitation guide to ensure program content was appropriate, respectful, and engaging for Hispanic participants. All translated materials were approved by the Committee for cultural appropriateness.

Conceptual Framework. The development of Spanish Baby Talk classes, materials, and resources was framed around the Health Belief Model[12] and the cultural appropriateness framework.[13] The Health Belief Model considers modifying factors and individuals' beliefs to impact behavior change; these include susceptibility, seriousness, benefits, and barriers to a behavior, cues to action, and self-efficacy. All perceived barriers and strategies for addressing them were reviewed. For example, the Committee considered Hispanic women's perceived threats during pregnancy, such as fear of not being able to communicate with doctors and staff at prenatal appointments, which coincided with literature on racial and ethnic disparities in health care.[14] Another example was lack of knowledge regarding methods of contraception and myths regarding certain methods. Benefits of participating in the program and implementing learned health practices to optimize participant's and baby's health also were addressed. Cues to action for both program participation (e.g., binders, reminder calls) as well as behavior change (e.g., safe sleep door hangers) were assessed for cultural appropriateness when modifying the curriculum.

The cultural appropriateness framework includes five strategies for enhancing cultural appropriateness in health promotion: 1) peripheral, 2) evidential, 3) linguistic, 4) constituent-involving, and 5) sociocultural.[13] Peripheral strategies focus on preparing program and/or materials so they appeal to specific groups, in this case pregnant Hispanic women. Videos and images featuring Hispanic women, infants, and families helped to address this strategy. Evidential strategies focused on perceived relevance of a health issue to a specific group. This was achieved by sharing trends in infant mortality, as well as behaviors that impact pregnancy outcomes. Linguistic strategies centered on ensuring content was linguistically appropriate, beyond a direct translation. To achieve this, the Committee focused on examples and how those would be perceived by different Hispanic communities. Using this information, a facilitator guide was created with talking points and appropriate ways to introduce topics. Constituent-involving strategies centered on drawing from the experiences of members of the priority group.[13] In efforts to achieve cultural appropriateness, the Committee consisted of Baby Talk program staff and Hispanic community members and professionals with lived experiences in perinatal health. Lastly, sociocultural strategies focused on building the cultural values of Hispanic communities and discussing health-related issues within the context of those value systems. For example, family connection is one of the most important values of Hispanic culture.[13] Participants were encouraged to bring family members (i.e., children, husbands, partners, cousins) with them to classes to participate in learning.

Due to the language and content modifications, the aim of this pilot study was to assess the newly developed Spanish Baby Talk curriculum to provide a baseline for program evaluation and improvement.

METHODS

This study was mixed methods research employing quantitative and qualitative methods; the latter of which utilized a thematic analysis methodology. Study procedures were approved by the University of Kansas School of Medicine-Wichita Human Subjects Committee.

Participants. Three cycles of Spanish Baby Talk (July 2017 to June 2018) were conducted at Hunter Health Clinic, a Federally Qualified Health Center (FQHC). Each cycle included six weekly 2-hour sessions taught by a bilingual instructor. Spanish-speaking pregnant women, less than 32 weeks gestational age, and their support persons were invited to attend. Potential participants were referred by clinic case managers or social workers at community events or had contacted the Baby Talk program to see if Spanish classes were available. If a participant missed a session, they were given the opportunity to participate in one of the subsequent cycles. Program consent was obtained prior to the initial session. At the initial session, participants received a 3-ring binder including handouts and resources pertaining to each session topic.[10]

At the conclusion of class cycles, participants were invited to participate in this study. Inclusion criteria were: 1) completion of four or more Spanish Baby Talk sessions, 2) preferred language Spanish, and 3) able to provide informed consent. Study consent was obtained

verbally for those who participated in phone interviews and written consent was obtained prior to focus group participation. Study participants received diapers ($20 value) following participation.

Data Collection

Surveys. Surveys were collected from all participants at three timepoints: 1) prior to the first session (initial survey; 45 questions), 2) after the sixth session (completion survey; 62 questions), and 3) by phone at 6-weeks postpartum (birth outcome; 26 questions). These surveys were translated versions of evaluation tools developed by Kansas Department of Health and Environment to assess Baby Talk and similar programs across the state. Most items were multiple choice, with a few open-ended questions. Due to skip logic, not all participants answered all questions. Participants had the right to refuse to answer any questions.

Initial and completion survey questions included knowledge and intentions regarding modifiable risk factors. On the completion survey, participants were asked to rate their overall experience with Baby Talk on a Likert scale from 1 (excellent) to 4 (poor), comfort level in the classes from 1 (strongly agree) to 5 (strongly disagree), Spanish curriculum difficulty from 1 (very hard) to 5 (very easy), and program value from 1 (not valuable) to 5 (extremely valuable). For instructor feedback, participants were given a list of descriptors such as lively, boring, did not know the topics well, helped me with my problems, and encouraged to ask questions and respondents were asked to select all that described the instructor. Participants were asked if they felt supported by the instructor and by other women attending the class on a scale of 1 (strongly agree) to 5 (strongly disagree). Birth outcome survey questions related to mode of delivery, gestational age, birthweight, breastfeeding, and other infant and self-care behaviors.

Phone Interviews. At the conclusion of the second cycle, brief phone interviews were conducted (January 2018 to April 2018). A trained bilingual research assistant not familiar to participants conducted interviews using a standardized script. The interview consisted of questions relating to motivation to participate in the prenatal education program, Spanish Baby Talk promotional strategies, program strengths, areas for improvement, and concerns regarding access to prenatal care within their community. The interviews lasted approximately 20 minutes.

Focus Group. Based on initial interview responses, program participants who attended the third cycle were invited to a focus group to build a shared understanding of Spanish Baby Talk's strengths and weaknesses. The focus group was held immediately following the final session of the third cycle (June 13, 2018). The focus group offered participants the opportunity to share opinions openly in the security of a group setting and for the facilitator to work toward group consensus. Facilitation and analysis of the focus group followed the standards of Stewart and Shamdasani[15] and Krueger and Casey[16]. The focus group followed a similar script as the phone interviews and was co-facilitated by the research assistant and a bilingual health professional; neither was familiar to the participants. The focus group lasted 30 minutes.

Statistical Analysis. Initial and completion surveys were matched to assess knowledge and behavioral intention changes. Quantitative data were summarized using central tendency and frequency measures using IBM® SPSS Statistics 23.

Focus groups and interviews were audio recorded, transcribed, and translated to English. Qualitative results were analyzed using the Consolidated Criteria for Reporting Qualitative Research Checklist (COREQ).[17] Transcripts were reviewed independently by two coders for common themes. Members of the research team reviewed the transcripts to ensure agreement with initial themes. Disagreements were discussed until group consensus was reached.

RESULTS

Three cycles of Spanish Baby Talk were held with a total of 15 pregnant women. Three participants were excluded from the study; one was unable to provide consent and two could not be reached for interviews. Of the remaining women (n = 12), six completed phone interviews and six participated in the focus group. As such, seven recordings were analyzed.

Demographics. Of the 12 participants, 75.0% (n = 9) were in their second trimester (14 - 27 weeks) at enrollment. Participants averaged 34 years of age (SD = 5 years) and had households of at least four people, with at least two children (33.3%; n = 4) in residence (Table 2). Only 25.0% (n = 3) reported any English proficiency. Most (75.0%; n = 9) were unemployed and uninsured or self-pay.

Survey Results

Knowledge and Intentions. Initial and completion surveys were completed by 91.7% of participants (n = 11; Table 3). On the initial survey, all participants (100.0%; n = 11) correctly identified full-term pregnancy as 39 weeks or more and that infants should sleep in a crib or portable crib. No participants were able to identify the benefits of a full-term pregnancy and only one (8.3%; n = 1) identified benefits of breastfeeding; both variables significantly increased at program completion. In addition, an increase in likelihood to inform other caregivers of safe sleep practices was noted. Participants were provided a list of 10 different potential postpartum symptoms and asked to select all that are considered normal for a mother to experience after delivery. The list included differences in bladder control, night sweats, baby blues for a day or two, and needing to nap; all of which are common symptoms, however, upon completion only two (18.2%) identified all symptoms. Other symptoms included in this list were excessive bleeding, fever, extreme fatigue, non-stop crying, panic for no reason, and lack of interest in your baby which are symptoms of a physical concern or postpartum depression.

Satisfaction. Completion survey results indicated all respondents (100.0%; n = 11) described their Spanish Baby Talk experience as "excellent". All felt a connection to and supported by other pregnant women in the classes and by the instructor. The instructor was described by all (100.0%; n = 11) as lively and knowledgeable. Most respondents indicated all sessions were "very" (54.5%; n = 6) or "extremely" (36.4%; n = 4) helpful; one (9.1%) indicated sessions were "somewhat" helpful. While most (90.9%; n = 10) reported the curriculum as "very easy" (54.5%; n = 6), "easy" (27.3%; n = 3), or "just right" (9.1%; n = 1) to understand, one (9.1%) reported it was "hard" to understand.

Table 2. Patient demographics (n = 12).

Demographics	Participants; n (%)
Household size	
4	4 (33.3)
5	2 (16.7)
6	2 (16.7)
7	2 (16.7)
8	1 (8.3)
Missing	1 (8.3)
Children < 18 years old in the home	
2	4 (33.3)
3	3 (25.0)
4	2 (16.7)
5	1 (8.3)
Missing	2 (16.7)
English proficiency	
Yes	3 (25.0)
No	9 (75.0)
Education level	
< High school	5 (41.7)
High school or GED	5 (41.7)
Vocational certification/license	1 (8.3)
Missing	1 (8.3)
Employment	
Unemployed	9 (75.0)
Occasional/seasonal	1 (8.3)
Missing	2 (16.7)
Insurance	
None/self-pay	9 (75.0)
KanCare/Medicaid	1 (8.3)
Missing	2 (16.7)
Gestation at enrollment	
1st trimester (1 - 13 weeks)	1 (8.3)
2nd trimester (14 - 27 weeks)	9 (75.0)
3rd trimester (28+ weeks)	2 (16.7)
Pregnancy risks	
High risk pregnancy	3 (25.0)
Barriers attending prenatal care	2 (16.7)

Birth Outcomes. Outcomes were collected from 72.7% (n = 8). Three (37.5%) delivered at 39 weeks gestation or after, four (50.0%) delivered between 37 to 38 weeks, and one (12.5%) delivered before 36 weeks due to pregnancy complications. Half (n = 4) were induced due to medical necessity. Six (75.0%) had vaginal deliveries and two (25.0%) had cesarean deliveries, one due to medical complications and one for unknown reasons. All (100%; n = 8) indicated infant birth weight of 5 pounds and 8 ounces or more.

Participants were asked three yes/no questions regarding whether any of the information from the Spanish Baby Talk classes (1) impacted their decision to breastfeed, (2) how long to breastfeed, and (3) their confidence to breastfeed. Six participants (75.0%) indicated Spanish Baby Talk classes impacted all three of these variables. At the time, outcomes were collected, 62.5% (n = 5) were breastfeeding. An additional 25.0% (n = 2) indicated having breastfed their baby in the past though were not breastfeeding currently.

Table 3. Initial and completion knowledge and behaviors (n = 11).

Maternal survey responses	Initial	Completion
Knowledge, n (%)		
Normal postpartum symptoms	1 (9.1)	2 (18.2)
Full-term is 39 weeks or more	11(100.0)	11 (100.0)
Benefits of full-term pregnancy	0 (0.0)	8 (72.7)*
Benefits of breastfeeding	1 (9.1)	8 (72.7)*
Signs of preterm labor	4 (36.4)	6 (54.5)
Resources to support breastfeeding	7 (63.6)	10 (90.9)
Behaviors, n (%)		
Daily prenatal vitamin	7 (63.6)	8 (72.7)
Daily moderate exercise	10 (90.9)	11 (100.0)
Very likely to breastfeed	7 (63.6)	11 (100.0)
Safe sleep, n (%)		
Back positioning	7 (63.6)	10 (90.9)
Crib or portable crib	11 (100.0)	10 (100.0)^
Inform other caregivers	8 (72.7)	11 (100.0)*

* Significant change, $p < 0.05$
^ One participant did not respond this question on the Completion survey.

All participants (100.0%; n = 8) indicated they had attended or planned to attend their postpartum visit, talked to their provider about contraception, and were using or planning to use a contraception method. The most prevalent method was hormonal injection (50.0%; n = 4).

Focus Group and Interview Results

Four themes were identified: 1) lack of accessible community resources, 2) sense of community, 3) program strengths, and 4) areas for improvements (Table 4).

Theme 1: Lack of Accessible Community Resources. Lack of accessible community resources and inability to identify available resources were acknowledged as barriers to optimal pre- and postnatal care. Participants reported struggling to determine what the Sedgwick County community was doing to support pregnant women and their children, especially those who had limited or no English proficiency. In this context, the term community was explained as both the geographic and environmental setting where participants lived, worked, played, and grew. Participants also reported a disconnection from the greater community that made it difficult to learn about existing resources. One participant stated, "In my experience, I have not received any support... right now if I were going through that [postpartum depression], I would not know where to go. I would not know who could help me."

Table 4. Qualitative findings.

Emerging themes	Definition	Quote(s)
Lack of accessible community resources	Language barriers within their communities caused a disconnect that perpetuated the lack of knowledge of available resources for Spanish-speaking women who are pregnant or have recently delivered.	*"The reality is that I do not know what is being done in my community to support women who are pregnant."*
Sense of community through Spanish Baby Talk	Group dynamics as sources of accountability and support.	*"I liked [the classes] a lot; you learn and get to spend time with people."*
Spanish Baby Talk strengths	Program provided a high-quality and safe setting to facilitate learning process.	*"The instructor was nice and helpful... great at explaining everything."*
Areas for improvement	Expansion of marketing and promotional strategies to Hispanic communities.	*"Having a direct line [with a] Spanish representative is important because there are people that get frustrated when they can't understand you."*

All focus group participants (n = 12) indicated limited English proficiency and a major concern was not being able to communicate with others in the community or in health care settings. One participant stated, "No one in my community speaks English". Some participants discussed the inability to vocalize concerns regarding their pregnancy to health professionals because of limited English or discomfort using a translator.

On the positive side, participants described Spanish Baby Talk as, "Helping to begin to break down resource barriers for pregnant women in [their] community". Participants shared that the program provided them with basic knowledge of what community resources were available. Instructors shared resources for insurance determination, provided state insurance applications in Spanish, and made referrals to Spanish-speaking Out-station State Insurance Eligibility Specialists who could help participants complete applications, navigate any questions or concerns, and connect them with other payment programs if not eligible. Additionally, the instructor shared transportation resources available through insurance providers or FQHCs for prenatal appointments for participants who identified transportation as a barrier to seeking care. Information on organizations that provided education and free infant safety items, such as portable cribs, also were shared. Most participants were not familiar with these resources or hesitated to call or ask for resources at appointments due to fear of facing language barriers. Participants expressed feeling confident in their ability to share what they had learned with other women. They also reported plans to promote Spanish Baby Talk to family and friends.

Theme 2: Sense of Community. Participants described the classes as fostering a sense of community and as a safe and inviting place where they could share stories and ask questions. One stated, "I enjoyed it because you learned something and get to share experiences with other women". Another said, "I like how they explained things, the topics that were discussed, and the sense of community that I felt with the people you came to class with". Participants mentioned originally being motivated to come to receive the educational support materials but found further benefit. One mentioned, "I went for the car seat but stayed for the people and the conversation". Participants reported Spanish Baby Talk offered them a safe space to build relationships with other expecting mothers, which created what participants described as a sense of trust and encouraged them to talk more freely about fears, concerns, and frustrations. Sharing stories, conversation, and fostering relationships with other pregnant women were their primary reasons for remaining in class. One participant said, "I really like the program because they inform you, they help clarify doubts and provide a space to express what you're feeling. If you have doubts you would just say it and [Baby Talk] would help resolve them".

Theme 3: Program Strengths. Participants appreciated the opportunity to learn new information even though most were not first-time mothers. One stated, "I have two children...The information that they [Baby Talk] give helps you understand, I don't know how I got through my other pregnancies without knowing this information". Other participants expressed gratitude and appreciation for the opportunity to learn, they shared, "There is a lot of us that do not know a lot of [this] information. I mean our world is different and I come from a ranch where you do not learn about many thing". Another said, "Many times we get pregnant, but we don't learn the precautions we should take while pregnant". A third participant added, "I was really confused about the family planning methods and the program really opened my eyes".

Participants discussed the high quality of the program, from instructors to content. They described instructors as open, willing to answer questions, kind, and knowledgeable about community resources and prenatal health. One stated, "The instructor's behavior was excellent". Another said, "She did not want us to leave with questions". While a third stated, "I think everything was explained and the instructor evoked trust and the material was very complete". Several participants also mentioned completeness of the material and, specifically, that it addressed pregnancy precautions and complications. Other participants described the tangible materials (i.e., handouts and brochures) and information as valuable and stated they felt confident in their ability to share information with other women. Program strengths were viewed as optimizing participants' prenatal care.

Theme 4: Areas for Improvement. Most participants indicated having seen flyers or brochures at clinics for English Baby Talk prior to its availability in Spanish but were not sure what the program entailed because content was in English. In reflecting on why they decided to attend, participants indicated being referred by hospital social workers, community programs, through community baby shower events, or seeing promotional materials. One said, "I would have liked to have learned about the program from the first moment I went to the clinic". Participants reported a greater need for marketing and promotional materials that clearly communicated the purpose of the program. One stated, "The promotion flyer could be interpreted as talking about your baby" and indicated that the direct translation of "Baby Talk" in Spanish may not be the optimal way to engage Spanish speakers, which other

participants echoed. Another shared, "I was too shy to ask someone in the clinic front desk because I didn't want to disturb, and they had other people to attend to". A third stated, "It would be good that this was included in both languages and had a direct contact number for Spanish representative". Participants further reported the need to expand Spanish Baby Talk marketing strategies outside of the clinic to Hispanic communities, especially stores, restaurants, and transit. Finally, participants reported needing essentials like formula, food, clothing, and diapers. As such, they recommend Spanish Baby Talk more directly promote organizations providing such resources.

DISCUSSION

The Spanish Baby Talk curriculum was developed to address a need for pregnancy education and support for Spanish-speaking women. The community collaborative provided a team to translate and review materials to ensure the curriculum would support Hispanic women from various origins. This study assessed the women's responses to the modified materials to evaluate whether they were appropriate for Spanish-speaking communities.

Findings from initial and completion surveys suggested the program curriculum can be translated successfully to educate non-English speaking communities, as evidenced by increases in participants' knowledge regarding benefits of full-term pregnancy and breastfeeding. This also was reflected in the birth outcome survey, where most participants reported breastfeeding or having tried to breastfeed. Positive trends also were seen for other knowledge and behavior variable though statistical significance was not reached.

Birth outcomes related to gestational age and delivery method reflected the high-risk nature of the population served by FQHCs, and the importance of collaboration with such entities. Differences in preterm birth rates for this population have not been explained fully, however, there is evidence that socioeconomic disparities[18] and acculturation[19] play roles. Early enrollment into prenatal education (i.e., first trimester) may allow more time to impact these outcomes.

Feedback from participants addressed program strengths and areas for improvement, as well as community needs regarding prenatal support. One common theme was the importance of addressing language barriers, as these can inhibit prenatal care experiences and likelihood of seeking further care.[8] While no specific needs for language changes were identified within the curriculum, participants highlighted the importance of clearly promoting Spanish Baby Talk and recommended community-based promotion to reach Hispanic women. Some participants were exposed to promotion materials for English Baby Talk, which may have introduced confusion. This informed an opportunity to grow and move towards cultural appropriateness by allowing program staff to review recruitment/engagement strategies and marketing materials to ensure messaging is clear but also relatable for potential participants. Tan and Cho[20] discussed the importance of ensuring health professionals do not assume that translating a message to a group's native language makes it more accessible. It is important to consider differences in customs, values, and belief systems when designing messaging not only for Hispanic communities but all groups. Although the curriculum was reviewed thoroughly to ensure examples and health practices presented in classes were respectful and mindful of cultural values and beliefs, more can be done with marketing and recruitment to enhance appropriateness and continue to move towards competence.

Both completion survey and qualitative findings indicated the instructor as a program strength. Participants highlighted the instructor's ability not only to project themselves as a health professional, but also as a peer to build rapport and promote questions and discussion. More specific instructor screening or training to ensure qualities, values, and characteristics match participants priorities would benefit the program. Another strength of the program was the group format, which allowed participants to build relationships with other Hispanic women in attendance. Participants indicated feeling thankful to be able to share and connect with other women who may face similar struggles. High levels of social support have been found to enhance healthy behaviors during pregnancy for women of Mexican descent.[21] Participants reported they wanted to access the support Baby Talk provided even after baby was born. Bridging the gap between services to be able to refer participants to other programs, especially postnatal support, is essential.

Limitations of this study included small sample size, lack of a control group, single class location, and potential for social desirability response bias. However, results appeared to be consistent across multiple forms of data collection and across three separate cohorts of participants.[22] Although some of the barriers and values shared by participants were generalizable to Hispanic communities, this study had a small sample size. Health educators must not assume all Hispanics are the same and face the same struggles with regards to pre- and postnatal care. Within Hispanic culture, values and beliefs are not necessarily universal. For this reason, when developing public health programs, health campaigns, or materials prioritizing Hispanic communities, it is essential to consider the primary audience, what is known about their culture and subcultures, and how these variables relate to health behaviors.[13] For example, in this study, most participants were unemployed. If women who participated primarily were employed, this could have impacted their flexibility to attend the program or simply yielded a different experience.

Future research should assess behavioral and health outcomes for program participants in comparison with a control group to assess impact on birth outcomes. More research is needed on implementing additional cultural appropriateness strategies to continue the move towards cultural competence. Public health practitioners should consider these findings in the development of programs or resources for women who speak Spanish. Facilitating resource attainment, breaking down language barriers, and developing a network for perinatal support may promote positive birth outcomes.

CONCLUSIONS

There is a dearth of literature regarding perinatal support and outcomes for Spanish-speaking U.S. women. This study began to fill the void by describing the development of a comprehensive prenatal educational program for Spanish-speaking pregnant women. Collaboration with community partners supported the development of a linguistically appropriate curriculum. Spanish prenatal education offered a space for participants to share stories and listen to other perspectives, which facilitated the development of a sense of community. Feedback from participants highlighted the importance of cultural competence, not only in program curriculum, but also in marketing strategies. Results illustrated the importance of the class environment to foster trust and a sense of community for Spanish-speaking pregnant women. Findings helped the program tailor tools and marketing strategies to engage this population better and can serve as a baseline for other community programs in how to move toward cultural competency as they serve diverse groups.

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Hematologic Involvement as a Predictor of Mortality in COVID-19 Patients in a Safety Net Hospital

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ABSTRACT

Introduction. COVID-19 affects the hematologic system. This article evaluated the impact of hematologic involvement of different blood cell line parameters of white blood cells including absolute neutrophil count (ANC), hemoglobin, and platelets in COVID-19 patients and their association with hospital mortality and length of stay (LOS).

Methods. This was a retrospective study of 475 patients with confirmed positive COVID-19 infection and hematologic abnormalities in the metropolitan New York City area.

Results. Elevated absolute neutrophil count (OR: 1.20; 95% CI: 1.02-1.42; $p < 0.05$) increased days of hematologic involvement (OR: 4.44; 95% CI: 1.42-13.90; $p < 0.05$), and persistence of hematologic involvement at discharge (OR: 2.87; 95% CI: 1.20-6.90; $p < 0.05$) was associated with higher mortality. Higher hemoglobin at admission (OR: 0.77; 95% CI:0.60-0.98; $p < 0.001$) and platelets peak (OR: 0.995; 95% CI: 0.992-0.997; $p < 0.001$) were associated with decreased mortality. Patients with higher white blood cell peak (B = 0.46; SE = 0.07; $p < 0.001$) and higher hemoglobin at admission (B = 0.05; SE = 0.01; $p < 0.001$) were associated with higher LOS. Those with higher hemoglobin nadir (B = -0.06; SE = 0.01; $p < 0.001$), higher platelets nadir (B = -0.001; SE = < 0.001; $p < 0.001$), and hematologic involvement at discharge or death (B = -0.06; SE = 0.03; $p < 0.05$) were associated with lower LOS.

Conclusions. These findings can be used by clinicians to better risk-stratify patients with hematologic involvement in COVID-19 and tailor therapies potentially to improve patient outcomes.

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INTRODUCTION

Coronavirus Disease (COVID-19), caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), was declared a pandemic crisis in March 2020 by the World Health Organization.[1] COVID-19 has claimed over 2 million lives and has had a profound public health impact worldwide.[2] The spectrum of COVID-19 disease varies from asymptomatic to severe cases requiring Intensive Care Unit (ICU) level of care and intubation. Severe COVID-19 commonly is complicated by development of multiorgan involvement,[3,4] including hematologic and hematopoietic dysfunction.[5] Studies of hematologic involvement in COVID-19 demonstrated its manifestation mostly in the form of thromboembolic events[6] with an unadjusted mortality of 24 - 50%.[7,8]

Several risk factors are described for severe COVID-19 disease, including older age, hypertension, diabetes mellitus type 2, morbid obesity, and chronic lung disease.[6] There are mixed findings for male gender where some report an increased association for severe COVID-19 disease,[9] while others do not report an association.[10] Race and ethnicity also has mixed findings where some report that Hispanics have a higher incidence of infection[11] and African-Americans have a higher mortality rate in COVID-19[12,13] while others do not report an association.[14,15] Some report that lack of health insurance was associated with increased SARS-CoV-2 infection.[12] The authors were not aware of any studies on the impact of many demographic variables for COVID-19 patients with hematologic involvement.

Anemia and abnormalities of iron metabolism markers may be associated with increased mortality in patients with COVID-19.[5,16] Similarly, thrombocytopenia is a common feature in patients with severe COVID-19.[17] The presence of elevated hematologic inflammatory markers (i.e., pro-inflammatory cytokines) and neutrophil-to-lymphocyte ratio may be indicators for severity of COVID-19 disease.[18] However, other key hematologic variables such as absolute neutrophil count (ANC) have not been studied as a predictor for mortality and disease severity in COVID-19. A meta-analysis of Chinese studies summarizing the impact of COVID-19 on all blood cell lines found an association between COVID-19 and increased hypercoagulability.[5] Another meta-analysis of Chinese studies that compiled laboratory findings in patients with COVID-19 suggested that increased white blood cells (WBC), low platelets, and high interleukin-6 (IL-6) levels may be useful clinically in predicting severe and fatal COVID-19.[7] The impact of hematologic involvement in all blood cell lines parameters and its association with COVID-19 disease mortality and length of stay (LOS) have not been well investigated.

This paper describes hematological involvement in patients with COVID-19. The authors conducted multivariate analyses for the association of demographics and different blood cell lines parameters of WBC including absolute neutrophil count (ANC), hemoglobin, and platelets to study their association with COVID-19 mortality and LOS in patients with hematological involvement.

METHODS

Study Subjects. This was a retrospective study of 475 patients with confirmed COVID-19 and hematologic involvement that were admitted to a safety-net hospital in suburban New York City from March 1, 2020 through May 15, 2020. All patients were 18 years of age or older. Diagnosis of COVID-19 was confirmed by a positive reverse transcriptase polymerase chain reaction (RT-PCR) showing SARS CoV-2 RNA. Hematologic involvement was defined as the abnormal laboratory value of any of the following blood cell lines components: WBC including ANC, hemoglobin, and platelets. All patients were followed until

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completion of their hospital course whether alive or deceased. Ethical approval was received from the hospital Institutional Review Board to conduct this study. A waiver for informed consent was received due to the retrospective nature of the study.

Variables. Demographic variables were age (years), gender (male/female), and race/ethnicity (Caucasian, Hispanic, African American, East Asian, and Southeast Asian (i.e., Indian, Afghan, Pakistani, Bangladeshi, Thai), and Other). Insurance status had categories of private, uninsured, or emergency Medicaid (i.e., Medicaid issued during this hospitalization), regular Medicaid, and Medicare.

Comorbidities were obesity (body mass index (BMI) ≥ 30.0 kg/m^2), sickle cell disease, other hematologic disorders, excluding those that are included in the Charlson Comorbidity Index (CCI), and use of immunosuppressive medications in the past six months such as chemotherapy, steroids, disease-modifying antirheumatic drugs, and others (i.e., tacrolimus, sirolimus, JAK-inhibitors). The CCI was calculated (range: 0 - 37), which predicts a 10-year survival rate based on a series of comorbid conditions of age, history of myocardial infarction, heart failure, peripheral vascular disease, cerebrovascular accident, dementia, chronic obstructive pulmonary disease, connective tissue disease, peptic ulcer disease, chronic liver disease, diabetes mellitus, renal disease, solid tumor, leukemia, lymphoma, and AIDS status.[19,20]

Disease severity indicators were Intensive Care Unit (ICU) level of care (defined as hospitalization in a critical care area, use of vasopressor medication, or supplemental oxygen use with requirement of a fraction of inspired oxygen (FiO_2) above 55%), Quick Sepsis Related Organ Failure Assessment (qSOFA) score (range: 0 - 3) upon admission (identifies non-ICU high risk patients and estimates their mortality based on a 3-point scoring),[21] invasive mechanical ventilation upon admission, and highest supplemental oxygen requirement during hospitalization (none, low $FiO_2 \leq 55\%$, high $FiO_2 > 55\%$, and use of invasive mechanical ventilation).

Treatment and management included the use of any vasopressor medication, any antibiotic, nonsteroidal anti-inflammatory drugs (NSAIDs), angiotensin converting enzyme inhibitors (ACEI), and angiotensin II receptor blockers (ARBs), antiviral (remdesivir), antimalarial, any steroid medication regardless of dosage, convalescent plasma from COVID-19 survivor donors, interleukin inhibitors (anti-IL-6 monoclonal antibodies - tocilizumab), and therapeutic dosage of anticoagulant medications.

Number of organs involved was defined as the sum of organs that were impaired or involved during admission. This involved organs of neurological system, renal system, cardiovascular system, liver organ system, endocrine system, musculoskeletal system, and hematologic system.

Hematologic involvement was considered if one of the following parameters were present: hemoglobin more than 16.0 g/dL or less than 12.0 g/dL, WBC less than 4,000 k/mm^3 or more than 11,000 k/mm^3, ANC of less than 1.80 k/mm^3 or more than 7 k/mm^3, and platelet count less than 150 k/mm^3 or more than 450 k/mm^3. Authors collected the WBC peak and nadir, ANC nadir, platelet peak and nadir, and hemoglobin at admission and nadir. Peak and nadir were defined as the highest and the lowest recorded value during the hospitalization respectively, regardless of normal or abnormal. WBC proportion days involved was defined as the total number of days that WBC count was abnormal divided by the total number of days of hospitalization. ANC proportion days involved was calculated by dividing the total number of days that ANC was abnormal by the total number of days of hospitalization. Days-to-hematologic-involvement was defined as the total number of days from admission until the first day of hematologic involvement. Persistent hematologic involvement at the time of discharge or death also was recorded. The outcome variables were mortality and LOS. Admission levels of lactate dehydrogenase (LDH), erythrocyte sedimentation rate (ESR), interleukin-6 (IL-6), ferritin, D-dimer, C-reactive protein (CRP), fibrinogen, prothrombin time (PT) peak level, and International Normalized Ratio (INR) peak level also were collected and described.

Statistical Analysis. Mean and standard deviation were used to describe the continuous variables. Frequency and percentage were used to describe the categorical variables. Two models were used to analyze the separate outcome variables of mortality and LOS. Model 1 consisted of univariate analyses that included demographic, comorbidities, disease severity, and treatment management variables. Model 2 consisted of a multivariate analysis that included all the significant variables in the univariate analyses from Model 1 and added hematology variables. Mortality was analyzed with logistic regression. LOS was analyzed with linear regression. Logarithmic transformations were calculated for the skewed variables. The p values were two-sided. IBM® SPSS Statistics version 26 was used for the analyses (IBM® SPSS Statistics for Windows®. Version 26. Armonk, NY: IBM® Corporation; 2019).

RESULTS

Table 1 describes the sample characteristics. Mean age was approximately 61 years, more than one-third were female, slightly less than two-thirds were those from either African American or Hispanic race/ethnicity, more than one third had regular Medicaid, and more than a third met criteria for obesity. Almost two thirds of patients that met the criteria of ICU level of care, and less than 10% of patients were intubated on the day of admission. Slightly over a third of patients with hematologic involvement required mechanical ventilation, and only 10% of patients did not require supplemental oxygen during the admission. The mean CCI was 3.0 (the CCI score of 3 signifies that there is a 77% 10-year survival)[20] and the mean qSOFA was 1.5 (the qSOFA score of 2 signifies 3-to-14-fold increase in in hospital mortality)[21]. The mean number of organs involved was 4.8 organs. The most frequent interventions were antibiotics, antimalarial medications, and steroids. Mortality was at 42.9% and mean length of stay was 12.8 days.

Table 1. Sample characteristics of 475 COVID-19 patients.

Variables	Mean (SD) or Frequency (%)
Demographics	
Mean age (years)	60.9 (15.75)
Sex (female)	171 (36.0)
Race/ethnicity	
Caucasian	125 (26.3)
African American	115 (24.2)
Hispanic	198 (41.7)
East Asian	16 (3.4)
Southeast Asian	11 (2.3)
Other	10 (2.1)
Insurance	
Private	103 (21.7)
Uninsured/emergency Medicaid	98 (20.6)
Regular Medicaid	179 (37.7)
Medicare	95 (20.0)
Comorbidities	
Sickle cell disease (yes)	3 (0.6)
Other hematologic disorders (yes)	3 (0.6)
Immunosuppressive medications at home (yes)	24 (5.1)
Obese (yes)	177 (37.3)
CCI [mean]	3.0 (2.45)
qSOFA [mean]	1.5 (0.65)
Disease severity	
ICU (yes)	301 (63.4)
Intubation admission (yes)	41 (8.6)
Oxygen requirement hospitalization	
None	48 (10.1)
Low FiO_2 (< 55%)	130 (27.4)
High FiO_2 (> 55%)	127 (26.7)
Ventilation	170 (35.8)
Treatment management	
Vasopressor (yes)	117 (24.6)
Antibiotic (yes)	454 (95.6)
NSAID (yes)	118 (24.8)
ACEi/ARBS (yes)	61 (12.8)
Antiviral (yes)	14 (2.9)
Antimalarial (yes)	392 (82.5)
Steroid (yes)	206 (43.4)
Convalescent plasma (yes)	50 (10.5)
Interleukin inhibitor (yes)	72 (15.2)
Anticoagulant (yes)	121 (25.5)
Organ involvement	
Mean number organs involved	4.8 (1.62)
Hematology	
Mean white blood cell peak	16.4 (11.45)
Mean white blood cell nadir	6.7 (3.80)
Mean absolute neutrophil count nadir	6.2 (3.92)
Mean hemoglobin admission	12.8 (2.36)
Mean hemoglobin nadir	10.5 (2.56)
Mean platelets peak	350.7 (154.67)
Mean platelets nadir	191.6 (92.52)
Mean white blood cell proportion days involved	0.4 (0.30)
Mean absolute neutrophil count proportion days involved	0.2 (0.19)
Mean days to hematology involvement	2.2 (2.37)
Hematology persistent involvement at discharge (yes)	367 (77.3)
Mean lactate dehydrogenase	663.8 (504.63)
Mean erythrocyte sedimentation rate	69.9 (32.60)
Mean interleukin level (pg/mL)	179.8 (496.07)
Mean ferritin level (ng/mL)	1,612.1 (1,919.01)
Mean D-dimer (µg/ml)	4.6 (5.71)
Mean C-reactive protein (mg/L)	18.2 (10.62)
Mean fibrinogen (mg/dL)	565.1 (209.10)
Mean prothrombin time peak (seconds)	16.0 (5.45)
Mean international normalized ratio peak	1.3 (1.09)
Outcomes	
Mortality (yes)	204 (42.9)
Mean length of stay (days)	12.8 (13.17)

Abbreviations: SD, standard deviation; CCI, Charlson Comorbidity Index; qSOFA, quick Sepsis Related Organ Failure Assessment; ICU, intensive care unit; FiO_2, fraction of inspired oxygen; NSAID, nonsteroidal anti-inflammatory drug; ACEi, Angiotensin-converting-enzyme inhibitors; ARB, angiotensin II receptor blockers.

The following variables were missing data and are only shown for descriptive purposes: lactate dehydrogenase level (n = 295), erythrocyte sedimentation rate (n = 133), interleukin (n = 67), ferritin (n = 300), D-dimer (n = 252), C-reactive protein (n = 301), fibrinogen (n = 161), prothrombin time peak (n = 357), and international normalized ratio peak (n = 365).

Table 2 shows logistic regression analyses for mortality. In the univariate analyses shown in Model 1, increased age, insurance of regular Medicaid and Medicare, increased CCI, increased qSOFA, ICU care, intubation at admission, oxygen requirement during hospitalization of high FiO_2 and ventilation, vasopressor, antiviral, steroid, and increased number organs involved each were associated significantly with increased odds for mortality. Hispanic race/ethnicity was associated significantly with decreased odds for mortality. In the multivariate analysis shown in Model 2, increased age, insurance of regular Medicaid, oxygen requirement during hospitalization of ventilation, increased number organs involved, increased absolute neutrophil count nadir, increased days to hematology involvement, and hematology persistent involvement at discharge each were associated significantly with increased odds for mortality. Increased platelets peak and increased hemoglobin admission were associated significantly with decreased odds for mortality.

Table 2. Logistic regression analyses for mortality.

Variables	Model 1 Univariate OR (95% CI)	Model 2 Multivariate OR (95% CI)
Demographics		
Age (years)	1.05 (1.04, 1.07)***	1.04 (1.01, 1.08)*
Sex (female)	0.98 (0.67, 1.44)	---
Race/ethnicity		
Caucasian	1.00	1.00
African American	0.78 (0.47, 1.30)	0.37 (0.13, 1.03)
Hispanic	0.56 (0.35, 0.88)*	0.66 (0.26, 1.68)
East Asian	1.31 (0.46, 3.73)	0.22 (0.03, 1.54)
Southeast Asian	0.85 (0.25, 2.92)	0.39 (0.05, 3.20)
Other	4.07 (0.83, 19.91)	10.67 (0.93, 122.22)
Insurance		
Private	1.00	1.00
Uninsured/emergency Medicaid	0.94 (0.52, 1.70)	1.21 (0.40, 3.68)
Regular Medicaid	1.75 (1.06, 2.91)*	3.68 (1.41, 9.61)**
Medicare	3.64 (2.02, 6.54)***	2.35 (0.68, 8.16)
Comorbidities		
Sickle cell disease (yes)	2.67 (0.24, 29.69)	---
Other hematologic disorders (yes)	2.67 (0.24, 29.69)	---
Immunosuppressive medications at home (yes)	1.92 (0.84, 4.42)	---
Obese (yes)	0.96 (0.66, 1.40)	---
CCI	1.30 (1.19, 1.41)***	1.03 (0.84, 1.26)
qSOFA	1.66 (1.24, 2.22)**	0.72 (0.42, 1.24)
Disease severity		
ICU (yes)	17.89 (10.03, 31.91)***	2.22 (0.38, 12.88)
Intubation admission (yes)	7.54 (3.27, 17.40)***	0.44 (0.11, 1.80)
Oxygen requirement hospitalization		
None	1.00	1.00
Low FiO_2 (< 55%)	1.92 (0.40, 9.08)	1.75 (0.32, 9.56)
High FiO_2 (> 55%)	15.94 (3.71, 68.61)***	7.82 (0.86, 70.91)
Ventilation	107.33 (24.69, 46.63)***	98.43 (8.84, 1,095.89)***
Treatment management		
Vasopressor (yes)	14.37 (8.19, 25.22)***	2.41 (0.83, 7.04)
Antibiotic (yes)	2.50 (0.90, 6.93)	---
NSAID (yes)	1.34 (0.88, 2.03)	---
ACEi/ARBS (yes)	0.84 (0.49, 1.46)	---
Antiviral (yes)	5.09 (1.40, 18.50)*	2.33 (0.29, 18.65)
Antimalarial (yes)	1.10 (0.68, 1.79)	---
Steroid (yes)	1.50 (1.04, 2.16)*	0.95 (0.44, 2.04)
Convalescent plasma (yes)	1.15 (0.64, 2.07)	---
Interleukin inhibitor (yes)	1.49 (0.90, 2.47)	---
Anticoagulant (yes)	1.00 (0.66, 1.52)	---
Organ involvement		
Number organs involved	2.94 (2.43, 3.57)***	1.69 (1.21, 2.36)**

Table 2. Logistic regression analyses for mortality. *continued.*

Variables	Model 1 Univariate OR (95% CI)	Model 2 Multivariate OR (95% CI)
Hematology		
White blood cell peak	---	0.70 (0.08, 6.30)
White blood cell nadir	---	0.93 (0.06, 15.59)
Absolute neutrophil count nadir	---	1.20 (1.02, 1.42)*
Hemoglobin admission	---	0.77 (0.60, 0.98)*
Hemoglobin nadir	---	1.25 (0.99, 1.57)
Platelets peak	---	0.995 (0.992, 0.997)***
Platelets nadir	---	1.00 (0.999, 1.01)
White blood cell proportion days involved	---	1.17 (0.27, 5.12)
Absolute neutrophil count proportion days involved	---	2.35 (0.24, 22.55)
Days to hematology involvement	---	4.44 (1.42, 13.90)*
Hematology persistent involvement at discharge (yes)	---	2.87 (1.20, 6.90)*

Abbreviations: OR, odds ratio; CI, confidence interval; CCI, Charlson Comorbidity Index; qSOFA, quick Sepsis Related Organ Failure Assessment; ICU, intensive care unit; FiO_2, fraction of inspired oxygen; NSAID, nonsteroidal anti-inflammatory drug; ACEi, Angiotensin-converting-enzyme inhibitors; ARB, angiotensin II receptor blockers.
*p < 0.05, **p < 0.01, ***p < 0.001, Model 2 Nagelkerke R Square = 0.76.

Table 3 shows linear regression analyses for LOS. In the univariate analyses shown in Model 1, ICU care, oxygen requirement during hospitalization of high FiO_2 and ventilation, vasopressor, antibiotic, NSAID, steroid, convalescent plasma, interleukin inhibitor, anticoagulant, and increased number organs involved each were associated significantly with increased LOS. East Asian race/ethnicity was associated significantly with decreased LOS. In the multivariate analysis shown in Model 2, steroid, convalescent plasma, interleukin inhibitor, white blood cell peak, increased platelets peak, and increased hemoglobin admission each were associated significantly with increased LOS. Increased white blood cell nadir, increased platelets nadir, increased hemoglobin nadir, increased white blood cell proportion days involved, increased absolute neutrophil count proportion days involved, and hematology persistent involvement at discharge each were associated significantly with decreased LOS.

Table 3. Linear regression analyses for length of stay.

Variables	Model 1 Univariate B (SE)	Model 2 Multivariate B (SE)
Demographics		
Age (years)	-0.001 (0.001)	---
Sex (female)	-0.07 (0.04)	---
Race/ethnicity		
Caucasian	Reference	Reference
African American	-0.07 (0.05)	-0.03 (0.03)
Hispanic	0.01 (0.04)	-0.03 (0.03)
East Asian	-0.23 (0.10)*	-0.03 (0.06)
Southeast Asian	0.02 (0.11)	-0.01 (0.07)
Other	0.19 (0.12)	0.03 (0.07)
Insurance		---
Private	Reference	
Uninsured/emergency Medicaid	0.07 (0.05)	
Regular Medicaid	-0.05 (0.05)	
Medicare	0.01 (0.05)	
Comorbidities		
Sickle cell disease (yes)	-0.28 (0.21)	---
Other hematologic disorders (yes)	0.31 (0.21)	---
Immunosuppressive medications at home (yes)	-0.06 (0.08)	---

Table 3. Linear regression analyses for length of stay. *continued.*

Variables	Model 1 Univariate B (SE)	Model 2 Multivariate B (SE)
Comorbidities		
Obese (yes)	-0.03 (0.04)	---
CCI	-0.004 (0.01)	---
qSOFA	0.02 (0.03)	---
Disease severity		
ICU (yes)	0.25 (0.03)***	0.05 (0.06)
Intubation admission (yes)	-0.07 (0.06)	---
Oxygen requirement hospitalization		
None	Reference	Reference
Low FiO_2 (< 55%)	0.09 (0.06)	0.02 (0.04)
High FiO_2 (> 55%)	0.25 (0.06)***	-0.01 (0.07)
Ventilation	0.34 (0.06)***	-0.11 (0.07)
Treatment management		
Vasopressor (yes)	0.17 (0.04)***	-0.03 (0.03)
Antibiotic (yes)	0.22 (0.08)**	0.09 (0.05)
NSAID (yes)	0.08 (0.04)*	0.03 (0.02)
ACEi/ARBS (yes)	-0.04 (0.05)	---
Antiviral (yes)	0.15 (0.10)	---
Antimalarial (yes)	0.08 (0.04)	---
Steroid (yes)	0.31 (0.03)***	0.06 (0.03)*
Convalescent plasma (yes)	0.50 (0.05)***	0.12 (0.04)**
Interleukin inhibitor (yes)	0.37 (0.04)***	0.07 (0.04)*
Anticoagulant (yes)	0.29 (0.04)***	0.04 (0.03)
Organ involvement		
Number organs involved	0.07 (0.01)***	0.01 (0.01)
Hematology		
White blood cell peak	---	0.46 (0.07)***
White blood cell nadir	---	-0.27 (0.09)**
Absolute neutrophil count nadir	---	-0.01 (0.01)
Hemoglobin admission	---	0.05 (0.01)***
Hemoglobin nadir	---	-0.06 (0.01)***
Platelets peak	---	0.001 (< 0.001)***
Platelets nadir	---	-0.001 (< 0.001)***
White blood cell proportion days involved	---	-0.14 (0.04)**
Absolute neutrophil count proportion days involved	---	-0.21 (0.07)**
Days to hematology involvement	---	0.02 (0.04)
Hematology persistent involvement at discharge (yes)	---	-0.06 (0.03)*
Constant	---	0.54 (0.10)***

Abbreviations: B, unstandardized beta; SE, standard error; CCI, Charlson Comorbidity Index; qSOFA, quick Sepsis Related Organ Failure Assessment; ICU, intensive care unit; FiO_2, fraction of inspired oxygen; NSAID, nonsteroidal anti-inflammatory drug; ACEi, Angiotensin-converting-enzyme inhibitors; ARB, angiotensin II receptor blockers.
*p < 0.05, **p < 0.01, ***p < 0.001, Model 2 adjusted R Square = 0.65.

DISCUSSION

Results showed that increased age was associated with increased mortality. This finding was consistent with other studies that found increased age as an independent predictor of mortality in COVID-19.[14,15] This study had a large percentage of minorities consisting of Hispanics and African Americans and did not find an association of race/ethnicity with mortality. Some studies showed higher mortality among these minorities.[11,12] However, other studies that adjusted for many covariates did not find an association of Hispanics and African Americans with mortality.[14,15] Results found that regular Medicaid, but not those uninsured who were eligible for emergency Medicaid, had an association with increased mortality. The authors were not aware of any research of regular Medicaid status with COVID-19 mortality. However, studies done in other diseases found increased mortality in patients who have regular Medicaid.[22,23] Patients who have regular Medicaid were often of lower socioeconomic class, have barriers to care, and have increased burden of comorbidities.[24] Uninsured patients tend to be younger and healthier as many of them are undocumented in the country for work.[25] This could be a reason why there was no association of uninsured with mortality.

This study did not find a significant association between obesity and mortality. This was like other studies that did not find an association with obesity and mortality at BMI ≥ 30.[26] Studies that reported an association of obesity with mortality found this association for severe obesity at BMI ≥ 40.[27,28] This study found that mechanical ventilation was associated with higher odds for mortality, and this was consistent with other studies.[4] Results demonstrated that patients who developed hematologic involvement adjusted for other organ compromise and had increased mortality. Although previous research for hematologic involvement in COVID-19 showed increased mortality, these studies did not adjust for other organ involvement.[17,29,30] This study showed increased mortality adjusted for all other organ involvement.

The results demonstrated that increased ANC had higher odds for mortality. These results were consistent with findings of all COVID-19 patients reporting higher ANC associated with mortality.[31] Other studies in COVID-19 found neutrophilia to be a risk factor for development of Acute Respiratory Distress Syndrome and mortality,[29,32] suggesting that innate immune cell response might be the cause of pathogenesis in the pulmonary system.[33] This likely was related to the hyperinflammatory response in COVID-19 carried out mostly by neutrophils.[34,35] As part of the innate immunity response, neutrophils are recruited to the lungs by proinflammatory cytokines and form neutrophil extracellular traps (NETs). NETs consist of an extracellular network of DNA fragments, microbicidal proteins, and oxidant enzymes like myeloperoxidase (MPO) and neutrophils elastase (NE), whose function is to capture and eliminate viral particles.[34-36] Sustained NETs formation can induce a cascade of inflammatory reactions that ultimately causes tissue damage and cell death via the MPO and NE release.[34,35] This also was corroborated with reports of lung autopsies that showed neutrophil infiltration within lung capillaries and extravasation of neutrophils into the alveolar space in COVID-19.[37]

In this study, higher WBC peak was associated with higher LOS and an increased WBC nadir was associated with decreased LOS. In COVID-19, patients with leukocytosis tended to have more severe disease, more ICU admissions, and higher LOS.[38] One possibility of why patients with increased WBC nadir had decreased LOS was that the WBC nadir was in the normal range signifying a milder disease. Another possibility is that decreased WBC nadir often was caused by lymphopenia that in COVID-19 studies has been associated with more severe disease.[39]

This study found that patients with higher hemoglobin on admission was associated with decreased mortality. Studies in COVID-19 patients report that patients with baseline anemia on presentation had increased odds of mortality[16] and the more severe the degree of the anemia the higher odds of mortality.[30] The proposed pathophysiology is that patients with anemia have decreased oxygen delivery to peripheral tissues, leading to worsening organ function.[40] Also, the increased inflammatory state due to the cytokine storm makes iron unavailable for erythropoiesis resulting in anemia of inflammatory disease. This ultimately creates a deficit in organ perfusion during the increasing demand of oxygen secondary to the hyper-metabolic state of the COVID-19 disease.[16,40] Patients in this study who had higher hemoglobin nadir had lower LOS. This finding was similar to a study in COVID-19 patients that showed a significantly negative correlation between hemoglobin and LOS.[41] This also was consistent with other medical conditions where low hemoglobin was an independent risk factor for increased LOS.[42]

High platelet peak was associated with decreased mortality and increased LOS. There were no studies of platelet peak and its association with mortality or LOS in COVID-19. However, studies showed that having low platelets in COVID-19 patients was associated with increased mortality.[17,43,44] Thrombocytopenia can develop in COVID-19 patients through two possible approaches.[45,46] One approach is by affecting hematopoiesis. The virus can enter the bone marrow platelet precursors and platelets through their surface receptors and induce growth inhibition and apoptosis.[45,46] Another approach is by generation of antibodies. The antibodies that form in response to interaction of the host cells and the virus bind to surface antigens on platelets and are recognized by reticuloendothelial system which ultimately leads to platelets destruction.[45,46] This study found that patients with higher platelets nadir had decreased LOS. Previous research related to platelets and LOS showed an increased LOS if patients developed delayed thrombocytopenia after 14 days of admission.[44] The platelet nadir mean in this study was within normal range. The results suggested that our patients with higher platelets nadir had a milder disease and therefore a decreased LOS.

The results showed that increased days to hematologic involvement was associated with higher mortality. Other studies reported a similar association of abnormal hematologic parameters positively associated with mortality.[38,41,44] Patients that took longer to have WBC or ANC involvement had decreased LOS. The data on WBC or ANC and LOS were limited to a study that showed no association between ANC and

LOS.[47] In this study, it took an average of 2.2 days for hematologic involvement. The authors propose that a decrease in LOS with abnormalities in WBC and ANC later during hospitalization were likely no longer COVID-19 related and manifestations of a milder form of the illness.

This study found that treatment with convalescent plasma, interleukin inhibitors, or steroids were associated with increased LOS. The data on LOS and treatment of COVID-19 were limited. A study of interleukin inhibitor treatment for COVID-19 also had increased LOS for those receiving tocilizumab.[48] A study from China found increased LOS with steroid treatment; however, the study did not focus on those with hematologic involvement.[47] Data from COVID-19 patients administered convalescent plasma showed decreased LOS when convalescent plasma was applied early in the course of the disease.[49,50] This study's findings may differ since the sample was collected at the time when convalescent plasma was experimental and was started on patients with severe disease late in their course after they did not respond to other therapies. A possible reason for the findings may pertain to treatment with these therapies as indications for more severe cases that would have an increased LOS regardless of their administration.

Patients that had hematologic involvement at discharge had higher mortality and lower LOS than those who recovered to normal hematologic values. The authors propose that these patients likely were critically ill. This was consistent with other studies showing hematologic abnormalities being associated with increased mortality[16,17,29-32,43,44] and a decreased LOS.

This study had some limitations. First, it was done in a single center safety net hospital with a large minority population and may not be representative of other hospitals in the U.S. However, inclusion of a large proportion of minorities in the study group allowed a better description of the COVID-19 experience in this population. Second, data were collected from patients admitted during the peak of the pandemic in New York, where treatment management standards frequently were changing based on new guidelines. This could have affected patients' outcomes. Third, although guideline-based criteria were used for defining each hematologic cell line dysfunction, universally accepted criteria for hematologic organ system involvement were not available. We chose involvement as abnormalities in laboratory values for at least one cell line. Fourth, the retrospective nature of our study prevented any causative analysis. Fifth, there were some patients where the baseline information on hematologic parameters were not available.

In conclusion, patients with increased ANC, increased days to any hematologic involvement, and persistence of hematologic involvement at discharge were associated with increased odds for mortality while increased hemoglobin on admission and increased platelets peak were associated with decreased odds for mortality. Hematologic parameters consistent with milder disease (increased WBC nadir, increased hemoglobin nadir, and increased platelets nadir) or critical illness (hematologic involvement at discharge) were associated with shorter LOS. Hematologic parameters consistent with more severe form of the disease (increased WBC peak) were associated with longer LOS. These findings can be used by clinicians to risk-stratify patients with hematologic involvement in COVID-19 better and tailor therapies potentially to improve patient outcomes.

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Mental Health and Access to Medical Care in Patients with Chronic Cardiovascular Conditions: An Analysis of the Behavior Risk Factor Surveillance System

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ABSTRACT

Introduction. Poor mental health is associated with worse outcomes for chronic diseases. It is unclear whether mental illness predisposes to difficulties with healthcare access.

Methods. Using a combined dataset of the 2016-2019 Behavioral Risk Factor Surveillance System, this study focused on individuals who reported a chronic cardiovascular condition. Weighted multivariable logistic regression analyses were used to explore the association between domains of mental health and measures of healthcare access including delaying medical care, more than one year since last routine checkup, lack of a primary care physician, and cost-related medication nonadherence.

Results. Among 1,747,397 participants, 27% had a chronic cardiovascular condition, 12% had clinical depression, and 12% had poor mental health. Those with poor mental health (OR 3.20 [3.08 - 3.33]) and clinical depression (OR 2.43 [2.35 - 2.52]) were more likely to report delays in medical care. Those with greater stress frequency (OR 8.47 [6.84 -10.49] stressed all of the time), lower levels of emotional support received (OR 3.07 [2.21 - 4.26] rarely get needed emotional support), and greater life dissatisfaction (6.66 [4.14 – 10.70] very dissatisfied) reported greater delays in medical care.

Conclusions. Individuals with poor mental health have greater difficulty accessing medical care independent of socioeconomic variables.
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INTRODUCTION

Mental illness including depression and anxiety has been associated with poor outcomes in patients with history of cardiovascular diseas.[1] Previous studies have linked history of depression with increased chance of developing acute coronary syndrome.[2] Moreover, almost 15% percent of patients who suffer myocardial infarction experience severe depression following their hospitalization,[3] with those experiencing depression having increased risk of mortality.[4] In patients with stroke, depression was linked with higher mortality and worse quality of life.[5] Similar associations between depression and diabetes also have been demonstrated.[6]

The underlying reasons for the correlations are not established firmly, and there is debate regarding whether depression is merely a risk marker or a causative factor in cardiovascular disease. While plausible biological mechanisms exist, including elevated pro-inflammatory markers and autonomic dysregulation,[1,7,8] at least part of the association between depression and poor cardiovascular outcomes likely was due to psychosocial factors and disparities in care. Patients with history of depression have double the rate of medication nonadherence.[9-11] Moreover, previous studies have linked mental illness with receipt of less comprehensive medical care, including fewer guideline recommended screening practices.[12,13]

It is possible that patients with poor mental health have greater difficulty accessing and utilizing healthcare, either due to motivational issues or poor support systems that make accessing and having sustained follow-up in a complex healthcare system more challenging. Using a large, nationally representative sample, this study examined the relationship between mental health and different measures of healthcare access among individuals with history of chronic cardiovascular conditions. It also explored the association between mental health and cost-related medication nonadherence (CRMNA).

METHODS

Data were utilized from the 2016 to 2019 Behavioral Risk Factor Surveillance System (BRFSS), an annual U.S. national survey administered by the U.S. Centers for Disease Control and Prevention (CDC). Surveys were administered via telephone by trained professionals to adults 18 years and older, who were selected randomly from blocks of potential telephone numbers within an area.[14] Institutional review board approval was not necessary as BRFSS is a publicly available dataset. This study included all individuals who reported a history of chronic cardiovascular conditions including diabetes, hypertension, or atherosclerotic cardiovascular disease (ASCVD) including stroke or myocardial infarction.

Domains of mental health included subjective poor mental health, history of clinical depression, stress frequency, level of emotional support received, and life satisfaction. Poor mental health was defined as answering "at least 15 days" to the survey prompt, "Now thinking about your mental health, which includes stress, depression, and problems with emotions, for how many days during the past 30 days was your mental health not good?". The survey prompts used to derive other domains of mental health are listed in Table 1. Outcomes of interest utilized as measures of poor healthcare access included delaying medical care for any reason including cost within the last year, last routine checkup being greater than one year ago and lacking a primary care physician (PCP). Given the importance of medication adherence in the management of chronic cardiovascular conditions, CRMNA also was included as an outcome of interest. The survey prompts used to derive outcome measures are listed in Table 1.

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Table 1. Survey questions used to derive domains of mental health and measures of healthcare access.

Measure	Survey question
Domains of mental health	
Poor mental health	"Now thinking about your mental health, which includes stress, depression, and problems with emotions, for how many days during the past 30 days was your mental health not good?"
Clinical depression	"(Ever told) you have depression (including depression, major depression, dysthymia, or minor depression)?"
Stress frequency	"Stress means a situation in which a person feels tense, restless, nervous, or anxious, or is unable to sleep at night because his/her mind is troubled all the time. Within the last 30 days, how often have you felt this kind of stress?"
Emotion support received	"How often do you get the social and emotional support you need?"
Life satisfaction	"In general, how satisfied are you with your life?"
Measures of healthcare access	
Delayed medical care	"Was there a time in the past 12 months when you needed to see a doctor but could not because of cost?" and "Other than cost, have you delayed getting medical care for one of the following reasons in the past 12 months? Was it because..." • You couldn't get through on the telephone. • You couldn't get an appointment soon enough. • Once you got there, you had to wait too long to see the doctor. • The clinic or doctor's office wasn't open when you got there. • You didn't have transportation. • No, I did not delay getting medical care/did • Don't know/Not sure
Greater than one year since last primary care visit	"About how long has it been since you last visited a doctor for a routine checkup?"
Lack of primary care physician	"Do you have one person you think of as your personal doctor or health care provider?"
Cost-related medication nonadherence	"Not including over the counter (OTC) medications, was there a time in the past 12 months when you did not take your medication as prescribed because of cost?"

CDC-provided survey weights were utilized for all statistical analysis. The weighted prevalence of demographic characteristics of the overall population were estimated. The authors performed multivariable weighted logistic regression models to examine the association between mental health domains and measures of poor access to healthcare and CRMNA. Analyses were adjusted for age, gender, race, educational attainment, employment, household income, living in a Medicaid expansion state, healthcare coverage, language, living in a rural area, and number of comorbidities (hyperlipidemia, smoking history, chronic kidney disease, chronic obstructive pulmonary disease, arthritis, asthma, cancer). All analyses were performed using STATA version 16.1 (Statacorp, College Station, TX).

RESULTS

Among a total 1,747,397 survey respondents, 21% were above age 65, 63% were white, 12% were black, 17% were Hispanic, 51% were female, 18% were unemployed, 33% had hypertension, 11% had diabetes, and 9% had ASCVD. Mean household income was $60, 544 ± 39,527; 5% lived below the federal poverty line. In total, 88% had health coverage. Among those who had health coverage, 46% had employer sponsored insurance plans, 12% had individually purchased plans, 23% had Medicare, 10% had Medicaid, and 9% had other health types of health coverage. Regarding mental health domains, 18% reported history of clinical depression, 12% reported poor mental health, 20% received the emotional support they need sometimes or less frequently, 31% felt stressed some of the time or more frequently, and 5% were dissatisfied or very dissatisfied with their life.

In total, 592,401 (27%) individuals reported a history of at least one chronic cardiovascular condition. Among those, 15% reported having delayed medical care within the last year. Among those who delayed care for reasons other than cost, 5% delayed medical care because they could not get through on the phone, 30% could not get an appointment soon enough, 15% stated the wait was too long to see the doctor, 4% stated the clinic or doctor's office was not open when they got there, 19% did not have transportation, 23% had other unspecified reasons, 4% refused to answer or did not know. Survey weighted multivariable regression showed those who reported poor mental health were more likely to report having delayed medical care (OR 3.20 [3.08 - 3.33]), as were individuals with history of clinical depression (OR 2.43 [2.35 - 2.52]). There was a graded association between stress frequency and delays in medical care as follows: being stressed a little of the time, OR 1.99 [1.67 - 2.35], some of the time, OR 3.55 [3.01 - 4.20], most of the time, OR 5.45 [4.49 - 6.23], or all of the time, OR 8.47 [6.84 - 10.49]. Similar graded associations were observed for level of emotional support received and life satisfaction with delays in medical care (Table 2).

No routine checkup within the last year was reported by 13% of individuals with chronic cardiovascular conditions. Those with poor mental health were more likely to have not had a routine checkup within the last year (OR 1.32 [1.20 - 1.45]). There was no association between clinical depression and no routine checkup within the last year. Those with greater stress frequency were more likely to have gone greater than one year since their last routine checkup (stressed all of the time OR 1.72 [1.27 - 2.34]), as were those who reported dissatisfaction with their lives (dissatisfied OR 2.82 [1.33 - 5.96]).

Lack of PCP was prevalent in 11% of individuals with chronic cardiovascular conditions. Those who reported poor mental health also were more likely to lack a PCP (OR 1.29 [1.14 - 1.46]), whereas there was no association between clinical depression and lack of PCP (OR 0.93 [0.83 - 1.04]). Greater frequency of stress, lower levels of emotional support, and life dissatisfaction were correlated with lacking a PCP (Table 2).

Furthermore, 14% of individuals with chronic cardiovascular conditions delayed taking prescription medications due to cost within the last year. Similar correlations existed between the various domains of mental health and CRMNA. Those with subjective poor mental health were more likely to have delayed taking medications because of cost (OR 2.10 [1.50 - 2.94]), as were those with a history of clinical depression (OR 2.27 [1.70 - 3.05]). A graded association was present between stress frequency and CRMNA: being stressed a little of the time, OR 1.26 [0.76 - 2.07], some of the time, OR 3.28 [1.91 - 5.63], most of the time, OR 3.01 [1.67 - 5.44], or all of the time, OR 5.33 [2.40 - 11.84] (Table 3).

Table 2. Association between domains of mental health and measures of healthcare access in patients with history of cardiovascular disease.

Variable	Delayed medical care[1]	> 1 year since last primary care visit[2]	Lack of primary care physician[3]
Poor mental health[a]			
No	Ref	Ref	Ref
Yes	3.20 [3.08 - 3.33]*	1.32 [1.20 - 1.45]*	1.29 [1.14 - 1.46]*
Clinical depression[b]			
No	Ref	Ref	Ref
Yes	2.43 [2.35 - 2.52]*	1.09 [0.99 - 1.18]	0.93 [0.83 - 1.04]
Stress frequency[c]			
None of the time	Ref	Ref	Ref
A little of the time	1.99 [1.67 - 2.35]*	1.29 [1.08 - 1.55]*	1.33 [1.03 - 1.72]*
Some of the time	3.55 [3.01 - 4.20]*	1.32 [1.07 - 1.62]*	1.31 [1.00 - 1.72]*
Most of the time	5.45 [4.49 - 6.23]*	1.88 [1.42 - 2.50]*	1.81 [1.19 - 2.75]*
All of the time	8.47 [6.84 - 10.49]*	1.72 [1.27 - 2.34]*	1.82 [1.22 - 2.69]*
"How often do you get the emotional support you need?"[d]			
Always	Ref	Ref	Ref
Usually	1.42 [1.16 - 1.72]*	1.28 [0.88 - 1.86]*	1.58 [0.95 - 2.64]
Sometimes	3.11 [2.53 - 3.83]*	1.72 [1.03 - 2.88]*	2.23 [1.16 - 4.30]*
Rarely	3.07 [2.21 - 4.26]*	2.38 [1.16 - 4.89]*	3.59 [1.58 - 8.17]*
Never	1.66 [1.25 - 2.21]*	0.90 [0.43 - 1.91]	1.39 [0.55 - 3.49]
Life satisfaction[e]			
Very satisfied	Ref	Ref	Ref
Satisfied	2.12 [1.78 - 2.52]*	1.75 [1.28 - 2.40]*	1.41 [0.92 - 2.17]
Dissatisfied	5.59 [4.19 - 7.46]*	2.82 [1.33 - 5.96]*	1.58 [0.61 - 4.11]
Very dissatisfied	6.66 [4.14 - 10.70]*	4.44 [0.93 - 21.31]	6.98 [1.38 - 35.42]*

[1] "Was there a time in the past 12 months when you needed to see a doctor but could not because of cost?" and "Other than cost, have you delayed getting medical care for one of the following reasons in the past 12 months? Was it because...?"
[2] "About how long has it been since you last visited a doctor for a routine checkup?"
[3] "Do you have one person you think of as your personal doctor or health care provider?"
[a] "Now thinking about your mental health, which includes stress, depression, and problems with emotions, for how many days during the past 30 days was your mental health not good?"
[b] "(Ever told) you have depressive (including depression, major depression, dysthymia, or minor depression)?"
[c] "Stress means a situation in which a person feels tense, restless, nervous, or anxious, or is unable to sleep at night because his/her mind is troubled all the time. Within the last 30 days, how often have you felt this kind of stress?"
[d] "How often do you get the social and emotional support you need?"
[e] "In general, how satisfied are you with your life?"
* Significant association.

Table 3. Association between domains of mental health and cost-related medication nonadherence in patients with history of cardiovascular disease.

Variable	Cost-related medication nonadherence[1] OR [95% CI]
Poor mental health[a]	
No	Ref
Yes	2.10 [1.50 - 2.94]*
Clinical depression[b]	
No	Ref
Yes	2.27 [1.70 - 3.05]*
Stress frequency[c]	
None of the time	Ref
A little of the time	1.26 [0.76 - 2.07]
Some of the time	3.28 [1.91 - 5.63]*
Most of the time	3.01 [1.67 - 5.44]*
All of the time	5.33 [2.40 - 11.84]*
"How often do you get the emotional support you need?"[d]	
Always	Ref
Usually	1.27 [0.69 - 2.35]
Sometimes	1.32 [0.60 - 2.93]
Rarely	3.03 [1.13 - 8.10]*
Never	1.38 [0.31 - 6.07]
Life satisfaction[e]	
Very satisfied	Ref
Satisfied	1.13 [0.59 - 2.14]
Dissatisfied	2.56 [0.90 - 7.29]
Very dissatisfied	1.10 [0.08 - 15.61]

[1] Cost-related medication nonadherence was derived from the survey prompt "Not including over the counter (OTC) medications, was there a time in the past 12 months when you did not take your medication as prescribed because of cost?"
[a] "Now thinking about your mental health, which includes stress, depression, and problems with emotions, for how many days during the past 30 days was your mental health not good?"
[b] "(Ever told) you have depressive (including depression, major depression, dysthymia, or minor depression)?"
[c] "Stress means a situation in which a person feels tense, restless, nervous, or anxious, or is unable to sleep at night because his/her mind is troubled all the time. Within the last 30 days, how often have you felt this kind of stress."
[d] "How often do you get the social and emotional support you need?"
[e] "In general, how satisfied are you with your life?"
* Significant association.

DISCUSSION

This study found that among individuals with a history of chronic cardiovascular conditions, those with poor mental health have relatively greater difficulties in accessing healthcare, reporting more delays in care, fewer routine checkups, lower rates of having a PCP, and higher rates of CRMNA. Similar associations existed with other domains of mental health, with those reporting the greatest levels of stress frequency, lowest levels of emotional support, and greatest life dissatisfaction also reporting the greatest difficulty accessing medical care.

Poor mental health is an established risk marker for poor prognosis in cardiovascular disease, but its role as a risk factor is unclear as causal links and explanatory mechanisms remain incompletely defined.[1] Previous studies in which depression was treated medically have failed to yield an improvement in outcomes.[15] As such, in addition to biological mechanisms, it is equally important to consider how psychosocial determinants of health may impact prognosis. Medication nonadherence may be one component of how mental health modulates cardiovascular outcomes.[2,10] Our findings further raise the question of disparities in healthcare access, demonstrating a graded association between poor mental health and difficulties accessing medical care.

This relationship between poor mental health and healthcare access persisted despite adjusting for socioeconomic variables including employment status, household income, and healthcare coverage. Potentially, those with poor mental health have lower motivational levels and less social support, which make navigating a complex and sometimes convoluted healthcare system more difficult. Previous

studies have linked depressive symptoms with lower "self-efficacy" scores that may predispose patients to be less proactive with regards to their medical management, which in addition to rendering close follow up less likely could compromise other aspects of medical management such as medication adherence and making healthy lifestyle choices.[16-18] Moreover, other social conditions that may be coincident with and contributing to poor mental health could exacerbate the observed disparities in healthcare access.

Lapses in medical care such as those observed in our study are important to address, especially in the management of chronic cardiovascular conditions requiring meticulous follow-up and medical management. Potential interventions could include screening patients with cardiovascular conditions for mental illness and deploying resources to ensure adequate healthcare access. Whether deploying resources to alleviate such disparities would improve outcomes is uncertain as previous efforts to treat depression and to ensure optimal medical adherence have failed to improve outcomes.[15]

The results of this study were limited by the self-reported nature of the variables and the ability to only control for variables present within the BRFSS dataset. As such, factors in detail including regimen complexity, disease severity, and comprehensiveness of insurance coverage could not be adjusted. Also, the data were unable to distinguish between treated and untreated depression. Also, it was possible the results were biased by confounders that have been unaccounted for. Lastly, given the cross-sectional nature of the analyses, delays in accessing medical care made inferences regarding causality difficult.

CONCLUSIONS

Poor mental health was associated independently with poor healthcare access and CRMNA among patients with cardiovascular conditions. More research is needed to explore the relationship between mental health and access to care in those with chronic cardiovascular conditions. Improving access to healthcare could improve cardiovascular outcomes among this high-risk population.

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Octogenarian Motor Vehicle Collisions: Injury Patterns Matter

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ABSTRACT

Introduction. Motor vehicle collision (MVC) is the second most common mechanism of injury among octogenarians and is on the rise. These "oldest old" trauma patients have higher mortality rates than expected. This study examined potential factors influencing this increased mortality including comorbidities, medications, injury patterns, and hospital interventions.

Methods. A 10-year retrospective review was conducted of patients aged 80 and over who were injured in an MVC. Data collected included patient demographics, comorbidities, medication use prior to injury, collision details, injury severity and patterns, hospitalization details, outcomes, and discharge disposition.

Results. A total of 239 octogenarian patients were identified who were involved in an MVC. Overall mortality was 18.8%. An increased mortality was noted for specific injury patterns, patients injured in a rural setting, and those who were transfused, intubated, or admitted to the ICU. No correlation was found between mortality and medications or comorbidities.

Conclusions. The high mortality rate for octogenarian patients involved in an MVC was related to injury severity, type of injury, and in-hospital complications, and not due to comorbidities and prior medications. ***Kans J Med 2022;15:22-26***

INTRODUCTION

Similar to the rest of the developed world, the average age of the population in the U.S. continues to increase. The proportion of the U.S. population aged 65 and older in 1950 was only 8% compared to 16.5% of the population in 2019, and the proportion is projected to increase to 22% in 2050.[1] Simultaneously, the proportion of licensed drivers over the age of 65 continues to rise.[2] In 2019, 20.2% of all U.S. drivers were over the age of 65 and 3.7% of the population was over the age of 79.[3,4] While the octogenarian population is less likely to be licensed to drive, older drivers are keeping their licenses longer and driving more miles.[5,6]

In 2011, the number of injury-related emergency room visits per 100 persons per year was 18.3 for persons aged 75 years and older, the highest rate for any age group.[7] Falls remained the most common mechanism of injury for this population;[8] however, motor vehicle collisions (MVCs) represented the second most common mechanism of injury leading to trauma activation among octogenarians.[5,6,9] While older drivers only accounted for 9% of all individuals injured in MVCs in 2012, they accounted for over 17% of all traffic fatalities.[2] Individuals aged 80 years and older have the highest rate of fatal crash involvement in passenger vehicles per miles driven, and are ten times more likely to die than drivers aged 25-44.[10] Many studies have commented on these "oldest old" trauma patients and have hypothesized their outcomes are dismal due to medical comorbidities,[11-14] decreased physiologic reserve,[15,16] and increased susceptibility to injury,[17-19] particularly chest injuries[20] and polypharmacy.[21] Some authors suggested frailty or fragility as the major contributing factor to poor outcomes.[6,19,22]

According to 2019 Kansas collision statistics, drivers over the age of 79 accounted for 2.0% and 5.4% of all MVCs and fatal MVCs, respectively.[23] These individuals experience poor outcomes such as longer hospital stays,[11] discharge to long-term care facilities,[24] or mortality when compared to their younger counterparts. The families of these individuals can face difficulty in deciding how aggressive they should be in continuing care to keep their loved ones alive, and their decisions are made more difficult by a lack of sound evidence to guide their decisions.

The purpose of this study was to examine the distribution of injury patterns, advanced directives, and discharge disposition of drivers and passengers, aged 80 or older, who were involved in MVCs. Further, the study sought to determine if pre-existing comorbidities and polypharmacy were associated with higher mortality in these patients.

METHODS

The trauma database and electronic medical records at an American College of Surgeons verified level-1 trauma center were used to identify individuals 80 years of age and older who were involved in an MVC and were evaluated by the trauma team between November 1, 2000 and October 31, 2010. This study included all trauma patients aged 80 years and older and are hereafter referred to as octogenarians for the sake of simplicity. A retrospective chart review was conducted to abstract the following information: patient demographics; place of collision (urban vs. rural); motor vehicle collision information; whether the patient arrived intubated or was intubated on arrival; comorbid conditions as reported by patients or family members; medications upon admission as reported by the patient, family members, or local pharmacy; Injury Severity Score (ISS) and Abbreviated Injury Scale (AIS); Glasgow Coma Scale (GCS) score; Focused Assessment with Sonography for Trauma (FAST) findings; blood transfusion requirements; individual injuries and the need for operative or procedural management; information on comfort care, advanced directives, power of attorney, and living will; intensive care unit (ICU) or wards admission; ICU length of stay; ventilatory requirements and number of ventilator days; complications; hospital length of stay; discharge destination (i.e., home, rehabilitation, or skilled nursing facility); and mortality. Legal documentation regarding end-of-life wishes (i.e., advanced directives) was not recorded routinely for patients before 2008. This study was approved for implementation by the Institutional Review Board of Via Christi Hospitals Wichita, Inc.

Data initially were summarized and stratified by survival status at discharge. Comparisons of continuous and categorical data were conducted using one-way analysis of variance and Chi-square analysis, respectively. All statistical tests were two-sided, and analyses were considered significant when the resultant p value was less than or equal

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to 0.05. All analyses were conducted using SPSS release 19.0 (IBM® Corp., Armonk, New York).

RESULTS

A total of 239 subjects met inclusion criteria. Of these, 45 (18.8%) died of their injuries, while 194 (81.2%) survived to discharge. An initial comparison was made between those patients who died and who survived to discharge. Patients who died were older (85.7 ± 3.4 vs. 84.2 ± 3.3 years, p = 0.005), more severely injured as shown by increased ISS (22.3 ± 15.4 vs. 9.2 ± 8.1, p < 0.001), had decreased GCS (10.8 ± 5.3 vs. 14.3 ± 2.4, p < 0.001), and were more often injured in a rural setting (64.4% vs. 47.7%, p = 0.043) than those who survived. As expected, the mortality rate was higher in those who were more severely injured (ISS > 15, mortality = 39.2%) when compared to those less severely injured (ISS = 1 to 15, mortality = 9.7%, p < 0.001).

The remaining analyses were conducted comparing mortality rate for each variable studied. Patient sex, location within the vehicle (driver vs. passenger), and vehicle ejection were not associated with increased mortality (data not shown). Mortality rate was significantly higher in those patients who were intubated in the field (64.7% vs. 15.3%) or upon arrival (69.6% vs. 13.4%), had a positive FAST examination (53.8% vs. 15.2%), or required a transfusion (40.8% vs. 13.2%; Table 1; p < 0.001).

Table 1. Comparison of mortality rates based upon presence or absence of parameter.

Parameter	Yes		No		p Value
	Number/ total	Mortality rate (%)	Number/ total	Mortality rate (%)	
Arrived intubated	11/17	64.7	34/222	15.3	< 0.001
Intubated on arrival	16/23	69.6	29/216	13.4	< 0.001
Positive FAST* examination	7/13	53.8	32/211	15.2	< 0.001
Required transfusion	20/49	40.8	25/190	13.2	< 0.001

*Focused Assessment with Sonography for Trauma

Comparisons were made for the most common comorbidities and medications voluntarily offered by patients or their family members upon admission to the hospital or updated throughout their hospitalization. Comorbid conditions evaluated included: Alzheimer's disease, cerebrovascular accident, coronary artery disease, congestive heart failure, atrial fibrillation, myocardial infarction, stenting, chronic obstructive pulmonary disease, chronic renal failure, diabetes mellitus, and hypertension. Medications evaluated included: anti-hypertensives, aspirin, beta-blockers, warfarin, diuretics, inhalers, insulin, lipid-lowering agents, oral anti-hyperglycemics, and clopidogrel. No medications or comorbid conditions were associated significantly with mortality rate (data not shown).

The mortality rates for major and minor head injuries are reported in Table 2. Surprisingly, the only major head injuries significantly associated with an increase in mortality were intraparenchymal hematoma (33.3% vs. 15.0%) and skull fracture (75.0% vs. 15.7%). This unexpected finding may have been due in part to the low number of subjects in this study that suffered major head injuries, thereby limiting statistical power. Simple concussion (29.6% vs. 11.9%, p < 0.002) and loss of consciousness (26.9% vs. 12.6%, p < 0.014) also were shown to be associated with a significant increase in mortality. Cervical (31.9% vs. 13.4%, p = 0.003) and thoracic (38.9% vs. 15.3%, p = 0.011) spine injuries, spinal injuries treated with a cervical collar (31.0% vs. 15.1%, p = 0.033), and those requiring spinal surgery (62.5% vs. 15.9%, p = 0.005) were associated with statistically significant increases in mortality (Table 3).

Table 2. Comparison of mortality rates based upon cranial injuries.

Head injury	With specified injury		Without specified injury		p Value
	Number/ total	Mortality rate (%)	Number/ total	Mortality rate (%)	
Major head injury	10/40	23.3	30/191	15.7	0.235
Intraparenchymal hematoma	6/18	33.3	32/214	15.0	0.043
Subarachnoid hemorrhage	3/14	21.4	35/218	16.1	0.707
Subdural hematoma	4/21	19.0	34/211	16.1	0.757
Skull fracture	3/4	75.0	36/229	15.7	0.016
Minor head injury	19/68	27.9	20/165	12.1	0.004
Concussion	16/54	29.6	21/177	11.9	0.002
Loss of consciousness	14/52	26.9	22/174	12.6	0.014
Facial fracture	4/11	36.4	35/222	15.8	0.092

Table 3. Comparison of mortality rates based upon spinal injuries.

Spinal injury/ treatment	With specified injury		Without specified injury		p Value
	Number/ total	Mortality rate (%)	Number/ total	Mortality rate (%)	
Spine injury	16/60	26.7	24/174	13.8	0.022
Cervical	15/47	31.9	25/187	13.4	0.003
Thoracic	7/18	38.9	33/216	15.3	0.011
Lumbar	2/10	20.0	38/224	17.0	0.682
Cervical collar	9/29	31.0	31/205	15.1	0.033
Required surgery of the spine	5/8	62.5	36/227	15.9	0.005
Spinal cord injury	2/4	50.0	38/230	16.5	0.136
Spinal cord paralysis	1/2	50.0	39/232	16.8	0.313

All thoracic injuries recorded were associated with a significantly increased mortality rate ($p < 0.001$, Table 4). Patients with bilateral rib fractures, cardiac injuries, sternal fractures, and patients presenting with a pneumothorax all had mortality rates greater than 50% compared to their counterparts without these injuries (< 16%).

Table 4. Comparison of mortality rates based upon thoracic injuries.

Thoracic injury	With specified injury		Without specified injury		p Value
	Number/ total	Mortality rate (%)	Number/ total	Mortality rate (%)	
Thoracic injury	23/55	41.8	19/181	10.5	< 0.001
Thoracic requiring surgery	9/18	50.0	33/218	15.1	< 0.001
Rib fracture	20/51	39.2	22/185	11.9	< 0.001
Bilateral rib fractures	6/7	85.7	36/229	15.7	< 0.001
Pulmonary	15/32	46.9	27/204	13.2	< 0.001
Pneumothorax	14/27	51.9	28/209	13.4	< 0.001
Sternal fracture	10/18	55.6	32/218	14.7	< 0.001
Cardiac	6/10	60.0	35/225	15.6	0.002

The mortality rates associated with different fractures are displayed in Table 5. Upper extremity, femur, pelvic, and pubic rami fractures were associated with statistically significant increases in mortality. A trend was found towards increased mortality in those patients suffering lower extremity and acetabular fractures.

Table 5. Comparison of mortality rates based upon fractures.

Extremity or pelvic fracture	With specified fracture		Without specified fracture		p Value
	Number/ total	Mortality rate (%)	Number/ total	Mortality rate (%)	
Upper extremity	13/44	29.5	27/190	14.2	0.015
Lower extremity	13/49	26.5	28/186	15.1	0.060
Femur	9/18	50.0	32/217	14.7	< 0.001
Pelvic	6/13	46.2	37/224	16.5	0.007
Pubic rami	3/5	60.0	40/232	17.2	0.043
Hip	3/9	33.3	40/228	17.5	0.211
Acetabular	3/6	50.0	40/231	17.3	0.075

Table 6 displays the mortality rates for patients with or without abdominal injuries. The presence of an abdominal injury was associated with an increased mortality rate (50.0% vs. 15.8%, $p = 0.001$); however, the only specific abdominal injury associated with an increase in mortality was a hollow viscus injury (75.0% vs. 16.5%, $p = 0.018$). Patients requiring abdominal surgery also had significantly increased mortality rates when compared to those patients not requiring abdominal surgery (50.0% vs. 16.4%, $p = 0.007$).

Table 6. Comparison of mortality rates based upon presence or absence of abdominal injuries.

Abdominal injury/ surgery	With specified injury		Without specified injury		p Value
	Number/ total	Mortality rate (%)	Number/ total	Mortality rate (%)	
Abdominal	7/14	50.0	35/222	15.8	0.001
Hollow viscus	3/4	75.0	38/231	16.5	0.018
Kidney	1/1	100.0	40/234	17.1	0.174
Liver	1/3	33.3	40/232	17.2	0.439
Spleen	3/7	42.9	38/228	16.7	0.104
Required abdominal surgery	5/10	50.0	37/226	16.4	0.007

The only in-hospital complications associated with a significantly higher mortality rate were myocardial infarction (66.7% vs. 17.6%, $p = 0.012$) and line infections (100% vs. 18.1%, $p = 0.035$; Table 7). Patients with pneumonia or acute respiratory distress syndrome had mortality rates over 35%, but these rates did not reach statistical significance when compared to uncomplicated cases.

Table 7. Comparison of mortality rates based upon presence or absence of complications.

Complication	With specified complication		Without specified complication		p Value
	Number/ total	Mortality rate (%)	Number/ total	Mortality rate (%)	
In-hospital myocardial infarction	4/6	66.7	41/233	17.6	0.012
Line infection	2/2	100.0	43/237	18.1	0.035
Pneumonia	6/17	35.3	39/222	17.6	0.072
Acute respiratory distress syndrome	3/6	50.0	42/233	18.0	0.082
MRSA infection	1/1	100.0	41/228	18.0	0.183
Urinary tract infection	3/20	15.0	42/219	19.2	0.774
Deep vein thrombosis	0/2	0.0	45/237	19.0	1.000
Delayed diagnosis	1/6	16.7	25/150	16.7	1.000

With regard to patient hospitalization, those patients admitted to the ICU and those requiring mechanical ventilation had significantly higher mortality rates than those not admitted to the ICU or ventilated (Table 8). As expected, mortality was higher in patients with advanced directives who proceeded to comfort care measures. Of note, only 117 of 239 (49.0%) of the cohort had advanced directives. Approximately

one-third of the patients were discharged to home (34.7%, n = 83) with an additional 5% (n = 12) being discharged to home with home health. Forty-four patients (18.4%) died in the hospital and one additional patient was sent to hospice (0.4%) where they later died, resulting in an overall mortality rate of 18.8%. Nearly one-half of the patients (41.5%) required some form of extended care post-discharge, which included skilled nursing unit care (n = 59, 24.7%), rehabilitation (n = 20, 8.4%), nursing home (n = 14, 5.9%), assisted living (n = 5, 2.1%), or a mental health facility (n = 1, 0.4%).

Table 8. Comparison of mortality rates based upon hospitalization and advanced directives.

Parameter	Yes		No		p Value
	Number/ total	Mortality rate (%)	Number/ total	Mortality rate (%)	
Intensive care unit admission	34/109	31.2	11/130	8.5	< 0.001
Mechanical ventilation (Y)	29/49	59.2	16/190	8.4	< 0.001
Tracheostomy	12/86	14.0	33/153	21.6	0.148
Advanced directives	19/56	33.9	11/61	18.0	0.003
Comfort care	26/26	100.0	19/213	8.9	< 0.001

DISCUSSION

A population of octogenarian MVC victims was evaluated to identify factors associated with increased mortality. Older, more severely injured patients, and patients injured in a rural setting had a significantly higher mortality rate. Higher mortality rates were noted among patients who arrived intubated or were intubated shortly after arrival to the hospital. The finding of increased mortality in those requiring transfusion was in accord with that of Zhao et al.[25] Whether a patient was the driver or passenger did not affect mortality rate significantly.

These findings suggested higher mortality rates among octogenarians involved in MVCs when compared to the available literature on geriatric trauma patients.[6,13,14] Most trauma research focusing on a geriatric population use an age of 65 years as the lower inclusion.[8,9,12,14,15,20] These studies commented on the elderly population having increased mortality rates, but few studies focused exclusively on octogenarian patients. This population had a mortality rate of 18.8%, which is significantly higher than the 5 to 12% published mortality rate for geriatric patients 65 years of age or older.[9,12] Older patients had a decreased ability to tolerate thoracic injuries, and subsequently had a higher mortality.[13,14,22] This fact was likely to be true for most injuries as an increased mortality was demonstrated for head, spine, thoracic, and abdominal injuries.

Previously published studies disagreed on the role comorbidities and medications play in affecting mortality. Many studies suggested an increased mortality,[12,22] some referred to increased morbidity and prolonged hospitalization,[11,24] while others refuted comorbidities or medications as a cause of increased mortality in this population.[8,12,24] Among octogenarians involved in MVCs, no specific comorbidities were shown to correlate with increased mortality. Similarly, mortality was not found to increase in association with the use of any medications, including anticoagulants and antiplatelet therapies. One possible explanation for our finding was that individual comorbid conditions and medications were evaluated rather than the combined effect of multiple comorbidities or medications. For example, Bartolomeo et al.[21] found that anticoagulant or antiplatelet therapy, when evaluated individually, had little or no increased impact on the odds of older patients (older than 74 years) being admitted for traumatic injuries. However, the authors found increased odds for admission in patients taking antiplatelet therapy and anticoagulants in combination. Another possible explanation was that while a patient's list of prescribed medications may be readily available, obtaining information on an individual patient's compliance with these medications is difficult at best.

Despite their comorbidities and the medications a patient has been taking, the decrease in physiologic reserve has been suggested as a factor in the higher mortality rate observed.[15,16] Given that this population had a relatively high mortality rate of 9.7% in those patients with an ISS of 15 or less, any detrimental effect from comorbidity may have been overshadowed by the effect of frailty. However, this quantification was not done via direct measurement of physiologic reserve or calculation of a frailty index as this was a retrospective review and these data were not available.

This study was limited by the fact that it was retrospective. It also was limited by the fact that major injuries were observed in a limited number of the subjects. Further, while some information about living situation prior to injury can be obtained through chart review, it was possible that a percentage of the population required assistance with activities of daily living prior to the MVC that was not available through chart review. However, it was likely that the percentage of patients who required assistance with activities of daily living pre-injury was significantly less than the 41.4% of patients needing such assistance on discharge. As we could not determine with a high degree of confidence the patient's pre-injury level of functioning or requirements for daily assistance, discharge destination did not provide an objective measurement of patient return to previous functioning. But discharge destination has been suggested as a proxy measure when that is all that is available.[26]

Advanced Trauma Life Support (ATLS) continues to teach that the geriatric trauma population can return to their previous level of functioning with appropriate management.[16] This assumption was based on an accepted geriatric population of all individuals aged 65 and older. Based upon the findings of this study, this may not hold true for octogenarian trauma patients involved in MVCs. Only 34.7% of patients returned home upon discharge from the hospital, with an additional 5% returning with home health. The remainder of the patients (41.5%) required additional assistance with activities of daily living following discharge (i.e., skilled nursing unit, long-term acute care hospital, rehabilitation hospital, nursing home). When the geriatric population is defined as ages 65 and older, most of these patients may be returning to their previous level of functioning, as stated by ATLS. However, the majority of patients aged 80 and older likely either succumb to their injuries or require additional assistance upon dismissal from the

hospital after presenting as a trauma activation following MVC.

A minority of the patients in this study was known to have legal documents stating their wishes for end-of-life care. However, this information was not recorded until 2008, as trauma surgeons were not trained specifically to ask for patient requests for end of life care prior to 2008. Considering these findings concerning the relationship of medical history and medications upon mortality, it may be of more significant benefit to obtain a "do not resuscitate" status and end-of-life wishes during our AMPLE history. AMPLE (Allergies, Medications, Past medical history, Last meal or other intake, and Events leading to presentation) often is useful as a means of remembering key elements of the history.

CONCLUSIONS

Octogenarian trauma patients injured as a result of MVCs are being seen with increasing frequency. These patients have an increased mortality that is not explained by underlying comorbid conditions or medications, but is related to injury pattern, setting, and hospital interventions. These factors can be predictive of mortality and discharge disposition and may prove valuable in discussing desires for level of care and interventions with patients and family.

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Thromboelastography after Cardiopulmonary Bypass: Does it Save Blood Products?

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ABSTRACT

Introduction. This study aimed to determine if thromboelastography (TEG) is associated with reduced blood product use and surgical re-intervention following cardiopulmonary bypass (CPB) compared to traditional coagulation tests.

Methods. A retrospective review was conducted of 698 patients who underwent CPB at a tertiary-care, community-based, university-affiliated hospital from February 16, 2014 to February 16, 2015 (Period I) and from May 16, 2015 to May 16, 2016 (Period II). Traditional coagulation tests guided transfusion during Period I and TEG guided transfusion during Period II. Intraoperative and postoperative administration of blood products (red blood cells, fresh frozen plasma, platelets, and cryoprecipitate), reoperation for hemorrhage or graft occlusion, duration of mechanical ventilation, hospital length of stay, and mortality were recorded.

Results. Use of a TEG-directed algorithm was associated with a 13.5% absolute reduction in percentage of patients requiring blood products intraoperatively (48.2% vs. 34.7%, $p < 0.001$). TEG resulted in a 64.3% and 43.1% reduction in proportion of patients receiving fresh frozen plasma (FFP) and platelets, respectively, with a 50% reduction in volume of FFP administered (0.3 vs. 0.6 units, $p < 0.001$). Use of TEG was not observed to decrease postoperative blood product usage or mortality significantly. The median length of hospital stay was reduced by one day after TEG guided transfusion was implemented (nine days vs. eight days, $p = 0.01$).

Conclusions. Use of TEG-directed transfusion of blood products following CPB appeared to decrease the need for intraoperative transfusions, but the effect on clinical outcomes has yet to be clearly determined. ***Kans J Med 2022;15:27-30***

INTRODUCTION

Reversal of anticoagulation and re-establishment of hemostasis following cardiopulmonary bypass (CPB) always has been a challenge for the surgical team. The accurate assessment of anticoagulant reversal not only affects operative times, but also has significant implications, including use of blood products.[1] Blood product administration carries its own risk profile medically and also results in significant cost to healthcare. Additionally, patients requiring blood transfusion during or after CPB have increased long-term mortality.[2] Therefore, accurate assessment of coagulability following CPB best ensures hemostasis and minimizes the unnecessary transfusion of blood products and its associated morbidity and mortality.

Traditional tests for assessment of coagulability include activated clotting time (ACT), partial thromboplastin time (PTT), prothrombin time (PT), fibrinogen level, and platelet count. Collectively, these laboratory tests are used to direct blood product administration following cardiac surgery. However, some evidence suggested that functional coagulation tests, such as thromboelastography (TEG), can lead to reduced blood product transfusion rates following cardiac surgery.[3-7] It was hypothesized that measuring mechanical properties of blood clot formation and fibrinolysis predicts bleeding more accurately as compared to the traditional coagulation assessments. However, little evidence existed showing the ultimate clinical implications of such changes.[3,5,7] Thus, there is still disagreement as to whether TEG results are equivalent, or superior, to traditional testing.

Some investigators found that TEG findings were not comparable to traditional tests,[8-10] while Shore-Lesserson et al.[4] found TEG to be accurate in assessing coagulability and associated with lower transfusion rates. The effect of TEG-directed transfusions following CPB on long- and short-term clinical outcomes such as infections, immunological reactions, or mortality have yet to be determined.[11] In an effort to reduce unnecessary transfusions, many hospitals have adopted transfusion protocols, as opposed to clinician-directed transfusion based on professional discretion.[12] As TEG use has been shown to be associated with reduced transfusion rates in the trauma resuscitation setting, it also has been adopted for assessment of coagulability following CPB in some centers.[13] Therefore, the purpose of this study was to evaluate whether adoption of TEG-directed transfusion for CPB was associated with improved patient outcomes and reduced blood product use.

METHODS

This study was approved for implementation by the Institutional Review Board of Ascension Via Christi Hospitals Wichita, Inc.

A retrospective chart review was conducted of all patients who underwent CPB at a single tertiary-care hospital from February 16, 2014 to February 16, 2015 (Period I) and from May 16, 2015 to May 16, 2016 (Period II). Period I represented a time in which patient coagulability was assessed using traditional coagulation tests (platelets, INR, PTT, ACT, and fibrinogen) and comprised our control group. Period II represented the period in which TEG was implemented fully as the standard for assessment of coagulability intra-operatively and comprised our comparison group. A three-month washout period was implemented for the transition as to allow for adoption of TEG as the primary laboratory test for evaluation of blood coagulability. Patient data during this three-month washout interval between the two periods was not used, as TEG use was initiated at the start of the washout period. Upon completion of the CPB, standard labs including coagulation values and TEG were drawn to direct proper heparin reversal. The TEG specimens were collected with and without heparinase to eliminate confounding from any additional heparin yet to be reversed by protamine. The anesthesia team received the results and directed any need for intraoperative transfusion of blood products.

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Data collection was performed by retrospective review of both the local Society of Thoracic Surgeons (STS) registry and patient medical records for those who met inclusion criteria. The information collected from each subject meeting the inclusion criteria included: demographics (age, gender, race), intra-operative and post-operative blood products transfused (packed red blood cells (RBC), fresh frozen plasma, platelets, cryoprecipitate), need for reoperation, length of time on mechanical ventilation, length of hospital stay, and mortality. The TEG values collected and used to evaluate patient coagulability included: reaction time (R), amplification (K), propagation (α-angle), maximum amplitude (MA), clot lysis (CL), and clot stability (LY30%).

Intraoperative transfusions were directed by the cardiac anesthesia team in both periods. For Period II, lab referenced normal values were used to determine necessity of blood product usage based on TEG values.

Patient data were abstracted and summarized as means ± standard deviations for continuous variables with approximately normal distributions [~N(0,1)]. For ordinal variables and continuous variables with either skewed distributions or distributions not assumed to follow a normal distribution, medians and interquartile ranges are presented. For nominal variables, proportions were used to summarize the data. Comparisons between study groups were made using t-tests for continuous variables that were distributed normally. A Mann-Whitney U test was used to compare variables with skewed or ordinal distributions. Comparisons between nominal variables were completed with the use of a Chi squared test or Fischer's Exact test. All tests were conducted as two-tailed tests and were considered statistically significant if the resultant p value was less than or equal to 0.05. All analyses were conducted using SPSS version 19 (IBM® Corp., Somers, New York).

RESULTS

Overall, there were a total of 689 patients included with 311 (45.1%) in the traditional coagulation testing arm (Period I) and 378 (54.9%) in the TEG testing arm (Period II). There was no significant difference between groups with regard to age or gender; however, there was a slightly higher proportion of Caucasian and Asian patients in the TEG group (Table 1).

A significant difference was observed in blood product administration intra-operatively, with a 13.5% absolute reduction, and 28.0% overall reduction in the percentage of patients in the TEG guided group receiving blood products as compared to those in the control group (34.7% vs. 48.2%, respectively, $p < 0.001$; Table 2). There was no significant difference in proportion of patients receiving RBC's or cryoprecipitate, and the volume of RBCs and cryoprecipitate administered to these patients was also equivalent for those requiring transfusion of these products. As with total intraoperative products received, the proportion of patients requiring transfusion of FFP and platelets was reduced significantly in Period II with a 64.3% and 43.1% overall reduction in proportion of patients needing FFP and platelets, respectively. Those patients requiring FFP also received less FFP in the TEG group intraoperatively. Of all patients requiring FFP, those in the TEG group received 50% less FFP than those in the control group. While fewer patients in the TEG group required platelets, platelet requirements of those needing platelets were not different between the two study groups. Total volume of blood products received intraoperatively for those patients that required transfusion was not different between the study groups. There was no significant difference observed in the post-operative blood product usage between groups (Table 3).

Table 1. Comparison of demographics between study groups.

Parameter*	Study Period I Coagulation panel guided	Study Period II TEG guided	p Value
Number of observations	311 (45.1%)	378 (54.9%)	---
Age, years	65.4 ± 11.4	66.4 ± 12.4	0.284
Male sex	205 (65.9%)	262 (69.3%)	0.343
Race†			0.050
White or Caucasian	252 (85.7%)	332 (89.0%)	
Black or African American	25 (8.5%)	28 (7.5%)	
Asian	6 (2.0%)	11 (2.9%)	
Native American	4 (1.4%)	2 (0.5%)	
Native Hawaiian or Pacific Islander	3 (1.0%)	0(0.0%)	
Other	4 (1.4%)	0 (0.0%)	

*Data are expressed as the number of observation (percent) or Mean ± SD.
†Variable contains missing values; reported percentages are based on number of cases with values entered.

Table 2. Comparison of intraoperative blood product administration between study groups.

Parameter*	Study Period I Coagulation panel guided	Study Period II TEG guided	p Value
Number of observations	311 (45.1%)	378 (54.9%)	---
Received intraoperative blood products	150 (48.2%)	131 (34.7%)	<0.001
Received red blood cells	99 (31.9%)	97 (25.7%)	0.070
Red blood cell units†	1.3 ± 1.3; 1 (0 - 2)	1.2 ± 1.0; 1 (0 - 2)	0.684
Received fresh frozen plasma	39 (12.6%)	17 (4.5%)	<0.001
Fresh frozen plasma units†	0.6 ± 1.2; 0 (0 - 1)	0.3 ± .8; 0 (0 - 0)	0.004
Received platelets	85 (27.4%)	59 (15.6%)	<0.001
Platelet units†	0.7 ± 0.7; 1 (0 - 1)	0.6 ± .7; 0 (0 - 1)	0.197
Received cryoprecipitate	28 (9.0%)	27 (7.1%)	0.363
Cryoprecipitate units†	0.3 ± 0.6; 0 (0 - 0)	0.4 ± .7; 0 (0 - 0)	0.563
Total blood products, units†	2.8 ± 2.7; 2 (1 - 4)	2.4 ± 1.8; 2 (1 - 3)	0.414

*Data are expressed as the number of observations, Mean ± standard deviation, or Median (interquartile range).
†Data provided only for those patients that received that blood product.

Table 3. Comparison of post-operative blood usage between study groups.

Parameter*	Study Period I Coagulation panel guided	Study Period II TEG guided	p Value
Number of observations	311 (45.1%)	378 (54.9%)	---
Received blood products	112 (36.0%)	123 (32.6%)	0.351
Received red blood cells	100 (32.2%)	110 (29.2%)	0.399
Red blood cell units†	1.8 ± 1.5; 1 (1 - 2)	1.9 ± 1.4; 1 (1 - 3)	0.817
Received fresh frozen plasma	14 (4.5%)	9 (2.4%)	0.125
Fresh frozen plasma units†	0.3 ± .8; 0 (0 - 0)	0.1 ± .5; 0 (0 - 0)	0.179
Received platelets	25 (8.0%)	35 (9.3%)	0.565
Platelet units†	0.3 ± .5; 0 (0 - 0)	0.4 ± .7; 0 (0 - 1)	0.210
Received cryoprecipitate	17 (5.5%)	25 (6.6%)	0.525
Cryoprecipitate units†	0.2 ± .5; 0 (0 - 0)	0.3 ± .7; 0 (0 - 0)	0.234
Total blood products, units†	2.5 ± 2.1; 2 (1 - 3)	2.7 ± 2.3; 2 (1 - 3)	0.949

*Data are expressed as the Number of observations, Mean ± standard deviation, or Median (interquartile range).
†Data provided only for those patients that received that blood product.

Quality markers of the STS registry including reoperation for bleeding, reintervention for graft occlusion, mechanical ventilation hours, and mortality were not significantly different between the two groups (Table 4). However, median hospital length of stay was significantly shorter in the TEG guided group (p = 0.010).

Table 4. Comparison of complications and hospital outcomes between study groups.

Parameter	Study Period I Coagulation panel guided	Study Period II TEG guided	p Value
Number of observations	311 (45.1%)	378 (54.9%)	---
Number of coronary grafts	112 (36.0%)	123 (32.6%)	0.351
Reoperation for bleed	100 (32.2%)	110 (29.2%)	0.399
Reintervention for graft occlusion*	1.8 ± 1.5; 1 (1 - 2)	1.9 ± 1.4; 1 (1 - 3)	0.817
Mechanical ventilation hours	7.2 (5.4 - 12.1)	6.5 (5.0 - 11.6)	0.157
Hospital length of stay (d)	9 (7 - 12)	8 (6 - 12)	0.010
Mortality	6 (1.9%)	11 (2.9%)	0.413

*Variable contains missing values; reported percentages are based on number of cases with values entered.

DISCUSSION

Comparisons of TEG-directed transfusion versus traditional coagulation tests directed transfusion have been explored in several different surgical and resuscitation settings.[5,6,13,14] A review by Wikkelsø et al.[6] found that TEG-directed resuscitation in patients with bleeding may reduce need for blood products. Similarly, a review by Deppe et al.[7] found that TEG-based coagulation management decreased the risk of allogenic blood product exposure. However, routine use of TEG as a test to measure coagulability in patients needing massive transfusion or with trauma induced coagulopathy have been shown to have variable outcomes.[11,15] With the hope to reduce transfusion rates, our institution adopted a transfusion model directed by TEG following CPB. This model appeared to be the most successful in the literature thus far for minimizing blood product usage.[6,12] Our findings were in concordance with this idea as we saw a 13.5% absolute reduction and 28% overall reduction in the percentage of patients requiring blood product usage intraoperatively. However, once patients were deemed to need transfusions, the units of blood products administered per patient (with the exception of FFP) were not significantly different between TEG and traditional coagulation tests groups.

Effect of TEG on Blood Product Use in Cardiac Surgery. Others have found utilization of blood products during complex cardiac procedures to be reduced with implementation of TEG-directed algorithms.[3,5-7] Boliger et al.[3] found TEG-directed transfusion to result in a 73% decrease in FFP use and a 38% decrease in RBC use. Similarly, Fleming et al.[5] showed that TEG-directed management of blood product administration during complex cardiac surgeries reduced units of blood products received perioperatively by 40%. However, similar to our study, they found no significant reduction in blood product usage more than 24 hours postoperatively. Shore-Lesserson et al.[4] found TEG-directed transfusion following cardiac surgery to be restrictive in the transfusion of RBCs, FFP, and platelets. However, unlike our study, and that of Fleming et al.[5], they also found decreased post-operative transfusions.

Effect of TEG on Clinical Outcomes. We also were interested in the impact of adopting TEG-directed transfusions on the clinical course following CPB related to rebleeding, need for reoperations, and mortality. Re-operative rates for bleeding were similar between treatment groups in our study with five re-explorations for bleeding (1.6%) in Period I and eight re-explorations (2.1%) in Period II. Similarly, some others in the literature also have not found significant differences in re-operation rates when adopting TEG-directed transfusion algorithms.[5,13] In contrast though, in a review by Deppe et al.[7], TEG-based coagulation management not only decreased risk of allogeneic blood product exposure, but also resulted in a 44% decrease in surgical re-explorations. Impacts on mortality also were not significant both in our findings and by others in the literature.[3,5,7] Specifically, the review by Bolliger et al.[3] found that transfusions triggered by TEG were more restrictive, but they did not observe improvements in mortality or additional clinical outcomes.

Challenges to TEG Implementation. Surgeons have been wary of changes to standard assessments of coagulability because the implications are significant and adjusting to differences in how the values are reported takes time. At our institution, TEG can be reported live in

the operating room as the sample is being processed; however, the final values generally are reported over a period of 30 minutes, and reporting is slower than the traditional coagulation lab result times. Lack of system-wide integration has made it difficult for TEG to function in the same capacity outside the operating room because the proprietary software was not available throughout the entire hospital. This often led the team managing the patient to use traditional coagulability labs beyond the operating room and was a possible reason why we did not show a difference in blood product utilization in the post-operative period. With resolution of this systems limitation, it would be easier to explore the impact of TEG on the post-operative management of patients after CPB at our facility.

Heparinase was used in the TEG samples collected after CBP. This was intended to mitigate the effects of heparinization on the sample given its short half-life and use of protamine. Further analysis directly comparing traditional coagulation tests and TEG with heparinase may be warranted to determine if any discrepancy exists.

Limitations. Our study was limited by its retrospective design. Inconsistency in clinical charting contributed to areas of missing data, as data were collected prior to knowledge of this study. Also, as the study data were collected retrospectively, clinical decision-making dictated timing of lab orders and what labs were ordered, rather than how and when labs would have been ordered in a prospective study setting, and as such may have affected the results obtained. Additionally, our sample size was likely too small to sufficiently analyze the confounding variables on very low occurrence events such as re-operation or mortality. The ability to determine confounding influence of clinical variables also was limited by the retrospective nature of this study. Large randomized prospective trials with strict adherence to transfusion algorithms would be best suited to obtain generalizable conclusions to evaluate the effect of TEG implementation on clinical outcomes including morality and need for surgical re-intervention.

CONCLUSIONS

Use of a TEG-directed algorithm for transfusion of blood products following CPB appeared to decrease the need for intraoperative transfusions, but effects on other clinical outcomes have yet to be determined clearly. Further investigation with the utilization of TEG throughout the recovery period following CBP may impact utilization of specific blood products. Also, the effect of heparinase on blood product utilization must be clarified further.

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Understanding Medication Adherence in Patients with Limited English Proficiency

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ABSTRACT

Introduction. Approximately 41.6% of the U.S. population who speak a language other than English (20% of the total population) have limited English proficiency (LEP) status. Health outcomes for patients with LEP status or who are language discordant (speak a different language than their clinicians) have been studied in several settings, including hospital and outpatient, with results widely demonstrating that these patients have worse outcomes when a professional interpreter is not used consistently. The aim of this study was to investigate the impact of preferred language and language discordance on medication adherence.

Methods. Data were collected through the review of pharmacy-acquired medication profiles for three primary language cohorts: English, Nepali, and Spanish. Total Days of Adherence, Adherence Ratio, and Maximum Days Non-Adherent were calculated and compared between language groups. The statistics were examined for regular and long-acting insulin, metformin, and ACE inhibitors, testing for differences between language groups, and those who experienced greater and less than the median value for language concordant clinical encounters.

Results. The most adherent group overall (highest Adherence Ratio) were the Nepali-speaking patients, but the results showed high variability across outcomes and medications.

Conclusions. After adjustment and stratification for greater and lesser language concordant patient visit experience, it was found that language-spoken plays an important role in the clinical encounter, and that LEP patients could have improved outcomes in their adherence to medications by having providers who speak their language or use an interpreter. ***Kans J Med 2022;15:31-36***

INTRODUCTION

The 2009-2013 American Community Survey reported that 41.6% of the U.S. population who speak a language other than English (20% of the total population) have limited English proficiency (LEP) status.[1] Health outcomes for patients with LEP have been studied in a number of settings, including hospital and outpatient, with results widely demonstrating that LEP patients have worse outcomes when a professional interpreter was not used consistently.[2,3] Refugees and new immigrants often have LEP status during their early resettlement period in the U.S.; data have shown that 62% of refugees are limited in their English proficiency.[4]

When compared to non-refugees, refugees have a higher prevalence of chronic disease.[5] Even when compared to their U.S.-born ethnic counterparts, refugees have higher rates of diabetes.[6,7] Health education promoting physical activity and optimal self-care for LEP patients with Type 2 diabetes mellitus (T2DM) in primary care settings is often ineffective, leading to poorer control of blood glucose and poorer health outcomes than among English-speaking patients.[8] Other significant barriers to effective management of chronic disease, including diabetes mellitus, in refugees with LEP include: varying cultural beliefs about illness,[2] ineffective communication between provider and patient,[9] decreased access to pharmacy and medication services,[10] and decreased health literacy.[11] However, a significant paucity of published research explored barriers to medication and pharmacy services among resettled refugees.[10]

Thus, the aim of this study was to quantify the impact of LEP status on diabetes-related medication adherence over the course of 12 months. The authors hypothesized that speaking English would correlate with higher Adherence Ratios and that LEP status would correlate with lower Adherence Ratios (other studies have demonstrated improvement in clinical outcomes with use of interpreters).[9]

Patients with LEP who speak Nepali or Spanish were compared with English-speaking patients as a control group. The primary outcome of interest was number of days of nonadherence with their medication regimen as determined by days adherent to medication divided by days prescribed medication.

METHODS

This study was approved as a quality improvement study by the University of Kansas Medical Center Institutional Review Board.

Study Design. Data collection for this observational study was accomplished through chart review of patient medical records at the Family Medicine clinic of the University of Kansas Health System. Access to protected health information (PHI) was limited to researchers who were members of the treatment team directly providing care to study participants. Pharmacy data were collected over a six month period from June 1, 2018 to May 31, 2019.

Participants. All participants were established patients of the University of Kansas Health System. Participants in the study were selected via electronic medical record (EMR) chart review to meet the following qualifications: preferred language as Nepali, Spanish, or English; at least 18 years old; diagnosis of T2DM prior to study enrollment; and a hemoglobin A1c (HbA1c) of at least 8% (representing uncontrolled diabetes mellitus). English speaking patients were included as a control if they identified as Latin(x) for their ethnic status. The Nepali-speaking patients were ethnically Bhutanese former refugees. Most patients in the Nepali cohort were served by a single Nepali-speaking bilingual physician. This was not the case for the Spanish and English-speaking cohort. The English-speaking cohort was composed largely of bilingual, Spanish-speaking patients whose preferred language was English.

Measures. Patients did not contribute patient-reported information in this study. Medication adherence data were collected through a retrospective chart review and through contacting patients' pharmacies. Each patient's medication profile was obtained by contacting the patient's pharmacies, where the investigators determined actual medications

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filled at each pharmacy and which medicines a patient had access to fill. Data collected from the EMR included: patient's medication record (to allow for consideration of longitudinal data), self-reported preferred language, number of language concordant visits, most recent HbA1c, medication refill dates of all diabetes-related medications, total number of medications of any type, and patient demographics (e.g., age, sex, ethnicity, living situation, insurance status, marital status, and presence of currently active EMR patient portal). Language concordance with providers was assessed by review of patient's preferred language status and the bilingual status of the provider in question. All those preferring English as their language also identified "Spanish/Hispanic" as their ethnic group. All language discordant encounters were conducted with the use of a professional medical interpreter, either live or by phone.

Outcomes of Interest. The outcome of interest was Actual Days of Medication Adherence, Adherence Ratio, and Maximum Days Non-Adherent. The Adherence Ratio was calculated based on the cumulative number of days of medication supply afforded a patient as a ratio with number of days the patient had been prescribed the medicine, such that:

$$Adherence\ Ratio = \frac{actual\ number\ of\ days\ adherent\ to\ regimen}{expected\ number\ of\ days\ adherent\ to\ regimen}$$

The Actual Days of Medication Adherence was the number of days possible for the patient to use the medication properly based on the quantity dispensed by the pharmacy for each refill over the time of the study. The expected adherence was the total number of days the patient had been prescribed that medicine, starting from their first refill at the pharmacy. This ratio was used as a surrogate for medication adherence because there was a paucity of validated metrics in the literature for measuring patient medication adherence using objective data without collecting information on patient reported medication use directly.[12,13] The Adherence Ratio was calculated for each medication reported. Maximum Number of Days Non-Adherent was calculated for each medication based on gaps in medication refill data collected from pharmacy medication profiles, such that:

$$Maximum\ Days\ Nonadherence = \#\ of\ total\ days\ prescribed\ medication - \#\ of\ days\ supply\ of\ medication$$

In other words, Maximum Days Nonadherence revealed the number of days that the patient did not have access to the medication because it was not picked up from the pharmacy. The three language groups were compared to each other in terms of these outcomes, as well as their most recent HbA1c value and the number of visits with a language-concordant provider.

Analysis. Stata Inter-cooled Version 10 (Statacorps, Austin, TX) was used for analyses. Demographic variables were centered (subtracted the mean value of each variable from each value) to produce variables that would allow an estimate of baseline values for outcome variables in regression models that had real-world meaning once adjusted. Medication use was measured over 180 days from the time of enrollment. The number of days of medication use was doubled to produce an annualized estimate. This procedure was used for the actual days of medication use and maximum number of days patients were non-adherent.

A one-way analysis of variance was calculated to compare each outcome variable by language group (English, Spanish, or Nepali). A two-tailed significance using F-statistics was calculated, accepting an alpha p value of 0.05 as significant. Bartlett's test of equal variance tested for heteroskedasticity in the dependent variable distribution of each outcome for each different language group. If Bartlett's test was significant, median and interquartile ranges were calculated and a non-parametric median test determined significance.

Next, an ordinary least squares regression was conducted, using a dependent variable for each of the different medication parameters for actual days of medication use and maximum days of non-adherence, separately. Models included data for all participants taking each type of medication. Models were examined for the effect of potential confounding by centered age, sex, marital status, current health insurance (insured or not), total number of medications, most recent HbA1c, and presence of a currently active electronic medical record patient portal. The independent variable of primary interest was self-reported preferred language. Only age and sex were retained in final models, as including other potential confounders had little impact on final adjusted results. All models were weighed by the amount of time data were collected (which varied between patients). For these models, the Breusch-Pagan test (also known as the Cook-Weisberg test) was used for heteroskedasticity. The Breusch-Pagan test approximates the Bartlett's test for heteroskedasticity for one way analysis of variance.

Outcomes for Spanish- and Nepali-only speakers were compared to those who reported bilingual status in English and either Spanish or Nepali. Outcomes were estimated using the linear combination of the constant model term and the beta-coefficient for each language using the Stata post-estimation lincom command, which estimated the 95% confidence intervals. Non-equivalence of outcomes compared Spanish-only to Nepali-only speakers, using a post-estimation Wald test.

Finally, all models were examined for evidence that language discordant visits impacted the models. The proportion of visits were calculated for each participant that was provided by a language concordant provider (concordance ratio). Participants who preferred English always had a language concordant provider. This was not true for those preferring Spanish or English. Models were examined for evidence of interaction between language and the concordance ratio. Interaction in terms of significance of the Wald test for the multiplicand of the values of those two variables were reported. Mean and standard deviation were reported for each language with a concordance ratio greater than the median value (67%) against those with lesser values.

RESULTS

Table 1 shows the demographics of the study participants. In general, Spanish-speaking patients were more often bilingual in English when compared to the Nepali-speaking patients. In fact, the English demographic was comprised of Latin(x) patients who listed English as their preferred language on EMR review and did not require an interpreter for clinical encounters.

Table 1. Demographics (n = 59).

Mean age (SD)	56.4 (13.1)
Sex	*n (%)*
Female	36 (61.0%)
Male	23 (39.0%)
Preferred language	*n (%)*
English	15 (25.4%)
Spanish	21 (35.6%)
Nepali	23 (39.0%)

On average, the Nepali-speaking group had a higher recent HbA1c [10.6 (2.0 SD)] than the Spanish-speaking group [9.8 (1.6 SD)] while taking a greater number of medications overall. The mean number of total medications taken was 18.7 (4.4 SD) for Nepalis and 16.4 (6.8 SD) for Spanish-speaking patients. The English and the Nepali groups were similar regarding total number of medications taken and average HbA1c.

Table 2 reports medication adherence for insulin, metformin, and ACE inhibitors. Some drugs prescribed (i.e., thiazolidinediones, DPP-4 inhibitors, and others) had insufficient data to perform statistical analysis and are not reported. The unadjusted values have been reported for comparison. After adjustment for potential confounders, adherence, as reflected by the total number of days adherent and Adherence Ratio, were higher for both Spanish- and Nepali-speakers compared to English-preference patients for regular insulin and metformin, as well as for the use of ACE inhibitors. This was also true for Neutral Protamine Hagedorn (NPH) insulin for Nepali- but not Spanish-speakers. Nepalis were significantly more adherent than Spanish-speaking patients for ACE inhibitors and regular insulin (but not NPH), in terms of the total number of days adherent; however, the Adherence Ratio only differed between Nepali- and Spanish-speaking patients for ACE inhibitors (Nepali-speakers' ratio was higher). Correspondingly, Maximum Days of Non-Adherence was significantly less for Nepali- and Spanish-speakers compared to English-preference speakers for NPH insulin. This was true for metformin and ACE-inhibitors for Nepalis compared to English preference speakers, but not for Spanish-speakers.

The Maximum Consecutive Days of Non-Adherence demonstrated opposing trends with higher values in the English- and Spanish-speaking groups compared to Nepali-speaking. English- and Spanish-speaking groups had, on average, a longer Maximum Number of Days Non-adherent than their Nepali-speaking counterparts.

After controlling for language concordance between patient and provider, language groups remained significantly different only for regular insulin actual days of use. For medication ratio and maximum days of medication adherence for regular insulin, and for all other medication and all other outcomes, there were no significant differences between language groups once language concordance was controlled. Tests of interaction between preferred language and language concordance were non-significant for all medications and all outcomes.

Because of the systematic variation introduced by the design (i.e., English-speaking patient encounters were language concordant by design), mean and standard deviation values for each medication and outcome by language and concordance group were calculated, using one-way analysis of variance (Table 3). Significant differences between language groups were found only when comparing language concordant Nepali- to English-preference patients. For some comparisons, Bartlett's test for heterogeneity was significant (metformin Adherence Ratio and Maximum Days Non-adherence for language concordant encounters, and ACE Inhibitor actual days and ratio for language non-concordant encounters, and maximum non-adherent days for concordant encounters). For those comparisons, to determine if there was a significant difference between languages in each instance, the outcome variable was transformed by subtracting a constant k (different for each outcome) from the natural log of the outcome (i.e., for Metformin ratio, this = ln(metformin ratio +1.014)). This transformed variable had skewness equal to about 0. The analysis using the transformed variable was repeated. This result effectively corrected the heterogeneity for each of the above comparisons for which it was problematic. None of the transformed comparisons were significant between language groups.

DISCUSSION

The aim of this study was to investigate medication adherence among LEP patients. To that end, medication profiles collected from pharmacies and the Adherence Ratio for diabetes-related medications differed amongst the studied language groups. Surprisingly, the patients who were least compliant with their medication regimen were the Latin(x) English-preference patients. Despite this finding, the most recent HbA1c measurement in the Nepali and English groups were comparable to each other. This result suggested factors not assessed in this study contributed to adequate control of diabetes other than medication adherence as we measured it and as has been demonstrated elsewhere.[12] In support of this assertion, the Maximum Days of Non-Adherence was more often longer in the Spanish-speaking and English-preference cohort than in the Nepali-speaking. Since almost all of the English-speaking cohort were assumed also to speak Spanish, the differences noted between the English-speaking cohort and the Nepali-speaking cohort included both cultural and linguistic factors, whereas between Spanish- and English-speaking cohorts, the main differences were more likely to have been linguistic. Most of the Spanish- and English-speaking patients studied were of Mexican descent, thus having a similar cultural background. These findings were at odds with our hypothesis that speaking English would correlate with higher Adherence Ratios and that LEP would correlate with lower Adherence Ratios.[9]

It is possible that the language spoken by the patient was only one among many factors influencing medication adherence. One study has found that LEP patients with language-discordant physicians were more likely than LEP patients with language-concordant physicians to have poor glycemic control.[7] Thus, outcomes were improved for LEP patients when the patient and provider can communicate more easily. Our data supported this finding given that the observed differences among language groups dissipated after stratifying patients by language concordance with their providers. The only exception was for

actual days of using regular insulin, and only for those with above the median level of language concordant visit. Thus, language concordance accounted for most of the above findings.

Table 2. Adjusted† and unadjusted values of medication.

	Actual Days Medication Adherence		Adherence Ratio (actual days/expected days of adherence)		Maximum Days Non-Adherent	
Regular insulin (n = 17)	**Adjusted mean (95% CI)**	**Unadjusted mean (SD)**	**Adjusted mean (95% CI)**	**Unadjusted mean (SD)**	**Adjusted mean (95% CI)**	**Unadjusted mean (SD)**
English	106 (19-192)**	44.3 (44.4)	0.648 (0.258-1.04)	0.444 (0.381)	78.6 (-23.7-181)	127 (164)
Spanish	183 (123-242)**	163 (117)	0.718 (0.450-0.986)**	0.669 (0.376)	35.1 (-35.3-106)	41.0 (50.0)
Nepali	273 (188-358)**+	241 (86.7)	0.796 (0.412-1.180)**	0.714 (0.256)	60.0 (-40.8-161)	68.7 (62.1)
NPH/ glargine insulin (n = 25)	**Adjusted mean (95% CI)**	**Unadjusted mean (SD)**	**Adjusted mean (95% CI)**	**Unadjusted mean (SD)**	**Adjusted mean (95% CI)**	**Unadjusted mean (SD)**
English	146 (18.9-272)*	171 (169)	0.611 (0.259-0.963)**	0.676 (0.452)	125 (39.9-209)*	102 (176)
Spanish	122 (32.5-211)*	139 (109)	0.531 (0.283-0.779)**	0.587 (0.302)	90.1 (30.5-150)**	58.7 (44.0)
Nepali	212 (114-311)**	209 (128)	0.673 (0.398-0.947)**	0.705 (0.362)	80.7 (14.7-147)*	79.6 (111)
Metformin (n = 32)	**Adjusted mean (95% CI)**	**Unadjusted mean (SD)**	**Adjusted mean (95% CI)**	**Unadjusted mean (SD)**	**Adjusted mean (95% CI)**	**Unadjusted mean (SD)**
English	139 (15.7-263)*	134 (121)	0.601 (0.239-0.963)**	0.672 (0.456)	107 (24.0-190)*	85.3 (120)
Spanish	173 (100-246)**	170 (81.8)	0.803 (0.590-1.015)**	0.835 (0.206)	42.7 (-5.98-91.3)	40.9 (47.3)
Nepali	200 (145-254)**	205 (115)	0.741 (0.582-0.900)**	0.761 (0.328)	49.6 (13.1-86.1)*	49.8 (83.4)
ACE inhibitors (n=21)	**Adjusted mean (95% CI)**	**Unadjusted mean (SD)**	**Adjusted mean (95% CI)**	**Unadjusted mean (SD)**	**Adjusted mean (95% CI)**	**Unadjusted mean (SD)**
English	116 (17.9-215)*	97.7 (102)	0.511 (0.166-0.856)**	0.427 (0.493)	153 (58.8-248)**	188 (178)
Spanish	186 (118-255)*	184 (111)	0.701 (0.460-0.942)**	0.692 (0.331)	65.1 (-1.05-131)	64.0 (69.3)
Nepali	275 (208-342)*+#	286 (42.1)	0.914 (0.680-1.15)**+	0.908 (0.133)	24.0 (-40.3-88.3)+	24.9 (36.1)

†Adjusted for age, sex
*p < 0.05
**p < 0.01
+Group significantly varies from English, p < 0.05
#Group significantly varies from Spanish, p < 0.05

Table 3. Values of medication by language concordance.

	Actual Days Medication Adherence (Mean, SD)		Adherence Ratio (actual days/expected days of adherence) (Mean, SD)		Maximum Days Non-Adherent (Mean, SD)	
	Concordant visits	Non-concordant visits	Concordant visits	Non-concordant visits	Concordant visits	Non-concordant visits
Regular insulin						
English (n = 4)	51 (43)	n/a	0.51 (0.35)	n/a	127.5 (164)	n/a
Spanish (n = 6)	n/a	158 (125)	n/a	0.67 (0.41)	n/a	37 (56)
Nepali (n = 2)	260 (84)*	231 (99)	0.78 (0.31)	0.68 (0.27)	75 (106)	65.5 (51.3)
NPH-insulin						
English (n = 4)	208 (155)	n/a	0.89 (0.04)	n/a	12 (8)	n/a
Spanish (n = 9	n/a	142 (112.5)	n/a	0.60 (0.33)	n/a	58 (46)
Nepali (n = 12)	291 (32)	176 (136)	0.86 (0.11)	0.62 (0.41)	40 (41)	99 (121)
Metformin						
English (n = 3)	142 (130)	n/a	0.61 (0.46)	0.61 (0.46)	85 (120)	n/a
Spanish (n = 9	90 (0)	194 (88)	0.43 (0)	0.87 (0.16)	118 (0)	35.7 (41)
Nepali (n = 20)	273 (74)**	174 (112)	0.93 (0.11)	0.69 (0.35)	19 (30)	42 (45)
ACE inhibitor						
English (n = 3)	135 (135)	n/a	0.65 (0.64)	n/a	125 (237)	n/a
Spanish (n = 8)	n/a	179 (112.5)	n/a	0.65 (0.33)	n/a	73 (69)
Nepali (n = 10)	294 (54)	272 (32)	0.91 (0.16)	0.88 (0.13)	26 (44)	30 (33)

*$p < 0.05$, **$p = 0.07$

This was contrary to the authors hypothesis that patients' adherence to medications could be impacted by the patient's LEP status. The primary driver of participants' adherence was not their preferred language, but whether they had a provider who spoke the same language. It is important to reiterate that all encounters were conducted either with a language concordant provider or with the use of a professional medical interpreter. We also noted the high number of total medications patients consumed, on average. This too may have impacted medication adherence. Other unmeasured factors, such a high carbohydrate, culturally preferred diet also may have confounded our results. The study was underpowered, leading to wide confidence intervals in the language concordance analysis. Further research, recruiting more study participants, should be directed at studying provider-patient factors, such as level of education about refugees, cultural awareness, language(s) spoken by provider and patient, and availability of interpreters in the clinical encounter. Qualitative interviews also may be a useful way to assess these factors.

The finding that Nepali-speaking patients had higher average HbA1c, took more medications, and had higher average Adherence Ratios (i.e., more compliant with regimen) compared to the English-preference patients, suggested that, although these patients were filling their medications consistently, the actual administration, dosing, and consistent use of these medicines may not have matched the physician-directed regimen. Again, qualitative interviews would be useful to investigate this further.

The Adherence Ratio provided the most interpretable and actionable information and could be used clinically to assess a patient's adherence to medication regimen. As this was a quality improvement study, the goal was to use a metric that could, at least in theory, be utilized in a clinic as an objective measure to assess medication adherence, and for successful disease management. One systematic review demonstrated studies using various methods for assessing medication adherence including patient report, Medication Event Monitoring System, electronic monitoring systems, qualitative interviews, and urine assays.[14] The authors concluded that there was a lack of congruence among studies in the way adherence was measured and reported. As the literature did not show a consistent, validated metric for the proposed question and the study design did not permit the adoption of patient reporting or direct patient contact as means for collecting medication adherence, it was decided to use to medication Adherence Ratio as the most efficient and useful means to answer the question. However, as stated, the usefulness of the metrics may be limited in that they do not assess how administration of medication occurs once the patient has the medicine in hand, or any other more qualitative factor in the use of the drug. On the other hand, the data provided by the metrics provided a valuable step in assessing medication adherence, since a patient cannot take prescription medication that they have not received from a pharmacy.

This study was limited by the small number of participants. Some of the medication data collected, such as that for sulfonylureas, DPP-4

inhibitors, and thiazolidinediones, did not have adequate data points to be meaningful or draw statistical inferences from them and were excluded from the results. Additionally, one of the primary endpoints, Maximum Days Non-Compliant, showed significant heteroskedasticity by the Breusch-Pagan/Cook-Weisberg test, suggesting that this outcome may not be valid for comparing language groups. Another limitation of the study was that it was possible the patients were filling medications at pharmacies other than what was listed in the EMR. Some patients had more than one pharmacy documented in the EMR, but it is conceivable that they were using other, unlisted pharmacies without the awareness of the clinical team. Finally, an important limitation of the study was that the authors assumed that the Latin(x) English-speaking patients also spoke Spanish. This was not data collected from the EMR but it was inferred from the patients' stated ethnicity.

CONCLUSIONS

Patients with LEP often have worse clinical outcomes than their American-born and English-speaking counterparts.[6,9] A way to improve these outcomes is to ensure proper adherence to medication regimen. This study found that on average, Nepali-speaking patients with LEP had higher rates of adherence as measured by the Adherence Ratio for diabetic medications than English-preference or Spanish-speaking patients who identified as Latin(x). Yet, these same Nepali-speaking patients, who were largely Bhutanese refugees, had higher HbA1c measurements than the Spanish-speaking patients while being similar to the English-preference cohort in respects to HbA1c. Additionally, the observed differences in the language groups resolved upon stratification by patient-provider language concordance. More research is needed to evaluate other underlying causes of medication non-adherence in these populations and improve management of chronic conditions.

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Keywords: patient compliance, diabetes mellitus, communication barriers, physician-patient relations, medication adherence

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Neurosyphilis Presenting as the Lateral Medullary Syndrome

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INTRODUCTION

Syphilis is known as "the great imitator" because its clinical presentation mimics many other diseases.[1] Syphilis is classified as having primary, secondary, tertiary, and latent stages based on its clinical features and timing of symptoms. Neurosyphilis represents syphilitic infection of the central nervous system (CNS) and can occur at any timepoint of infection.[1] The presentation of neurosyphilis varies depending on the involved CNS site; with respect to temporality, early symptomatic forms include meningeal and meningovascular syphilis, and the late forms include tabes dorsalis and general paresis.[1,2] Ischemic stroke from meningovascular syphilis is uncommon; however, it is modifiable with early recognition and treatment. This case report described an ischemic stroke caused by meningovascular syphilis with literature review.

CASE REPORT

A 30-year-old male with a past medical history of human immunodeficiency virus (HIV) infection, who had not been on antiretroviral therapy (ART) for the last two years, presented with acute onset dizziness upon waking from sleep the day prior to his emergency department presentation. The patient complained of nausea and vomiting and falls from poor balance. He also noticed left eyelid droop, left facial tingling, and left-sided weakness. He developed hiccups associated with the onset of his cluster of neurological symptoms. There was no history of trauma or neck manipulation. Past medical history was otherwise noncontributary. Further questioning revealed a generalized headache for one month, night sweats for two weeks, and mild neck stiffness for one week.

His exam showed normal vital signs, miosis and ptosis in the left eye, right beating nystagmus, and increased sensitivity to cold temperature on the left side of his face and both his right upper and lower extremities. Strength and reflexes were normal.

Initial labs showed absolute lymphopenia, normocytic anemia, and a grossly unremarkable comprehensive metabolic panel. Erythrocyte sedimentation rate was 72 mm/hour. CD4 cell count was 7 cells/μL.

Head computed tomography with and without contrast revealed no acute hemorrhage or enhancing lesion. Cerebrospinal fluid (CSF) testing showed cloudy fluid with white blood cell (WBC) count of 534 cells/μL that consisted of 63% neutrophils and 26% lymphocytes. The red blood cell (RBC) count was 96 cells/μL. Glucose levels were 17 mg/dL and protein levels were 194 mg/dL. A Gram stain of the CSF showed only neutrophils.

Given the CSF findings and the patient's immunocompromised status, he was started on broad spectrum antimicrobial therapy with ceftriaxone, vancomycin, ampicillin, and acyclovir. Dexamethasone initially was added due to concern for *Streptococcus pneumoniae* etiology.

Subsequent magnetic resonance imaging (MRI) of the head showed an acute infarct in the left inferior and posterolateral medulla (Figure 1). It also showed punctate foci of T1 hypointensity with surrounding fluid-attenuated inversion recovery (FLAIR) hyperintensity and subtle enhancement near the left internal capsule.

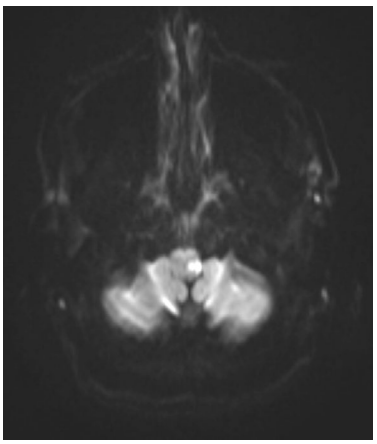

Figure 1. Axial diffusion-weighted magnetic resonance imaging of the head demonstrates restricted diffusion in the left posterolateral medulla, consistent with posterior inferior cerebellar artery territory ischemia.

Transthoracic echocardiogram showed normal ventricular function and was negative for structural abnormalities and vegetative lesions that would suggest infective endocarditis. Electrocardiography showed a sinus rhythm.

Further CSF testing showed a positive result for the venereal disease research laboratory (VDRL) test. Additional serum testing was positive for treponemal-specific IgG with an elevated rapid plasma reagin (RPR) titer. Extensive testing for other bacterial, viral, fungal, and parasitic etiologies was negative.

Given the elevated CSF WBC count, CSF VDRL titer, serum RPR titer, and treponemal antibodies, a diagnosis of stroke caused by meningovascular syphilis was made. Magnetic resonance angiography of the brain revealed multifocal areas of luminal irregularity and intracranial arterial stenoses in both the anterior and posterior circulations (Figure 2), consistent with CNS vasculitis secondary to meningovascular syphilis.

With the diagnosis of meningovascular syphilis, intravenous penicillin G was started. The patient also was started on trimethoprim-sulfamethoxazole prophylaxis given his CD4 count of 7 cells/μL. He was restarted on an ART regimen contingent on HIV genotype. Aspirin was initiated for secondary stroke prevention. Baclofen was started for the patient's intractable hiccups. He completed inpatient rehabilitation and received close primary care follow-up, as well as screening for other sexually transmitted diseases. His RPR titer decreased with penicillin therapy and follow-up CSF VDRL testing was scheduled to monitor treatment response.

As an aside, the patient's reported left-sided weakness was thought to be related to his central vestibular disturbance impairing normal ambulation, as the initial exam revealed no weakness or abnormal reflexes.

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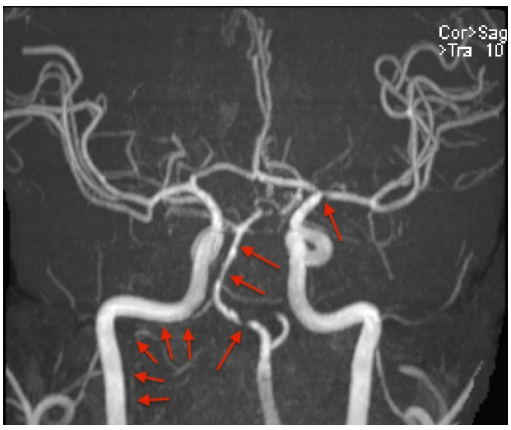

Figure 2. Tumble image from magnetic resonance angiography of the head demonstrates focal stenosis in the left vertebral artery, multifocal stenosis of the basilar artery, and left middle cerebral artery origin stenosis. In addition, there is a small caliber, nondominant right vertebral artery not well visualized in this image.

DISCUSSION

This was a case of a 30-year-old patient with HIV/acquired immunodeficiency syndrome (AIDS) and no other stroke risk factors presenting with acute onset lateral medullary syndrome, also known as the Wallenberg syndrome. The etiology was determined to be an ischemic stroke from meningovascular syphilis. History revealed subtle clues to the infectious etiology, including prodromal symptoms of headache, neck stiffness, and night sweats. These symptoms were important to highlight because half of patients with stroke from syphilitic vasculitis may present with these prodromal symptoms.[3]

Posterior circulation strokes and strokes in the young adult population remain challenging clinical diagnoses. An increased rate of misdiagnosis has been shown in patients under 35 years old and in cases that involve the vertebrobasilar territory, both factors likely contributed to our patient's diagnostic delay.[4] The delayed diagnosis with vertebrobasilar involvement may be due to the vague symptomatology involving dizziness and nausea. This patient's stroke was contralateral to his nondominant vertebral artery, even though vertebral territory strokes are reported more often ipsilateral to the nondominant vertebral artery.[5,6]

Early symptomatic neurosyphilis usually presents with symptoms of meningitis within 12 months of infection.[1] Meningovascular syphilis, as described in this patient's case study, represented endarteritis of the CNS vasculature resulting in thrombosis and infarction, a manifestation that occurs 5 to 12 years after initial infection.[1]

Patients with HIV often are co-infected with syphilis, such that the prevalence of syphilis in HIV infected people is much higher than in the general population.[7-9] Unfortunately, individuals with HIV are also more susceptible to neurologic involvement.[9] Our patient appeared to be severely immunocompromised given his CD4 cell count of 7 cells/μL, which likely contributed to his acute neurologic manifestation. His cell count mostly was attributed to his lack of compliance with ART; however, syphilis infection has been shown to decrease CD4 cell counts and may have contributed to the laboratory findings.[10,11]

While the differential diagnosis of stroke in the young adult population should remain broad, the increasing rate of syphilis infections in the U.S. suggested it is an important diagnosis to consider in this setting.[12] The association of syphilis with HIV makes the spirochete infection even more important to consider in those with HIV and stroke. Other recent case reports of strokes secondary to neurosyphilis reported these patients were HIV-infected.[13-16]

This case report demonstrated the clinical heterogeneity of neurosyphilis and the importance of extending stroke workup in patients with ischemic stroke who lack common stroke risk factors, especially in HIV-infected patients. Clinicians should be familiar with the clinical presentation of posterior circulation strokes. Syphilis should be considered as an etiology of stroke in HIV positive patients, as there is effective treatment.

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Keywords: neurosyphilis, ischemic stroke, lateral medullary syndrome, HIV coinfections, case reports

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WHAT'S INSIDE: ORIGINAL RESEARCH • CASE REPORT

KANSAS JOURNAL of MEDICINE

TABLE OF CONTENTS

KANSAS JOURNAL of MEDICINE

The COVID-19 Vaccines: A Description of Adverse Events of Reactions Reported in Kansas

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ABSTRACT

Introduction. Coronavirus disease 2019 (COVID-19) is caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and has spread rapidly throughout the world since its discovery in 2019. Three vaccines (Pfizer-BioNTech, Moderna/NIAID/BARDA, and Johnson & Johnson's Janssen) have been developed for use in the U.S. to aid in the fight against this virus, but have been scrutinized intensely for their efficacy and safety. It is important to understand and interpret the adverse events or reactions (AERs) associated with these vaccines in an objective and analytical manner. The goal of this descriptive study was to provide a resource outlining AERs associated with the three available vaccines in Kansas.

Methods. Reports were obtained from the Vaccine Adverse Event Reporting System (VAERS), representing AERs observed in Kansas from December 11, 2020 to May 13, 2021. All data were screened and coded, and descriptive statistics were used to describe AERs based on vaccine manufacturer, patient age and biological sex, and reported deaths.

Results. Only 0.00068% of COVID-19 vaccine doses given in Kansas were associated with an AER (1,445/2,120,350). There were 4,297 individual AERs reported, and the most common were fatigue/tiredness (266; 6.2%), tingling/itching (251; 5.9%), fever (226; 5.3%), hives (223; 5.2%), and muscle/joint pain (209; 4.9%). Only 0.002% of COVID-19 vaccine doses in Kansas were associated with a death (38/2,120,350). The majority of VAERS reports were by females (1,139; 78.8%) and those aged 30 to 39 years (297; 20.6%).

Conclusions. No reported AERs were unexpected compared to national data, and no VAERs report provided a causal relationship between vaccine administration and death. Vaccines are, and will continue to be, essential tools to fight COVID-19 in the quest to reach herd immunity. Providing a resource of potential AERs could aid in individual decisions to receive a vaccine and may help in the control of COVID-19. Future studies may include describing reported AERs for children under age 12 as the vaccines become available for those age groups, as well as reporting AERs for those who have received the vaccine after our study time period. ***Kans J Med 2022;15:39-47***

INTRODUCTION

On December 31, 2019, a respiratory virus of unknown etiology was detected in Wuhan City, Hubei Province of China and reported to the World Health Organization.[1] The virus, called Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), was linked to the development of the 2019 novel coronavirus (2019-nCoV), more commonly referred to as the "coronavirus" or "COVID-19." This novel coronavirus spread rapidly in the first months of 2020, with the first reported case in the U.S. on January 21, 2020. By March 20, 2020 there were a total of 250,000 confirmed cases of COVID-19 worldwide. As of August 31, 2021, the confirmed global case count of COVID-19 was more than 217.3 million people infected, with over 4.5 million deaths. In the U.S., there have been approximately 39.1 million confirmed cases and over 639,000 deaths.[2] Due to the morbidity and mortality rates associated with the proliferation of the virus, the U.S. Department of Health and Human Services (DHHS) launched a program called "Operation Warp Speed" to collaborate with the private sector to develop and distribute a vaccine to be used against COVID-19 quickly and effectively on March 30, 2020.[3]

On December 11, 2020, the U.S. Food and Drug Administration (FDA) announced an emergency use authorization (EUA) for the first COVID-19 vaccine approved for use in the U.S., manufactured by Pfizer-BioNTech.[4] An EUA is awarded by the FDA when the public health benefit of a medical product, such as a vaccine, outweighs the known and potential harm.[5] Officially named "Comirnaty" with the international non-proprietary name (INN) "tozinameran", the Pfizer-BioNTech COVID-19 vaccine is colloquially known as the "Pfizer vaccine".[4] With an efficacy rate of up to 95%, the Pfizer vaccine was approved conditionally for use in persons aged 16 and older in the U.S. and requires two doses given three weeks apart.[6-8] Recently, the U.S. Centers for Disease Control and Prevention (CDC) has been monitoring reports of myocarditis and pericarditis following vaccination, however, no suspension or pause in the use of the Pfizer vaccine has been issued.[9]

On December 18, 2020, just a week after the authorization of the Pfizer vaccine, a second COVID-19 vaccine from Moderna Therapeutics, the National Institute of Allergy and Infectious Diseases (NIAID), and Biomedical Advanced Research and Development Authority (BARDA) also received an EUA. The Moderna/NIAID/BARDA vaccine has the brand name "SpikeVax", INN "elasomeran", and is colloquially known as the "Moderna vaccine". This vaccine requires two doses to achieve a vaccine efficacy of 94.1%; however, the Moderna vaccine only was authorized for use in individuals 18 years of age and older.[7] On June 25, 2021, the FDA revised fact sheets related to the Moderna vaccine and disclosed that there may be an increased risk of myocarditis and pericarditis following vaccination, but this issue did not halt the FDA's EUA.[10]

On February 27, 2021, the FDA released the EUA for Johnson & Johnson's Janssen single dose COVID-19 vaccine (INN Ad26.COV2.S) colloquially known as the "J&J vaccine".[11] This marked the third vaccine approved for use in the U.S.[12] Following use for more than a month, the CDC and FDA recommended a temporary suspension for the use of the J&J vaccine on April 13, 2021, due to reports of cerebral venous sinus thrombosis (CVST) in vaccinated individuals, particularly women under age 50.[13,14] After a thorough safety review of the vaccine and the rare cases of CVST, the FDA and CDC lifted the pause on April 23, 2021.[15] Although shown to be effective in combatting COVID-19, the

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J&J vaccine has a slightly lower efficacy than the Pfizer or Moderna vaccines at 66.3%.[16]

Under the FDA's EUAs for the three vaccines, vaccine manufacturers and health care providers (such as local health departments, physicians, nurses, and pharmacists) who are administering the COVID-19 vaccines were mandated to report serious adverse events or reactions (AERs) that occur from any of the three vaccines through the DHHS's "Vaccine Adverse Event Reporting System" (VAERS), which is co-managed by the FDA and CDC, and accessible through the public resource, WONDER (Wide-ranging ONline Data for Epidemiologic Research).[17] Serious AERs are defined by VAERS as:

> *Death; a life-threatening adverse event; inpatient hospitalization or prolongation of existing hospitalization; a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions; a congenital anomaly/birth defect; an important medical event that based on appropriate medical judgement may jeopardize the individual and may require medical or surgical intervention to prevent one of the outcomes listed above; cases of multisystem inflammatory syndrome; cases of COVID-19 that result in hospitalization or death.*[17]

Health care providers are also encouraged to report any other AERs they observe in patients that they can reasonably conclude are due to the vaccine administered.

Individuals from the general public can report their AERs directly to the vaccination manufacturer or their health care provider, who are mandated to report the AERs to VAERS, or the person can report their vaccine side effects directly to VAERS by logging into the system and creating a report themselves.[17] Due to the fact that the general public can report unverifiable AERs to the VAERS system, these reports alone cannot be used to determine if a vaccine caused or contributed to the reported AERs and the threat of conviction under Federal law for submitting a fabricated report may not deter people from submitting false reports. The strengths of the VAERS system are that it can be used to detect unusual or unexpected patterns ("safety signals") that can be followed in a strategic manner, and VAERS staff regularly can monitor and remove entries made by the general public that cannot be verified.

This project was of interest due to the concerns regarding the potential side effects of the three COVID-19 vaccines authorized for use in the U.S. Data obtained for this study from the VAERS database provides the information needed to describe reported AERs, and specifically, this study was intended to provide a resource regarding potential AERs associated with the Pfizer-BioNTech (Pfizer), Moderna/NIAID/BARDA (Moderna), and Johnson & Johnson's Janssen (J&J) COVID-19 vaccines in the State of Kansas.

METHODS

The VAERS database was searched from vaccine inception on December 11, 2020 to May 13, 2021 for AERs related to the three COVID-19 vaccines. The study team chose this ending date as it was the day prior to the Pfizer vaccine receiving FDA EUA approval for use in adolescents 12 to 15 years old.[18] Results were grouped by vaccine manufacturer, whether the impacted patient resided in Kansas, patient age and gender, and included information on AER description, as well as any relevant or available data regarding labs, current illnesses, AERs after prior vaccinations, medications at time of vaccination, and medical history and/or allergies. The full description of the search strategy is available from the authors upon request. This study was approved by the University of Kansas School of Medicine Institutional Review Board as non-humans subject research.

Data Screening. The search identified 1,705 separate patient entries in VAERS. The initial data file was screened by two of the authors (AT and KN) for entries that needed to be removed. KN initially removed 270 entries and AT initially removed 239 entries, with an agreement rate of 96.3%. After discussion, a consensus was reached to remove 222 entries (Cohen's $\kappa = 0.85$, $p = 0.16$, 95% CI -0.7% to 4.1%). Entries were removed for four reasons, "unknown" vaccine manufacturer (four removed), report of unapproved underage administration (23 removed), duplicate entries (15 removed), and those entries that were not COVID-19 vaccine related AERs (180 removed). The break-down of the screening criteria by vaccine manufacturer is shown in Table 1.

Table 1. VAERS COVID-19 vaccine entry data screening procedure.

	Pfizer	Moderna	J&J	Total
Removed "unknown" vaccines	---	---	---	4
Start	**676**	**818**	**207**	**1,701**
Removed - underage administration	1	9	13	23
Removed - duplicate report	8	5	2	15
Removed - not COVID vaccine AER	102	58	20	180
Total after non-AER entries removed	**565**	**746**	**172**	**1,483**
Removed if death was indicated	16	18	4	38

Of the 180 entries related to the COVID-19 vaccines that did not indicate an AER occurred: 68 reported a patient had a positive COVID-19 diagnosis but no vaccine AER; 60 reported an unauthorized use of the vaccine (e.g., incorrect dose, incorrect vaccine given for second dose); 21 had another diagnosis after vaccination that accounted for the report (e.g., ruptured appendix, strep throat); 19 were unclear as to the specific AER experienced (e.g., "seen at ER", "just didn't feel right"); 11 were unremarkable clinic progress notes of follow-up calls to patients who had received a vaccination; and one was removed because the submitter indicated it was a report based on a friend's social media post. This left a total of 1,483 separate patient entries. Thirty-eight entries that reported the patient's death were removed and discussed separately below. This left a total of 1,445 VAERS entries to be coded by the research team.

Data Coding. Each VAERS entry was screened by one of the three authors, coded by another, and reviewed by the third, with a rotating list of entries for each author, ensuring that each entry was seen and checked by all three members of the authorship team. Any entries that were unclear were resolved by discussion. Each identified AER that appeared two or more times was coded into a separate category, for a

total of 58 identified categories of AERs related to the COVID-19 vaccines. Twenty-eight category names utilized wording obtained from the side effects listed on the information sheets provided by the manufacturer for each vaccine.[19-21] The additional 30 categories were named based on medical and lay terms for the AER identified (i.e., arrythmia/abnormal heart rhythm). Additionally, there was a category named "other" for 16 individual entries that did not fall into the identified AER categories. Within all 59 categories there were a total of 4,287 separate AERs reported. Table 2 shows the AER categories identified with the breakdown of number of coded entries in each.

Data Analysis. Descriptive statistics were used to describe AERs reported by vaccine manufacturer (Pfizer, Moderna, and J&J), age category (29 and younger, 30 to 39, 40 to 49, 50 to 59, 60 to 64, and 65 and older), and gender (male and female), as well as any reported deaths in the data file. Traditional statistical analyses were not performed beyond calculating the inter-rater reliability as this is a purely descriptive study of reported AERs and causal inferences are unable to be performed due to the nature of the VAERS system.

Table 2. COVID-19 vaccine reported adverse events or reactions categories identified from 1,445 patient entries.

	Total	Pfizer	Moderna	J&J
Fatigue/tiredness	**266**	84	144	38
Tingling/itching	**251**	80	153	18
Fever	**226**	12	163	51
Hives	**223**	18	199	6
Muscle/joint pain	**209**	136	6	67
Nausea	**189**	79	88	22
Headache	**187**	126	6	55
Chills/shaking	**175**	101	26	48
Confusion	**175**	8	165	2
Seizure	**174**	8	163	3
Rash	**146**	50	90	6
Numbness	**142**	21	112	9
Dizziness	**136**	107	3	26
Bruising at injection site	**133**	4	124	5
Redness at injection site	**131**	25	101	5
Dyspnea/hypoxia *(Shortness of breath)*	**118**	17	101	0
Pain at injection site	**98**	57	30	11
Eye pain	**88**	82	1	5
Arrythmia *(abnormal heart rhythm)*	**81**	31	34	16
Weakness	**76**	29	36	11
Blood clot	**75**	1	71	3
Syncope *(lightheadedness/fainting)*	**75**	28	34	13
Diaphoresis *(sweating)*	**70**	24	34	12
Vomiting	**69**	19	36	14
Sore throat	**65**	51	8	6
Diarrhea	**60**	20	34	6
Cough/congestion	**56**	34	16	6
Lymphadenopathy *(swollen lymph nodes)*	**56**	23	29	4
Arm pain	**54**	32	6	16
Xerostomia *(dry mouth)*	**52**	39	3	10

	Total	Pfizer	Moderna	J&J
Insomnia	**51**	8	37	6
Allergic reaction	**47**	24	15	8
Chest pain	**46**	35	2	9
Sensory issue/loss	**36**	10	20	6
Difficultly walking	**30**	2	25	3
Anxiety/panic/depression	**27**	11	16	0
Stroke	**25**	3	21	1
Abdominal pain	**24**	11	3	10
Ear pain/tinnitus *(ringing in ears)*	**22**	3	12	7
Metallic taste	**20**	6	10	4
Loss of appetite	**11**	3	4	4
Shingles	**11**	3	6	2
Epistaxis *(nosebleed)*	**10**	7	0	3
Bell's palsy	**9**	3	6	0
Hyperglycemia *(high blood sugar)*	**6**	1	4	1
Herpes labialis *(cold sores)*	**5**	2	3	0
Edema	**5**	2	3	0
Hematuria *(blood in urine)*	**4**	1	3	0
Vivid dreams	**4**	3	1	0
Gastrointestinal bleed	**3**	0	3	0
Myocardial infarction *(heart attack)*	**3**	0	3	0
Paralysis	**3**	2	1	0
Pneumonia	**3**	2	1	0
Asthma attack	**2**	1	1	0
Hallucinations/delusions	**2**	1	0	1
Hypoglycemia *(low blood sugar)*	**2**	1	1	0
Thrombocytopenia *(low blood platelets)*	**2**	2	0	0
Unexpected vaginal bleeding	**2**	1	1	0
Other	**16**	6	4	6
Total	**4,287**	**1,500**	**2,222**	**565**

RESULTS

Information from the Kansas Department of Health and Environment (KDHE) was obtained to determine how many people in Kansas had received at least one dose of the available COVID-19 vaccines (Andrea May, MPH, email communication, June 2021). From December 11, 2020 to May 13, 2021, the KDHE indicated that a total of 1,191,204 initial vaccine doses had been given, which translated to approximately 41% of the total population receiving at least one dose (1,191,204/2,911,641). VAERS did not indicate if someone submitted multiple reports, but this roughly indicated that for each vaccine dose given in Kansas, one in every 1,467 led to a report in VAERS (2,120,350/1,445), and one AER occurred per every 495 doses given in Kansas (2,120,350/4,287; Table 3). Of the 1,445 VAERS entries, 215 (14.9%) concerned patients younger than 29 years, 297 (20.6%) were age 30 to 39 years, 277 (19.2%) were between 40 and 49 years, 230 (15.9%) were age 50 to 59 years, 118 (8.2%) were age 60 to 64 years, and 263 (18.2%) were 65 years and older. Twenty-five entries had no age noted. In terms of gender, 296 (20.5%) entries reported male patients, 1,139 (78.8%) female patients, and 10 were unknown gender (0.7%).

Table 3. COVID-19 vaccines given in Kansas (December 11, 2020 to May 13, 2021).

	Pfizer	Moderna	J&J	Total
Total doses	**1,130,089**	**922,728**	**67,308**	**2,120,350**
Dose 1	624,528	499,808	67,308	1,191,056
Dose 2	505,561	422,920	---	929,069
Unknown vaccine received	---	---	---	225
Prevalence				
VAERS entry *(one per every)*	2,058 doses	1,267 doses	401 doses	1,467 doses
AER *(one per every)*	753 doses	415 doses	119 doses	495 doses

Adverse Events or Reactions Reported. Overall, there were a total of 4,287 AERs reported, with an average of 3.0 (± 1.9) AERs reported per VAERS entry, with a median number of 3 (range 1 to 12). The Pfizer vaccine had a total of 1,500 AERs reported with an average of 2.7 (± 1.8) AERs per patient entry, with a median number of 2 (range 1 to 11). The Moderna vaccine had a total of 2,222 AERs reported with an average of 3.1 (± 1.9) AERs reported per patient entry, with a median number of 3 (range 1 to 10). The J&J vaccine had a total of 565 AERs reported, with an average of 3.4 (± 2.0) AERs per patient entry, with a median number of 3 (range 1 to 12). Table 2 shows the breakdown of each AER by vaccine manufacturer.

Pfizer-BioNTech Vaccine. The Pfizer vaccine had a total of 549 entries in the VAERS system as of May 13, 2021, and 1,500 separate AERs. Of these entries, 92 (16.8%) included patients younger than 29 years, 117 (21.3%) were age 30 to 39 years, 93 (16.9%) were between 40 and 49 years, 91 (16.6%) were age 50 to 59 years, 37 (6.7%) were age 60 to 64 years, and 92 (16.8%) entries were 65 years and older. Twenty-seven had no age noted. In terms of gender, 103 (18.8%) were male patients, 1,139 (80.3%) were female patients, and 5 (0.9%) were unknown gender. The highest AER count was in female patients aged 30 to 39 reporting muscle/joint pain. The top five AERs for age and gender are shown in Tables 4 and 5.

Moderna/NIAID/BARDA Vaccine. The Moderna vaccine had a total of 728 entries in the VAERs system as of May 13, 2021, and 2,222 separate AERs. Of these entries, 91 (12.5%) concerned patients younger than 29 years, 141 (19.4%) were age 30 to 39 years, 155 (21.3%) were between 40 and 49 years, 115 (15.8%) were age 50 to 59 years, 66 (9.1%) were age 60 to 64 years, and 149 (20.5%) were 65 years and older. Eleven had no age noted. In terms of gender, 144 (19.8%) entries were for male patients, 580 (79.7%) female patients, and 4 (0.5%) were unknown gender. The highest AER count was for female patients aged 40 to 49 who reported hives (Tables 4 and 5).

Johnson & Johnson's Janssen Vaccine. The J&J vaccine had a total of 168 entries in the VAERs system as of May 13, 2021, and 565 separate AERs. Of the VAERS entries, 32 (19.0%) were reports for patients younger than 29 years, 39 (23.2%) were age 30 to 39, 29 (17.3%) were between 40 and 49 years, 24 (14.3%) were age 50 to 59 years, 15 (8.9%) were age 60 to 64 years, and 22 (13.1%) were 65 years and older. Seven had no age noted. In terms of gender, 49 (29.2%) entries concerned male patients, 118 (70.2%) female patients, and one (0.6%) had an unknown gender. The highest AER count was for female patients aged 30 to 39 reporting muscle/joint pain (Tables 4 and 5).

Other Adverse Events or Reactions Reported. Overall, there were 16 AERs that were outliers, meaning they were only reported in VAERS once and they did not fall into one of the 58 identified categories. There were six patients who received the Pfizer vaccine who reported "other" AERs: anemia, severe acid reflux, onychorrhexis (unexplained breaking of fingernails), flaring of Fothergill's disease (trigeminal neuralgia), Takotsubo cardiomyopathy (apical ballooning syndrome), and development of Willis-Ekbom disease (restless leg disease). There were four patients who received the Moderna vaccine who reported either the development of pyelonephritis (kidney infection), hemorrhoids, constipation, or a report of a pulmonary embolism (blood clot in lung). There were six patient entries related to the J&J vaccine: the worsening of multiple sclerosis symptoms, polyuria (excessive urination), hormonal changes, neuralgia (burning nerve pain), an acute adrenal (Addisonian) crisis, and priapism (prolonged painful erection).

Deaths. There were 38 patient deaths identified in the VAERs system from December 20, 2020 to May 13, 2021 (38/1,483; 2.6%). Of these, 16 had received Pfizer, 18 received Moderna, and four received the J&J vaccine. No deaths were reported in patients under age 39, and the majority (11/38; 28.9%) were 65 years or older. Fifteen of these deaths were due to unknown causes at time of report, but were not suspected to be related to the vaccines; 17 deaths were related to other verifiable diagnoses, such as cancer or falls, and were also not suspected to be related to the vaccines; five deaths were related to COVID-19 complications in between vaccine doses; and one death is being reported by KDHE as related to an allergic reaction from the Pfizer vaccine. Figure 1 shows the breakdown of deaths by age group, gender, and vaccine manufacturer.

Table 4. Top five reported adverse events or reactions for each COVID-19 vaccine by age group.

	Pfizer Vaccine			Moderna Vaccine			J&J Vaccine		
	AER	n	%	AER	n	%	AER	n	%
29 years and younger	Muscle/joint pain	37	40.2%	Hives	24	26.4%	Fever, headache*	14	43.8%
	Headache	27	29.3%	Confusion	23	25.3%	Muscle/joint pain	13	40.6%
	Nausea	21	22.8%	Fever	22	24.2%	Chills/shaking	10	31.3%
	Fatigue, dizziness*	17	18.5%	Numbness	20	22.0%	Dizziness	6	18.8%
	Eye pain	15	16.3%	Fatigue, seizure*	18	19.8%	Chest pain, fatigue*	5	15.6%
30 to 39 years	Muscle/joint pain	46	39.3%	Hives	44	31.2%	Muscle/joint pain	22	56.4%
	Chills/shaking	28	23.9%	Confusion	40	28.4%	Headache	19	48.7%
	Headache	26	22.2%	Seizure	37	26.2%	Fever	12	30.8%
	Eye pain, fatigue*	23	19.7%	Tingling/itching	33	23.4%	Chills/shaking	11	28.2%
	Dizziness	22	18.8%	Fever	32	22.7%	Fatigue	9	23.1%
40 to 49 years	Muscle/joint pain	32	34.4%	Hives	46	29.7%	Muscle/joint pain	10	34.5%
	Headache	22	23.7%	Seizure	41	26.5%	Fatigue	9	31.0%
	Chills/shaking	21	22.6%	Tingling/itching	37	23.9%	Headache	7	24.1%
	Dizziness, eye pain*	17	18.3%	Fatigue	35	22.6%	Chills/shaking, fever, pain at injection site*	6	20.7%
	Tingling/itching	15	16.1%	Numbness	33	21.3%	Arm pain/syncope*	5	17.2%
50 to 59 years	Muscle/joint pain	41	45.1%	Hives	40	34.8%	Muscle/joint pain	8	33.3%
	Headache	25	27.5%	Confusion	31	27.0%	Chills/shaking, headache*	7	29.2%
	Tingling/itching	21	23.1%	Fatigue	30	26.1%	Fatigue, tingling/itching*	6	25.0%
	Dizziness	18	19.8%	Bruising at injection site	29	25.2%	Dizziness, fever*	5	20.8%
	Chills/shaking	13	14.3%	Fever	28	24.3%	Ear pain/tinnitus	4	16.7%
60 to 64 years	Muscle/joint pain	10	27.0%	Fever	18	27.3%	Fever	4	26.7%
	Nausea	6	16.2%	Hives	17	25.8%	Muscle/joint pain	4	26.7%
	Dizziness, headache, tingling/itching*	5	13.5%	Confusion	14	21.2%	Nausea	4	26.7%
	Diarrhea/fatigue/pain at injection site/rash*	4	10.8%	Fatigue, seizure, tingling/itching*	13	19.7%	Chills/shaking, headache*	3	20.0%
	Arm pain, cough/congestion, difficulty walking/weakness*	3	8.1%	Dyspnea/hypoxia, nausea	9	13.6%	Abdominal pain, dizziness, numbness/weakness*	2	13.3%
65 years and older	Dizziness	27	29.3%	Tingling/itching	38	25.5%	Muscle/joint pain	9	40.9%
	Muscle/joint pain	20	21.7%	Seizure	32	21.5%	Chills/shaking	8	36.4%
	Headache	14	15.2%	Fever	30	20.1%	Fatigue	7	31.8%
	Chills/shaking	13	14.1%	Hives	26	17.4%	Fever	6	27.3%
	Eye pain	12	13.0%	Confusion	24	16.1%	Headache	5	22.7%
Total	Muscle/joint pain	196	35.7%	Hives	197	27.1%	Muscle/joint pain	67	39.9%
	Headache	125	22.8%	Confusion	164	22.5%	Headache	55	32.7%
	Dizziness	107	19.5%	Fever	163	22.4%	Fever	51	30.4%
	Chills/shaking	100	18.2%	Seizure	161	22.1%	Chills/shaking	48	28.6%
	Fatigue	82	14.9%	Tingling/itching	152	20.9%	Fatigue	38	22.6%

*Tie between reported AER type.

Table 5. Top five reported adverse events or reactions for each COVID-19 vaccine by gender.

	Pfizer Vaccine			Moderna Vaccine			J&J Vaccine		
	AER	n	%	AER	n	%	AER	n	%
Male	Muscle/joint pain	34	33.0%	Fever	42	29.2%	Muscle/joint pain, headache*	16	32.7%
	Headache	20	19.4%	Confusion	39	27.1%	Chills/shaking	15	30.6%
	Dizziness	17	16.5%	Hives	38	26.4%	Fever	14	28.6%
	Eye pain, nausea*	14	13.6%	Fatigue	33	22.9%	Fatigue	11	22.4%
	Chills/shaking, fatigue*	13	12.6%	Bruising	29	20.1%	Dizziness	7	14.3%
Female	Muscle/joint pain	162	36.7%	Hives	159	27.4%	Muscle/joint pain	51	43.2%
	Headache	105	23.8%	Seizure	150	25.9%	Headache	39	33.1%
	Dizziness	90	20.4%	Tingling/itching	139	24.0%	Fever	37	31.4%
	Chills/shaking	87	19.7%	Confusion	125	21.6%	Chills/shaking	33	28.0%
	Tingling/itching	72	16.3%	Fever	121	20.9%	Fatigue	27	22.9%
Total	Muscle/joint pain	196	35.7%	Hives	197	27.1%	Muscle/joint pain	67	39.9%
	Headache	125	22.8%	Confusion	164	22.5%	Headache	55	32.7%
	Dizziness	107	19.5%	Fever	163	22.4%	Fever	51	30.4%
	Chills/shaking	100	18.2%	Seizure	161	22.1%	Chills/shaking	48	28.6%
	Fatigue	82	14.9%	Tingling/itching	152	20.9%	Fatigue	38	22.6%

*Tie between reported AER type.

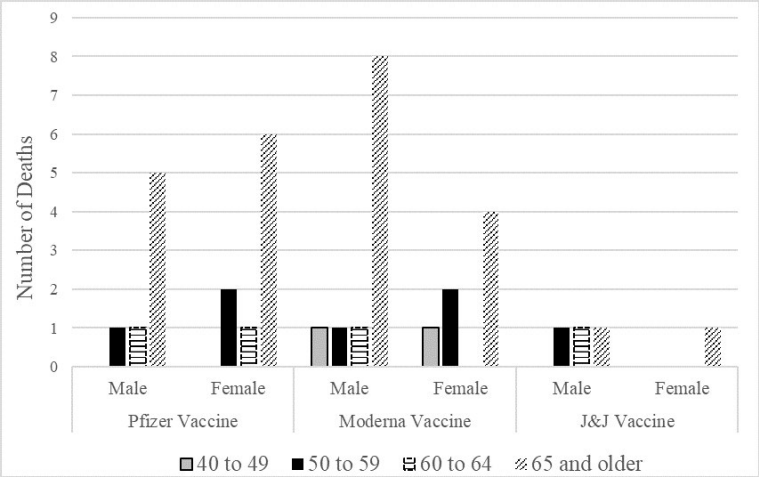

Figure 1. Number of deaths reported by age group, gender, and COVID-19 vaccine.

DISCUSSION

The information presented in this study can be used as a resource for those who are curious about the potential side effects of the three COVID-19 vaccines, especially those who may be hesitant for various reasons, such as fear of unknown risks, lack of trust in production, or personal safety. As of August 31, 2021, only 53.0% of the U.S. population and approximately 27.5% of the world population are fully vaccinated.[2] As of August 31, 2021, Kansas has had 369,890 confirmed cases of COVID-19 and 5,560 COVID-19 related deaths. Vaccine rates in Kansas were also slightly higher than previously reported on May 13, 2021, with 48.2% of the population being fully vaccinated. However, with more than 50% of the population of Kansas remaining unvaccinated, this indicated that many Kansans are either unable to get vaccinated (i.e., they are underage or have medical barriers) or they are unwilling. This hesitancy also may affect parental willingness to allow their children to get vaccinated, as uncertainty regarding the adverse effects of vaccines has been cited as a major barrier to adolescent vaccination in Kansas.[22]

Results from a June 2020 global survey of COVID-19 vaccine acceptance indicated that 71.5% of participants would be "very or somewhat likely" to receive a vaccine.[23] However, the survey results also indicated that the potential side effects and AERs related to the COVID-19 vaccines, as well as lack of trust in government and public health officials, have contributed to vaccine hesitancy. Despite the acceleration of the development of these three vaccines, the FDA has taken substantial and appropriate steps to ensure the validity and efficacy of these COVID-19 vaccines.[24]

Highlighting the fact that mild and likely short term side effects were present most often may aid individuals in their decision to receive a vaccine. The Pfizer vaccine mainly saw reports of mild AERs, including high incidences of muscle/joint pain and headache were somewhat consistent with manufacturer reports, with 21 of the 41 identified AERs listed on the supplied FDA fact sheet.[19] A prior study by Johnston and colleagues in 2021 reported allergic and neurologic reactions associated with the Moderna vaccine, with hives and seizure commonly reported.[25] Colloquially known as "COVID arm", hives at the vaccine site frequently have been reported with the Moderna vaccine. Cases of seizure have been reported with other common vaccines, such as tetanus, pertussis, poliovirus, and influenza,[26] especially in children; however, these cases were extremely rare and the vast majority of which were short and did not cause any long-term damage.[27] Confusion/delirium in the Moderna vaccine, like many other AERs, may be related to the systemic inflammatory response associated with COVID-19 vaccines as this response may be associated with modification in brain physiology.[28] Overall, 18 of the AERs identified in this study were indicated on the provided patient

fact sheet for the Moderna vaccine, while 40 of the AERs identified were not.[20] The presence of additional AERs indicated that there may be additional side effects that will need to be monitored with two mRNA vaccines.

The Johnson & Johnson vaccine saw very similar AERs compared to the Pfizer vaccine. Of the AERs reported for the Johnson & Johnson vaccine, 19 of the AERs we identified are listed on the patient fact sheet, while 30 were not.[21,29] Additionally, no reported cases of CVST were found through the VAERS system in Kansas for the study period.[15,16] Reported blood clots of any kind after receiving the vaccine were limited to just three cases total with the J&J vaccine, and unfortunately no specification of what kind of blood clot was indicated in VAERS. Additionally, on July 13, 2021, the FDA announced revisions to the fact sheets of the J&J vaccine to include an observed risk of Guillain-Barre Syndrome (GBS) following vaccination.[21] These cases are again exceedingly rare among J&J vaccine recipients as only 100 out of 12.5 million recipients reported cases of GBS after J&J vaccination, and no cases were noted in this study. Most people with GBS make a full recovery and as it stands there has been no definitive causal relationship established between the J&J vaccine and GBS.[30]

One of the most important AERs that must be investigated rigorously was the prevalence of death among those who receive a COVID-19 vaccine. Our study reported that there were 38 deaths reported in the VAERS system from December 20, 2020 to May 13, 2021. This translated to 0.0002% (38/2,120,350) of persons in Kansas who had recieved a COVID-19 vaccine being associated with a death. None of these cases provided a causal relationship between vaccine administration and death, but there was one report that is being investigated. Given the nature of the VAERS system, it is difficult to determine relationships from the reports and data that were available; however, the FDA and CDC follow-up on any reported deaths in the VAERS system and make a further determination in conjunction with state health departments.[17]

When weighing the choice of receiving any sort of medication, vaccine, or health-related intervention, the benefits and the risks must be weighed in any case.[31] All too often individuals suffer from omission bias, or the idea of favoring inaction over action when it comes to receiving a medical intervention, especially when it comes to vaccines. Additionally, the benefits and risks associated with other vaccines must also be considered. The flu vaccine, for instance, has common side effects including soreness, redness, and/or swelling from the shot, headache, fever, nausea, and muscle aches, which are very similar to the AERs reported with the COVID-19 vaccines.[32]

Combatting vaccine hesitancy is not a new phenomenon. However, given themes related to the COVID-19 vaccine hesitancy, such as vaccine efficacy, safety, pace of development, and fear of side effects, it is important for health care providers and public health officials to have information available as these groups play a critical role in combating vaccine hesitancy.[22,33-35] Of note, only 0.00068% (1,445/2,120,350) of COVID-19 vaccine doses given from December 11, 2021 to May 13, 2021 were associated with a report in VAERS, showing a particularly low rate of reactions associated with these vaccines thus far. By providing a clear statistical overview of the AERs associated with these vaccines, this study may be utilized as a resource for individuals and their medical providers to make informed and educated decisions on whether to receive a COVID-19 vaccine.

CONCLUSIONS

On June 10, 2021, Moderna petitioned the FDA to approve its vaccine for adolescents aged 12 to 17; and as of August 23, 2021, the Pfizer/Biotech COVID-19 was given full approval by the FDA for use in people ages 16 and older.[36] While Moderna has yet to be approved for adolescents, the EUA approval of the Pfizer/BioNTech vaccine for those aged 12 to 17 highlighted the confidence that the FDA has in the vaccine's efficacy and safety.[18] In addition, beginning in March 2021, Pfizer/BioNTech began conducting randomized control trials in children aged 6 months to 11 years old, which hopefully will cement the "tolerability, immunogenicity, and safety" of this vaccine in virtually all age groups.[37] With the first COVID-19 vaccine receiving full FDA authorization, there is the expectation that some of those who are vaccine hesitant may cease to be so.

One way to combat a virus is through herd immunity.[38,39] Herd immunity occurs when the majority of the population gets infected by a disease and, as a result, develops immunity and antibodies that makes the spread of the disease unlikely. Another way to reach herd immunity is through the use of vaccines. Prior to Spring 2021, when the global base reproduction number (R_0) of COVID-19 remained around 2.5, herd immunity was set at approximately 60%.[40] However, as the SARS-CoV-2 virus continues to mutate into variants of interest (VOIs), such as the Delta variant (B.1.617.2 lineage) and Lambda variant (C.37 lineage),[39] the global R_0 also has been increasing and was estimated at 4.1 (95% CI, 3.09-5.39), which pushed the need for global herd immunity close to 90%.[41] To approach herd immunity in the U.S., it is crucial to provide accurate and credible information to educate and encourage those who can be vaccinated to do so. The more people who can achieve natural immunity through infection (less desirable) or through vaccination (more desirable), the greater chance there is to lower the emergence of new VOIs that current vaccines may be less effective against.

With the augmentation and distribution of safe and effective COVID-19 vaccines, along with other mitigation efforts, the societal effects of COVID-19 will diminish. It is important for public health experts, health care providers, and elected officials to provide consistent and reliable information to the public to increase vaccine uptake.[35,42] Knowing that vaccine safety is an issue contributing to vaccine hesitancy, informing the public about the potential AERs of the COVID-19 vaccines is one step closer to fulfilling that gap.

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Qualitative Assessment of Access to Perinatal Mental Health Care: A Social-Ecological Framework of Barriers

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ABSTRACT

Introduction. Psychological distress affects up to 25% of pregnant women and contributes to poor birth outcomes. Screening with appropriate referral or treatment is critical, yet many women do not access services. This project aimed to identify knowledge of and barriers to mental health services in the perinatal period.

Methods. Interviews with low-income pregnant or postpartum women, primary care providers (PCPs), and mental health care providers were conducted in Sedgwick County, Kansas. Interviews were transcribed, independently reviewed using grounded theory, and stratified using a social-ecological model framework.

Results. Thirty-three interviews were conducted with 12 (36%) pregnant or postpartum women, 15 (45%) PCPs, and 6 (18%) mental health care providers. Barriers were categorized into three levels: individual, social, and society. Individual level barriers, including cost or lack of insurance and transportation, were consistent across groups, however, women identified barriers only at this level. Provider groups identified barriers at all levels, including lack of support, poor communication between providers, and Medicaid limitations.

Conclusions. Multi-level interventions are needed to improve access to mental health care for low-income women in the perinatal period.

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INTRODUCTION

Psychological distress during pregnancy, including depression, anxiety, and stress, can lead to poor birth outcomes, including preterm birth and low birthweight.[1,2] Perinatal mood and anxiety disorders (PMADs) lead to increased medical expenses, cessation of breastfeeding, and increase the risk of child abuse and neglect.[3] Perinatal depression, the most common pregnancy complication in the U.S., impacts the social, emotional, and cognitive development of infants,[1] increases stress hormone levels,[4] negative reactivity to stress,[5] sleep disturbance, attention-deficit hyperactivity disorder, conduct disorders, and cognitive deficits.[6] Perinatal women with depression are more likely to be uninsured, of low socioeconomic status, and have increased use of psychiatric and non-psychiatric services.[7]

The ability to identify and mitigate perinatal psychological distress properly is of upmost importance. Screening women for PMADs is recommended by the American College of Obstetricians and Gynecologists (ACOG),[8] the American Academy of Family Physicians (AAFP),[9] and the American Academy of Pediatrics (AAP).[3] Women who screen positive should be treated or referred to services. Yet, access to mental health services was an identified treatment barrier for women with lower socioeconomic status.[10] Other barriers included lack of knowledge, cultural complexities, and stigma around diagnosis.[11]

Previous studies assessed barriers to mental health care access based on perspectives of pregnant and postpartum women, health care providers, and mental health providers.[12-15] However, no identified studies assessed perceived barriers both within and across these three groups. As such, the aim of this project was to triangulate themes[16] from interviews with low-income pregnant or postpartum women, primary care providers (PCPs), and perinatal mental health providers regarding knowledge of and barriers to perinatal mental health services.

METHODS

This qualitative study evaluated knowledge of and perceived barriers to accessing perinatal mental health services in Sedgwick County, Kansas. The study was approved by the University of Kansas School of Medicine Institutional Review Board.

Participants. Pregnant (greater than 19 weeks) or postpartum women (infant less than one year of age) 18 years of age or older, able to understand English, and living in Sedgwick County were recruited from existing maternal and child health programs (e.g., prenatal education, home visitation, case management). Program staff, which were considered trusted sources of information, described the study and provided written information to participants. To reach women not connected to services, recruitment fliers were distributed through other community organizations (e.g., churches, schools).

PCPs practicing in Sedgwick County and able to understand English were recruited from the University of Kansas School of Medicine-Wichita, the Medical Society of Sedgwick County, and federally qualified healthcare centers. Perinatal mental healthcare (MHC) providers practicing in Sedgwick County and able to understand English were recruited through the University of Kansas School of Medicine-Wichita Department of Psychiatry and Behavioral Sciences, the Wichita State University Psychology Department, Postpartum Support International (Kansas Chapter), United Way 211 resource hotline, internet searches, and professional societies. Snowball sampling methods identified additional PCP and MHC providers from participants.

Structured interviews were completed over the telephone between October 2019 and March 2020. Participation was voluntary and informed consent was obtained prior to participation. Calls were recorded and lasted approximately 20 minutes. A standardized interview script for each participant group was followed. Interviews within each group were conducted until saturation of themes was reached.[17] Interview questions for participants included demographics (e.g., age, insurance), mental health (e.g., diagnosis, knowledge), mental health in terms of recent pregnancy (e.g., screening, comfort level), and knowledge of and access to mental health services (i.e., barriers or successes to accessing). PCP interviews included specialty and practice, standard

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practice for screening women for PMADS, knowledge of mental health services (e.g., medications, referral process, location, follow-up), and barriers or success in connecting women to resources. MHC provider interviews addressed specialty and practice, referral sources and follow-up, mental health medications, and barriers or successes in connecting women to resources.

Recordings were transcribed and identifying information removed. Transcripts were reviewed independently by researchers and community partners using grounded theory approach.[18] Within group themes were discussed until consensus was reached and crosscutting themes were identified by triangulation.[16] Reported barriers to accessing mental health care were organized using a social-ecological model,[19] distinguishing individual, social (interpersonal and community), and society (organizational and public policy) level barriers.

RESULTS

Thirty-four interviews were conducted. However, a discrepancy in gestation by weeks was identified for one interview and removed from analysis. A total of 33 interviews were included, 12 (36%) pregnant or postpartum women, 15 (45%) PCPs, and 6 (18%) MHC providers.

Pregnant and Postpartum Women. Of the 12 women interviewed, 17% (n = 2) were pregnant and 83% (n = 10) were postpartum with an infant less than one year of age. The average participant age was 24 years (range 18 - 33 years). One quarter of participants (25%; n = 3) had been diagnosed with a mental illness (Table 1). Participants described general stress and anxiety regarding pregnancy and fear of something happening to their child during pregnancy or after birth. One stated, "It's a scary feeling, we are looking into an abyss. I have no idea what I am getting myself into. Not only the physical caring for my child but the emotional. That's what's scary." Several mentioned breastfeeding challenges as a major contributor to stress and anxiety in the postpartum period. One reported, "I was struggling because I couldn't breastfeed. She wouldn't latch. Yeah. And I wanted to breastfeed. So, I was like, I planned on it and I didn't plan on nothing else."

Women reported varied experiences regarding screening and discussion of PMADs with healthcare providers. Only 67% (n = 8) reported ever completing a screening tool (e.g., Edinburgh Postpartum Depression Scale (EPDS), Patient Health Questionnaire (PHQ)); of those, 25% (n = 2) had the screening results discussed with them. One participant who completed a screening but was not given the results stated, "That's pretty annoying. I feel like it was a waste of time. But I feel like if they were concerned about something then maybe they would have went over it with me." Another shared dissatisfaction with the lack of information, stating, "I've never had anyone actually talk [about perinatal mental health] ... I'm thinking like yeah, why hasn't the doctor asked these specific questions? And it's kind of just, they sweep it under the rug, and these are normal feelings." Although most (83%; n = 10) were postpartum, no participants reported being screened by their child's doctor.

Table 1. Demographics of pregnant and recently delivered women (n = 12).[a]

Race/ethnicity	n (%)
Hispanic	4 (33%)
Non-Hispanic White	3 (25%)
Non-Hispanic Black	2 (17%)
Asian	1 (8%)
American Indian	1 (8%)
Multiracial	1 (8%)
Education	
High school or less	6 (50%)
Some college	4 (33%)
College degree	2 (17%)
Employment	
Unemployed	5 (42%)
Part-time	5 (42%)
Full-time	2 (17%)
Marital status	
Single	3 (25%)
Separated	1 (8%)
Partnered	2 (17%)
Married	6 (50%)
Insurance	
None	1 (8%)
Medicaid	5 (42%)
Military	1 (8%)
Private or parent's	5 (42%)
Financial status	
Struggling to keep up with the cost of living	4 (33%)
Comfortable keeping up with the cost of living	5 (42%)
Keeping up with the cost of living with extra money	2 (17%)
Missing	1 (8%)

[a]Data presented as f (%).

Despite differences in experience, all (100%; n = 12) women reported they would feel comfortable being asked about or completing a screening tool related to their perinatal mental health. One stated, "To me it was good. It was them showing they do care about us, the patients." However, responses were mixed regarding preference for face-to-face assessment or use of a paper or digital screening tool. Some expressed concern about receiving feedback from a paper screening; "Because there is no guarantee they will even look at the paper. Because if feels like when you do that, it feels like they just don't."

In terms of accessing mental health care, participants identified barriers only at the individual level; these included lack of transportation, cost or lack of insurance, issues with childcare while accessing services, lack of knowledge of available mental health resources, and scheduling difficulties with services (Table 2). Few (17%; n = 2) identified free or low-cost perinatal mental health care providers, and most (75%; n = 9) would use the internet to locate local resources. Others reported community organizations, pamphlets, doctor, or

family as means to locate resources. Several women also identified an interpersonal level success with social support from their husband or family, as making it easier to access care.

Table 2. Perinatal mental health access barriers as identified by interview cohorts.

Theme	Women[a]	FM providers[b]	OB providers[c]	Peds providers[d]	MHC providers[e]	Examples
Individual						
Transportation	x	x	x	x	x	"My patients definitely have issues with transportation. Transportation is a huge issue for a lot of people." (FM) "I am on a schedule. I can't be transported [by bus system] at certain times." (Postpartum)
Insurance	x	x	x	x	x	"Cost is probably the biggest issue with my patients." (FM). "There is a lot of anxiety with the cost." (OB).
Childcare	x	x	x		x	"It's kind of hard to bring a 4-year-old into a therapy session. She may not have anyone to watch." (MHC) "[It would be helpful if] somebody could help me take care of my baby while I went to therapy." (Postpartum)
Knowledge (women)	x			x		"Having that knowledge of available resources would be [a positive] change." (Peds)
Scheduling	x					"Finding [time] in my schedule with work." (Postpartum) "There is really no mental health help, like on the weekends or late in the afternoon when I have time to do these things." (Postpartum)
Knowledge (providers)			x	x	x	"Just knowing it is an issue and knowing how severe it can be. And then, understanding how to screen and what to do with positive screens." (Peds)
Social - Interpersonal						
Patient/provider communication		x	x			"A lot of patients don't have continuous cell phone service or have limited data plans...that's really an issue and they will tell us about that." (FM)
Social support		x	x	x	x	"There's a definite reluctance from the moms themselves who just don't want to go there. Or from their family members who don't think it is a big deal." (Peds) "What I hear from my patients is that they feel alone. They feel like they are the only ones going through things." (FM)
Social - Community						
Stigma		x	x	x	x	"I feel that there's still this stigma of depression/anxiety. Not being terrible happy about being pregnant...You're still not allowed to not be happy that you're pregnant." (OB)
Collaboration among providers		x			x	"There needs to be more networking events. There needs to be more just opportunity to come together and talk about what we do." (MHC)
Society - Organizational						
Provider to provider communication		x	x	x	x	"I would at least like some acknowledgement that the mom has made contact and that some sort of support is being given." (Peds) "[There needs to be] better communication, increased communication between physician and mental health providers. Both ways, honestly." (MHC)
Provider shortage		x		x	x	"There's just not enough providers. Not enough mental health providers in the city. Not in Sedgwick; I would say there are definitely not enough." (MHC)
Society - Public Policy						
Medicaid limitations		x	x	x	x	"Women on Medicaid lose their Medicaid. That's a big one. After six weeks." (MHC) "It would be great for them to have access to healthcare and to be the healthiest they can be before pregnancy." (Peds)

[a]Women = pregnant and recently delivered; [b]FM = Family Medicine; [c]OB = Obstetricians; [d]Peds = Pediatricians; [e]MHC = mental health care

Obstetrics Providers. Of the five obstetrics (OB) providers interviewed, four (80%) were practicing obstetrician-gynecologists, and one (20%) was a certified nurse midwife. All (100%; n = 5) were part of a group or hospital practice. Their length of practice in Sedgwick County ranged from 6 months to 36 years.

Regarding screening tools for PMADs, all (100%; n = 5) used the EPDS, and 20% (n = 1) also used the PHQ. Most (60%; n = 3) reported screening prenatally (at 28- or 36-weeks gestation) and at six weeks postpartum. One OB (20%) reported screening after delivery, prior to hospital discharge, and at two and six weeks postpartum, as well as administering the PHQ-2 for every patient (regardless of partum status) at every appointment. Those who screen positive on the PHQ-2 are screened further with the PHQ-9. The final provider (20%; n = 1) reported screening postpartum patients at every visit in the first year postpartum.

OB providers identified access to care barriers within all social-ecological levels. Formal training in PMADs was reported by 40% (n = 2) and varied levels of comfort were reported in prescribing medications. Transferring care between two members of the same healthcare team, known as a warm handoff, and integrated mental health services were perceived to improve access to care.

Regarding follow-up after a positive screening, OBs observed the challenges women who do not have a working telephone face in navigating the referral system. They also reported having a transient population can sometimes pose a barrier to follow-up.

Family Medicine Providers. All (100%; n = 4) family medicine (FM) providers were physicians and belonged to large group practices. Most (75%; n = 3) obtained additional certification beyond their family medicine residency; specifically, in maternal child health (50%; n = 2) or obstetrics (25%; n = 1). Length of time practicing in Sedgwick County ranged from 1.5 to 9 years. All FM providers (100%; n = 4) reported screening with a version of the PHQ; 75% (n = 3) screen at every visit and 25% (n = 1) screen at six weeks postpartum and the infant's one month well-check. If patients express additional concerns, one provider (25%) reported utilizing the Generalized Anxiety Disorder (GAD) screen and the Anxiety Symptoms Questionnaire (ASQ). Frustration was expressed related to screening. One stated, "Sometimes I don't want to screen" due to challenges connecting women to services.

The FM provider group reported barriers across all levels of the social-ecological model and identified warm handoffs and integrated mental health services as improving access to care. FM providers identified preconception counseling on the use of psychotropic medication during pregnancy as a positive factor in addressing PMADs.

Pediatric Providers. All (100%; n = 6) pediatric providers interviewed were physicians in group practices, ranging from small (17%; n = 1) to large (67%; n = 4); one (17%; n = 1) group practice size was unspecified. Years practicing in Sedgwick County ranged from 6 to 30. PMAD screening practices were focused on mothers of patients: 50% (n = 3) used the EPDS at varying intervals, including one, two, four, and six months postpartum, and unspecified time periods; 33% (n = 2) utilized a single question which was built into the electronic medical record (EMR) at two weeks and two months postpartum; and 16% (n = 1) used the PHQ for every patient in their predominantly adolescent practice, regardless of partum status. One (n = 16%) provider reported screening fathers as well.

As with the other PCPs, pediatricians identified barriers across all socio-ecological model levels. However, pediatric providers emphasized the importance of communication between providers, especially in cases where the mother's mental health status might have adverse effects on her ability to care for her child. Some pediatric providers (66%; n = 4) reported notifying the mother's PCP of a positive screen in addition to offering a list of resources. Warm handoffs and integrated mental health services remained ways to improve access.

Perinatal Mental Health Care Providers. The Mental Health Care (MHC) provider group (n = 6) included two clinical psychologists (33%) specializing in eating disorders, generalized anxiety, depression, and perinatal mental health, two (33%) licensed clinical social workers (one of whom specializes in trauma), one (16%) physician certified in general psychiatry, and one (16%) licensed master social worker specializing in perinatal mental health. Length of time practicing in Sedgwick County ranged from 1 month to 16 years. Most (66%; n = 4) were part of a large group practice, with 33% (n = 2) in small group practices. Regarding PMAD screening practices, 33% (n = 2) did not use a screening tool. The remaining 67% (n = 4) had varied practices: one used the EPDS; one used the EPDS and the Perinatal & Anxiety Screening Scale (PASS); one used the PHQ in conjunction with the GAD; and one used a specialized postpartum intake tool from Postpartum Support International (PSI).

Most (83%; n = 5) received referrals for PMAD treatment from OBs, other PCPs, hospitals, or self-referrals. All but one (83%; n = 5) MHC provider accepted Medicaid payments. One (n = 16%) mentioned that Medicaid patients were often not aware of the full scope of services that their insurance covers.

Consistent with PCPs, MHC providers identified access to care barriers across all levels of the socio-ecological model. All MHC providers (100%; n = 6) described processes or policies to address individual level barriers, such as letting children (especially infants) come to the appointment and providing space to breastfeed, and one offered in-home services. This group also echoed the need for warm handoffs and integrated mental health services, and identified home visitation as an avenue to improve access to services.

In addition, several talked specifically about the impact of birth trauma on maternal mental health. One also addressed the impact on PCPs, stating, "I think that if we could wrap around what we consider perinatal mental health is not just something that affects the mom. But partner and then extended family and then obviously the medical provider is part of that picture as well."

DISCUSSION

The purpose of this qualitative study was to identify the knowledge of and barriers to perinatal mental health services based on the perspectives of low-income pregnant or postpartum women, PCPs, and MHC providers. It was imperative to identify key drivers to accessing mental health services that can be leveraged for successful interventions to reduce negative birth outcomes.

Screening and Care Practices. Routine screening is recommended by ACOG,[8] AAFP,[9] and AAP,[3] as only 18 - 25% of PMADs (specifically postpartum depression and postpartum psychosis) are diagnosed without screening.[20] All interviewed PCP and MHC providers reported routinely screening women for mental health disorders in the perinatal period. However, a variety of protocols and tools were reported, which was reflected by the varied screening experiences reported by women. This variability may be a barrier to identifying women who have or are at risk for PMADs and is not unique to the community. A survey of Washington Academy of Family Physicians members found that while 70% (n = 254) always or often screened for postpartum depression, only 22% used a validated screening tool.[21] In the United Kingdom, PCPs perceived 7% of 176 women to be depressed, but EPDS scores were abnormal for 17%.[22] ACOG recommends screening for PMADs at least once during the perinatal period using a tool that has been validated for perinatal use, specifically EPDS, PHQ-9, Beck Depression Inventory, or Postpartum Depression Screening Scale.[23] ACOG further recommends having systems in place to ensure follow-up care when a diagnosis is made.

Providers should avoid screening due to perceived patient concerns, as women reported being open to PMAD screening, and those who had been screened reported providing honest responses. In addition, women reported feeling as though mental health concerns were brushed aside if the provider failed to raise the subject, and lack of feedback was interpreted as a negative screening result, which may not have been accurate. Educational interventions with providers, changes in EMRs, and use of standardized patient exercises regarding PMAD screening have improved screening adherence and referral/treatment for women who screened positive.[24]

Management practices of women who screened positive varied widely, with OB and FM providers more likely to manage, pediatric providers more likely to refer, and MHC providers' management depending on patient needs and expertise of the provider. Yet, Kansas Perinatal Risk Assessment and Monitoring (PRAMS) data suggested 17% of mothers who thought they needed treatment for depression did not receive it,[25] indicating barriers to perinatal health care remained.

Barriers to Access to Care. Barriers to perinatal mental health care access were identified at all levels of the social-ecological model. However, pregnant and postpartum women identified barriers only at the individual level. Individual level barriers, including cost or lack of insurance and transportation, were consistent across all respondent groups. These were expected as Sedgwick County has a very limited public transportation system and Kansas does not have Medicaid expansion. In contrast, half of women reported scheduling as a barrier, while no PCPs or MHC providers identified this barrier. Scheduling issues included conflict with work, lack of weekend and evening appointments, and long wait times to get an appointment. These barriers could be mitigated by increasing flexibility in scheduling, such as expanding or adjusting office hours to accommodate drop-in appointments and include more evenings and weekends.[15] Another individual level barrier cited by women (25%; n = 3) was a lack of knowledge of existing perinatal mental health services. Based on strategies reported by participants, MHC providers should partner with trusted community programs to promote their services and make sure organizations are optimized to be found in internet searches. Finally, childcare was a barrier to attending appointments and appointments were more difficult to navigate if a young child was present. Findings were consistent with PRAMS data, where over 50% of respondents did not get help for depression due to cost and childcare concerns.[25] However, all MHC providers reported allowing children when needed. Promotion of such accommodations may increase women's willingness to engage in services.

An interpersonal level barrier identified by all provider groups was lack of social support from the woman's family and friends. While not identified as a barrier, several women described the importance of family support in navigating mental health issues. An inverse relationship has been reported between social support levels and both perinatal depression screening scores and postpartum depression diagnosis.[26,27] Due to the significant impact, providers should consider the following strategies to increase social support for women in the perinatal period:[28,29]

1. Provide education to the woman's partner on how to support her, including communication and practical support strategies.
2. Connect women with other pregnant women and expectant couples.
3. Provide adequate information on pregnancy, childbirth, and parenting, that is consistent and accurate.

At the organizational level, lack of communication between providers regarding patients was identified across all provider groups. The majority (> 70%) of pediatricians, OB providers, and FM providers expressed a desire for feedback and closed-loop communication from MHC providers. However, MHC providers reported being intentional about providing feedback to PCPs and reported PCPs could be more effective following up on patients receiving perinatal mental health services, indicating there are likely significant communication gaps between medical and mental health providers. In general, closing the referral loop is a complex problem in health systems. Feedback regarding the outcome of a referral is important for patient safety because patients are medically vulnerable in the period of transition between providers; longer wait times can lead patients to forget about the referral appointment, seek out-of-network specialists, or forgo the referral due to perceived resolution of clinical concern.[30] Integrated behavioral health services and developing systems to support communication between providers better should be prioritized to enhance patient outcomes.

Stigma was a theme at the community level identified by all provider groups. No women cited this barrier, despite public stigma being a well-identified obstacle to seeking mental health services in the U.S.[14,15,31] Providers may address stigma through use of standardized screening questions, avoiding language that creates an "us" and "them" division, and paying adequate attention to mental health needs of perinatal women.[32]

At the public policy level, most providers (71%) identified being underinsured (i.e., being on Medicaid) as a barrier. For insurance purposes, postpartum depression belongs to the broader category of mental illness and many insurance companies do not cover mental illness. When coverage is provided, it is often below other categories of illness.[33] ACOG supports the expansion of pregnancy-related Medicaid coverage to one-year postpartum and provides tools for advocacy at the state level.[34] Even with Medicaid expansion, not having an adequate number of trained providers to support mental health in the perinatal period will lead to more demands on the limited providers comfortable to provide care in this area.

A major strength of this study was the use of triangulation between participant cohorts and the inclusion of researchers and community partners in the review and interpretation of the data.[16] Limitations are also present. Selection bias[35] was possible, especially among the pregnant and postpartum women groups, which may have excluded women who were uncomfortable discussing perinatal mental health. Further, while this study focused on physicians in the clinical setting, often nurses and social workers facilitate mental health screening and referral. As such, future research should include these critical groups in assessment of processes and barriers. Findings of stigma being a barrier within the PCP and MHC provider groups but not in the women group may be a result of this selection bias. Recall bias also may have influenced responses. Finally, though the focus of the study was on identifying barriers, many participants shared factors that improved access to perinatal mental healthcare services. Further study of facilitators (i.e., social support) may shed additional light on strategies to improve access.

CONCLUSIONS

Inadequate access to perinatal mental health care can lead to untreated PMADs, which may contribute to poor birth outcomes. This study identified barriers to accessing care from the perspectives of three unique populations and stratified these barriers across the social-ecological model. Interviews identified areas for improvement, including expanding scheduling options, standardizing screening practices to align with advisory organization guidelines, and advocating for legislation to expand Medicaid. Identification of perceived barriers can inform action steps, which may aid in the development of interventions to improve access to perinatal mental health care. Further, engaging community members in identifying and understanding barriers at various social-ecological levels enhances engagement in identifying and implementing interventions to address these barriers.

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A Preliminary Study of Clinical Practice and Prenatal Nutrition in Rural Kansas

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ABSTRACT

Introduction. The primary purpose of this study was to determine if new recommendations for prenatal supplements of docosahexaenoic acid (DHA) and choline have been implemented into care by physicians who care for pregnant women in rural Kansas communities. Both nutrients are inadequate in the diet of most pregnant women in the U.S., and not all prenatal supplements provide DHA and choline.

Methods. A cross sectional web-based survey was developed and provided by the University of Kansas Medical Center (KUMC) students to 44 rural Kansas clinics believed to have physicians who provide obstetrical care. Questions about DHA and choline were embedded in a larger survey focused on prenatal care. A total of 29 surveys were returned, however, only 21 were completed by physicians who provided obstetrical care.

Results. DHA (3/21) and choline (0/21) rarely were singled out for recommendation in contrast to folic acid (16/21) and iron (14/21). Participants stated that most women sought prenatal care during the first trimester of their pregnancy and indicated that they recommended prenatal vitamins at the first visit. Eleven gave patients a prescription for prenatal vitamins. The remaining patients either chose traditional over the counter prenatal vitamin capsules or less traditional chewable (gummy) vitamins, which provided lower concentrations of nutrients. Common barriers to nutritional counseling were limited resources and time constraints. Clinicians assessed their confidence and ability to provide nutritional counseling as moderate and competent, respectively.

Conclusions. New nutritional recommendations for DHA and choline have not been implemented into standard of care in rural Kansas.

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INTRODUCTION

Access to prenatal care is linked to infant mortality and morbidity.[1] The factors that were associated with infant mortality included preterm delivery, low birth weight, congenital malformations, and other maternal complications such as preeclampsia.[2] Infant mortality in rural counties was higher (6.55 deaths per 1,000 births) than in large urban counties (5.44 deaths per 1,000 births). Many rural counties are considered health professional shortage areas (HPSA); however, a study has not been done linking HPSA and infant mortality.[3]

The standard of care for prenatal counseling set forth by the American College of Obstetrics and Gynecology (ACOG) included education regarding labor and delivery, nutrition, exercise, and working during pregnancy.[4] ACOG recommended a daily prenatal vitamin which includes folic acid; however, the market contains a variety of prenatal vitamin supplements of varying quality. Most prenatal vitamins contain the important supplement folic acid, which is recommended by ACOG and the National Institute of Health (NIH),[5] and minerals including iron, iodine, and zinc; all of which have important roles in pregnancy and fetal development.[6]

Recent studies supported the recommendation to supplement pregnant women with docosahexaenoic acid (DHA) and choline. A 2018 Cochrane Review on the topic of DHA supplementation during pregnancy found a decrease in early preterm births from 4.6% to 2.7% and in all preterm births from 13.4% to 11.9% .[7] This was a relative risk reduction of 42% in early preterm birth (< 34 weeks gestation), and 11% in all preterm births (< 37 weeks gestation). Though this review clearly stated the benefits of DHA supplementation during pregnancy, it is important that gestation > 42 weeks was increased, as was large for gestation age (LGA) babies with DHA supplementation. While an optimal amount of DHA was not defined, the results largely were due to studies in which women were assigned randomly to a supplement of at least 500 mg/day of DHA. Meanwhile, two recent studies showed early preterm birth and preterm birth were reduced by doses of 800 and 1000 mg DHA/day in women starting pregnancy with low DHA status.[8,9] Dietary intake of DHA was low in women in the U.S., providing approximately 60 mg per day.[10] While DHA is included with some over the counter prenatal supplements, most provide 200 mg/day or less per dose.

The American Academy of Pediatrics highlighted choline and long chain polyunsaturated fatty acids, including DHA, as key nutrients to support fetal brain development during pregnancy and lactation;[11] however, choline was ranked last among common nutrients that doctors recommend for a healthy diet.[12] Only 6% of obstetricians and gynecologists reported they are likely to recommend foods that are good choline sources or supplements for pregnant women. A similar study has not been performed in family medicine physicians providing obstetric care. The Adequate Intake (AI) for choline during pregnancy is 450 mg/day,[13] while pregnant women consume only about 322 mg from food and supplements.[14] Evidence for the importance of ensuring good choline intake during the perinatal period continues to grow.[15] Meanwhile, there was also evidence that choline and DHA act synergistically in brain and eye development.[16,17]

Physicians can ensure that policy recommendations are implemented in patient care. However, it takes an average of 17 years for significant research to be implemented in clinical practice.[18] A delay in uptake of new findings by physicians can delay further implementation. This study was designed to determine if pregnant women in rural Kansas received information about the need for additional DHA and choline, as well as general information on prenatal nutrition counseling and resources. The study results will identify possible opportunities to amend prenatal

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nutrition counseling provided to women by obstetrical providers. We hypothesized that recommendations for DHA and choline have not been implemented into standard of care in rural Kansas.

METHODS

The study was approved by the Institutional Review Board at the University of Kansas Medical Center (KUMC). The survey used a cross sectional design. Prior to releasing the survey, nine physicians providing obstetrical care at KUMC completed the survey and made recommendations for clarifying the survey prior to implementation. Their data were not analyzed.

All 44 KUMC medical students in the Summer Training Option in Rural Medicine (STORM) program provided the web-based "Prenatal Nutrition Survey" as a REDCap® link to rural Kansas preceptors. Preceptors were considered rural if their practice took place in counties outside of the top six urban counties of Johnson, Wyandotte, Leavenworth, Sedgewick, Shawnee, and Douglas. All student researchers received basic interview training the week before the program began and completed a Human Subjects Committee (HSC) on-line training course.

Informed consent was sought at the beginning of the survey. Participants were asked about their practice demographics, patient choices on prenatal care, prenatal supplements, and barriers in providing that care in rural settings. Lastly, participants were asked about their confidence and self-assessed ability to provide patients with nutrition guidance. To be included in the analysis, surveys needed to be completed by participants with either a Doctor of Medicine (M.D.) or Doctor of Osteopathic (D.O.) degree and who provided prenatal care. A total of 29 of the 44 surveys were returned, however, eight were excluded from our analysis. Specifically, one was excluded because the individual who completed the survey did not provide informed consent, two others were excluded as they were not an M.D. or D.O., and five respondents did not provide obstetrical care. Statistical analysis included descriptive statistics and frequencies. Statistical Analysis Software (SAS) version 9.4 was used to complete data analysis.

RESULTS

Results are reported in frequency or sample size for each question and percentages. Of the 44 obstetric providers in rural Kansas, a total of 21 responses were used in analysis, giving a 47.7% response rate. The professions of the sample included 20 M.D.s and 1 D.O. Length of practice ranged from less than 1 year to 33 years. Of the 21 participants, five (23.8%) reported caring for one to ten pregnant women per year, six (28.6%) reported caring for 11 - 25, nine (42.9%) reported caring for 26 - 50, and one (4.8%) reported caring for 51 - 100. These physicians reported providing pre-pregnancy counseling, prenatal care, delivery services, and postpartum care. Nineteen participants (90.5%) reported that greater than half of their patients seek prenatal care in the first trimester.

Eighteen participants (85.7%) reported they would recommend prenatal supplements during pre-pregnancy counseling; although, most participants (90.5%) reported that less than 25% of their patients sought pre-pregnancy counseling. A comment by one participant clarified that they selected pre-pregnancy counseling on the questionnaire as the time they would recommend a prenatal supplement or vitamin, but so few women seek pre-pregnancy counseling that the recommendation for prenatal supplements or vitamins usually occurred at the first appointment patients are seen during the pregnancy.

Physicians were asked to select the type of supplements and vitamin options that patients in their practice choose. Eleven participants (52.4%) responded that women choose prescription prenatal supplements and 17 (81%) selected that women choose over-the-counter prenatal supplements. All 11 who chose prescription also selected over-the-counter supplements. Only one participant (4.8%) selected women choose to consume no prenatal supplements or vitamins. When asked to comment on preference on type of prenatal vitamin, respondents reported a preference for prescription prenatal supplements or vitamins, due to the increased amount of folic acid and preference and tolerance of patient. Most women selected over-the-counter prenatal supplements with about half selecting gummy prenatal supplements.

Participants were asked if they recommend specific nutrients to be included in prenatal supplements and could choose more than one option (Table 1). Folic acid and iron were chosen most frequently, with 16 (76.2%) and 14 (66.7%) of the participants, respectively. Less frequently recommended were vitamin B6 (8/21, 38.1%), vitamin D (6/21, 28.6%), and DHA (3/21, 14.3%). Choline and iodine were not chosen by participants. Two participants reported recommending other nutrients but did not offer comments. A comment by one participant stated that they sometimes recommended many of the nutrients, but on a case-by-case basis. As for herbal supplements, 19 participants reported that their patients do not choose to use herbal supplements during pregnancy. Comments on this topic included: herbal supplements are not safe or recommended as they are not well researched or regulated, and safety has not been established.

Table 1. Physician's recommendations for prenatal nutritional supplements.

Nutrient	N (%)
Folic acid	16/21 (76.2)
Iron	14/21 (66.7)
Vitamin B6	8/21 (38.1)
Vitamin D	6/21 (28.6)
DHA	3/21 (14.3)
Choline	0/21 (0)
Iodine	0/21 (0)
Other	2/21 (9.5)

Counseling on nutritional information in pregnancy was completed by a variety of clinic personnel (Table 2). All participants (100%) selected physicians provide education on nutrition. Nurses (12/21, 57.1%), midwives (2/21, 9.5%), and registered dietitians (7/21, 33.3%) were less frequently selected as providing additional counseling. The reported format of informational material provided to women were written handouts (17/21, 81%), prenatal classes (16/21, 76.2%), and guided internet searches (6/21, 29%). Barriers to providing

information on nutrition to patients included time constraints (13/21, 61.9%), lack of community resources (7/21, 33.3%), and other (1/21, 4.8%). Participants commented that limited community services and time are the chief barriers. Resources available to patients included a hospital or clinic registered dietitian (14/21, 66.7%), a referral less than 50 miles away (4/21, 19%), and a referral greater than 50 miles (3/21, 14.3%).

Table 2. Nutritional counseling during pregnancy.

Who provides counseling	**N (%)**
Physician	21/21 (100)
Nurse	12/21 (57.1)
Midwife	2/21(9.5)
Registered dietitian	7/21 (33.3)
Counseling format	
Written handouts	17/21 (81.0)
Prenatal classes	7/21 (33.3)
Guided internet searches	6/21 (28.6)
Barriers to counseling	
Time constraints	13/21 (61.9)
Lack of community resources	7/21 (33.3)
Other	1/21 (4.8)
Additional resources	
Registered dietitian	14/21 (66.7)
Referral less than 50 miles	4/21 (19.0)
Referral more than 50 miles	3/21 (14.3)

Participants answered questions on organizations and resources used to keep up-to-date on new information. The American Academy of Family Physicians/Kansas Academy of Family Physicians was the most frequently selected with 18 participants (85.7%) referring to this source, followed by ACOG being referred by 17 participants (81%), and 7 participants (33.3%) referring to the U.S. Centers for Disease Control and Prevention. No participants reported use of resources from the Academy of Nutrition and Dietetics or the World Health Organization (WHO). UpToDate® was reported as the most used resource with 90.5% (19/21) of participants selecting this option, followed by academic journals (8/21, 38.1%). Live continuing medical education was selected by 57.1% (12/21) of participants as a format of obtaining new knowledge. Other resources reported by participants included additional publication and texts, and their partners.

Finally, participants were asked to self-assess their ability to provide information on nutritional requirements during pregnancy and their confidence on this topic (Table 3). Self-assessed ability was rated from beginner, developing, competent, and advanced. Most participants reported competent ability (16/21, 76.2%), with three participants (14.2%) rating themselves developing and two (9.5%) as advanced. Confidence was rated as minimally, somewhat, moderately, and very confident. Most (14/21, 66.7%) reported they are moderately confident on nutritional requirements of pregnancy, five (23.8%) reported feeling very confident, and two (9.5%) were somewhat confident in their ability to provide prenatal nutritional counseling.

Table 3. Physician's confidence in their ability to provide prenatal nutritional counseling.

Confidence	**N (%)**	**Self-assessed ability**	**N (%)**
Minimally confident	0/21 (0)	Beginner	0/21 (0)
Somewhat confident	2/21 (9.5)	Developing	3/21 (14.3)
Moderately confident	14/21 (66.7)	Competent	16/21 (76.2)
Very confident	5/21 (23.8)	Advanced	2/21 (9.5)

DISCUSSION

These findings correlated to the hypothesis that new nutritional recommendations have not been implemented into standard practice in rural Kansas. Recent studies have shown that DHA is an important nutrient during pregnancy,[7] and the National Academy of Medicine has set a choline intake of 450 mg as an AI during pregnancy;[13] however, few of the respondents to our survey recommended DHA and none recommended choline. These results could be related to the time it takes for new information to become a standard of care. Even though an AI was set for choline during pregnancy in 1998,[13] implementation could have been delayed because it was understood only recently that dietary intake of choline did not meet the AI for most women.[14] The reported confidence and ability levels could be referring to nutrients like folic acid and iron that have been studied and in standard practice for many years. It also was possible that those surveyed misunderstood the question, considering one physician said each nutrient could be recommended on a case-by-case basis.

Americans living in rural communities face barriers in access to healthcare, especially women seeking prenatal care. According to the 2010 U.S. Census Bureau data, 17% of the U.S. population lives in rural communities, while only 9% of physicians practice in these areas.[17] The situation is similar in Kansas, where 25 of the 105 counties are designated as a whole county primary care HPSA and an additional 89 counties have some level of HPSA. This was reflected in the small number of physicians providing obstetrical care in rural Kansas. The work by Kennedy et al.[19,20] has identified just 44 physicians providing obstetrical care in this area, which were the sample we sought to obtain for this study.

A limitation of the research was the small sample size. Results were obtained from only 29 of the 44 physicians whose practice includes obstetrics, with only 21 of the 29 respondents meeting all inclusion criteria to be included in the study. The COVID-19 pandemic meant that not all physicians were able to be contacted in-person, decreasing the intended sample size. However, the sample size was large enough to serve as a starting point for further investigation and to consider how to best provide information on the importance of DHA and choline to physicians caring for pregnant women in Kansas. Our findings cannot be generalized to physicians practicing in urban and suburban settings, although there was evidence to suggest that the findings for choline could be similar.[12]

According to our study, rural physicians were using UpToDate®, ACOG, and the American Academy of Family Physicians most commonly for knowledge acquisition. Physicians have cited barriers of journal use to include "time, resource reliability, data credibility, and information overload".[21] With these barriers in mind, options for research dissemination in rural Kansas could include: open access to journal articles, increased time and funds for conference attendance (e.g., Kansas Academy of Family Physician conferences), continuing education courses specific to prenatal nutrition, and virtual education meetings from the academic research communities to rural Kansas providers. The efficacy and interest in these options would need to be assessed in further studies.

This preliminary study showed the need for further research, as well as offering educational ideas for shortening the time gap between evidence from research and recommendations for practice becoming standard of care. Bridging this gap can have more significant impacts such as reducing infant morbidity and mortality in the rural U.S.

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Cut Cortical Screw Purchase in Diaphyseal Bone: A Biomedical Study

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ABSTRACT

Introduction. During fracture osteosynthesis, traumatologists may remove screws which are too long, cut the excess length from the screw tip, then reinsert the cut screw (CS) to minimize implant waste. The purpose of this study was to determine if this practice influences screw purchase.

Methods. Using an axial-torsion load device, the maximal insertion torque (MIT) required to insert 3.5 mm stainless steel cortical screws into normal and osteoporotic bone models was measured. MIT was determined in three different test conditions: (1) long screw (LS) insertion; (2) LS insertion, removal, and insertion of a normal-length screw (NS); and, (3) LS insertion, removal, cutting excess length from the screw tip, and reinserting the CS.

Results. In the normal bone model, mean (± SD) MIT of LS insertion was 546 ± 6 Newton-centimeters (N-cm) compared to 496 ± 61 N-cm for NS reinsertion and 465 ± 69 N-cm for CS reinsertion. In the osteoporotic bone model, MIT of LS insertion was 110 ± 11 N-cm, whereas the values for NS and CS reinsertions were 98 ± 9 N-cm and 101 ± 12 N-cm, respectively. There was no significant difference in MIT between CS and NS reinsertions in the osteoporotic bone analog.

Conclusions. Cutting excess length from a 3.5 mm stainless steel cortical screw did not decrease its purchase regardless of bone density. During osteosynthesis, orthopaedists may remove screws which are too long, cut the screw tip, and reinsert the shortened screw as a cost-saving measure without compromising fracture fixation.

Kans J Med 2022;15:59-62

INTRODUCTION

Fracture fixation using plate osteosynthesis is a well-established treatment employing basic principles of biomechanics such as compression and torque. A successful fracture reconstruction depends largely upon the orthopaedist's ability to achieve adequate plate compression by maximizing torque applied to a screw. Many factors affecting screw purchase, including patient characteristics, such as bone density, and mechanical factors, such as screw and plate design features, are not within the surgeon's control. However, the surgical technique used to apply plate and screws to the fractured bone, including possible modification of the screw tip, is determined by the operating orthopaedist.

When cortical screws used during osteosynthesis are too long, they may protrude from the far cortex of bone, potentially causing pain and injury to adjacent soft tissue structures. In this setting, a shorter screw is warranted. How this is accomplished varies as some surgeons discard the long screw (LS) and replace it with a new screw (NS) of appropriate length, whereas others choose to remove the long screw, cut it to the required length, and reinsert the cut screw (CS). In the latter scenario, the orthopaedist saves the cost associated with wasting the LS, which may not be reused in another patient. One hospital system found that 3.5% of all trauma implant costs were due to wasted materials, adding an average of $83 to the cost of each case.[1] Incorrectly measured screw lengths were one of the most common reasons for wasted materials, the cumulative cost of which may be significant for a health care system.[1,2]

While other biomechanical studies have assessed the effect of insertion technique,[3] insertion angle,[4] and screw pitch[5,6] on screw purchase, the influence of reinserting a CS is unknown. The purpose of this study was to investigate whether removing an implanted screw, cutting excess length from the screw tip, and reinserting the implant has an effect on screw purchase as determined by the maximal insertion torque (MIT). As deformation caused by cutting a screw alters the distal thread, it was hypothesized that reinserting a CS would remove additional bone, decrease the contact surface area of the screw-bone interface, and decrease screw purchase. This hypothesis was tested by comparing the MIT required to reinsert CS and NS in synthetic bone models.

METHODS

Experimental Design. Stainless steel screws designed for fracture fixation were inserted into surrogate bone materials approximating normal and osteoporotic femoral diaphyseal bone to determine MIT in three different test conditions (Figure 1). In Condition A, a LS was introduced into each predrilled and untapped hole in the model specimen, MIT was measured, and the LS was removed. In Condition B, a LS was inserted and removed and then a screw of appropriate length, so-called "normal screw" (NS), was inserted, and MIT was measured. In Condition C, a LS was placed into a predrilled and untapped hole and then removed. The LS was then shortened by cutting the screw tip and the resulting cut screw (CS) was reinserted and MIT was remeasured. The values obtained for the three test conditions were statistically analyzed for both bone models.

Test Materials. The two bone analog models intended to simulate normal and osteoporotic bone in this study were like those used in previous biomechanical experiments.[7,8] A fourth generation Sawbones® (Pacific Research Laboratories, Vashon Island, WA) model with an outer diameter of 30 mm, wall thickness of 7 mm, and an internal fill of 20# density foam was used to mimic the normal bone of a mid-shaft femur. The common cylindrical shape of the specimen improved test repeatability as compared to testing with an anatomic model of varying geometry. To simulate osteoporotic bone, a custom Sawbones® foam laminate of 16 mm, thick 10# solid foam laminated on both sides with 5.5 mm 30# solid foam was used. Each test block had a finished size 120 mm wide, 170 mm long, and 27 mm thick.

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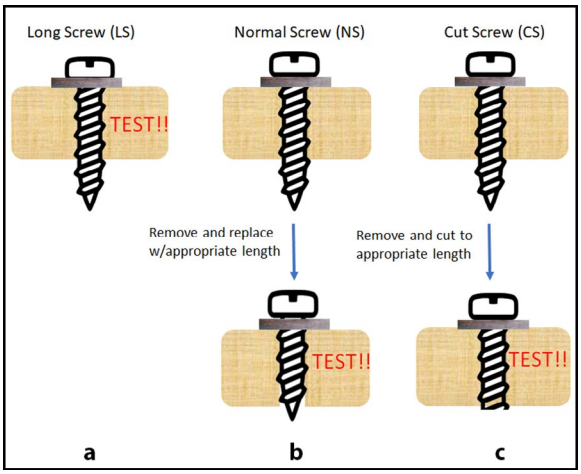

Figure 1. Testing algorithm. a) In Condition A, LS is inserted and test is done to determine MIT. b) In Condition B, LS is inserted, removed, NS is inserted, and MIT is determined. c) In Condition C, LS is inserted, removed, and screw tip is cut to shorten the screw. The resulting CS is reinserted and MIT is determined.

The stainless-steel cortical screws were 3.5 mm diameter screws manufactured by Stryker® (Mahwah, NJ). The LS measured 40 mm, CS 34 mm, and NS 34 mm. Images of a cut stainless steel screw are shown in Figure 2.

Figure 2. Two views of a stainless-steel cut screw showing mechanical deformation of the screw tip.

Maximal Insertion Torque Testing. Insertional torque was measured continuously on a Bose (Framingham, MA) ElectroForce® 3220 Axial-Torsion load frame (Figure 3). An axial preload of 10 N was applied and held constant for the duration of the screw insertion test. The test was driven at a rotational rate of five revolutions per minute. The time, axial load, axial displacement, rotation angle, and torque were recorded at a data acquisition rate of 10 Hz. The test was performed until failure of the bone-screw interface, screw head stripping, screw head fracture, or a machine torque limit was reached.

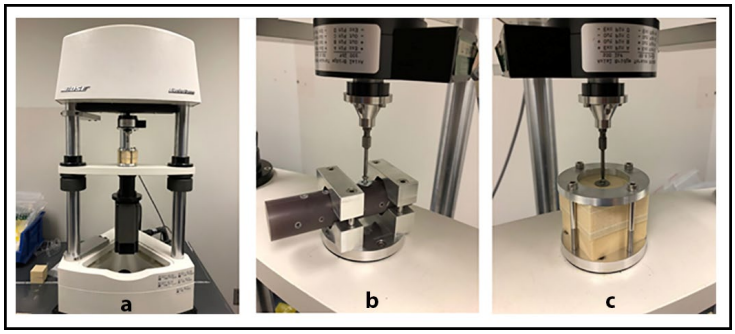

Figure 3. Maximal insertion torque (MIT) testing. a) Screw MIT testing setup; b) Screw insertion into normal cortical bone model; c) Screw insertion into osteoporotic bone model.

The torque measuring load frame limit of 550 N-cm is well above the torque applied to screws during osteosynthesis.[9] If the screw MIT was greater than 300 N-cm, the screw was considered not stripped under clinical conditions.[7,8,10,11]

To prepare the bone models for testing, 2.5 mm diameter holes were drilled perpendicular to the longitudinal axis of the test cylinder. A hole spacing of 12.5 mm was used to give a five times the diameter spacing between holes as specified by the American Society for Testing and Materials (ASTM).[12,13] The intent was to insert all screws perpendicular to the long axis of the test cylinder, penetrating both near and far sides of the specimen. A matched washer was used with each screw to simulate a standard bone fracture plate. Screws were started by hand and inserted until the screw head was approximately 4 mm from contacting the washer.

In the first series of tests using the normal cortical bone model, five replicates of LS, NS, and CS were tested to see if differences in MIT could be found. In the second series using the osteoporotic bone model, seven replicates were tested. Tested screws were removed by hand and each screw was examined for damage. The number of screws tested in each group of the study met or exceeded the number of screws tested in the published literature on MIT.[7,8]

Statistical Analysis. Statistical analysis of the results was performed by one-way ANOVA test with the Least Significant Difference formula for post hoc multiple comparisons (IBM® SPSS v23, Chicago, IL). Seven independent tests per test condition were summarized for analysis. A p value of less than 0.05 was considered as significant difference. Data were expressed as mean ± standard deviation (SD) of the mean.

RESULTS

Normal Bone Analog. The mean ± SD MIT of initial LS insertion was 546 ± 6 N-cm and the MIT values for NS and CS reinsertions were 496 ± 61 N-cm and 465 ± 69 N-cm, respectively (Table 1). The mean value for each test condition in the normal cortical bone model was significantly above the MIT clinically relevant threshold of 300 N-cm ($p < 0.05$). For the cortical bone surrogate, 70% of the screw heads broke prior to reaching the MIT machine limit of 550 N-cm.

Osteoporotic Bone Analog. The MIT of initial LS insertion was 110 ± 11 N-cm and the MIT values for NS and CS reinsertions were 98 ± 9 N-cm and 101 ± 12 N-cm, respectively (Table 1). There was no significant difference in MIT between CS and NS in osteoporotic bone.

Table 1. Maximal insertion torque (MIT).

Test condition	Screw type	Normal bone model*	Osteoporotic model*
A	Long screw (LS)	546 ± 6	111 ± 11
B	Normal screw (NS)	496 ± 61	98 ± 9
C	Cut screw (CS)	465 ± 69	101 ± 12

* Tabulated values are mean ± standard deviation in N-cm.

Within osteoporotic bone, insertional torque recorded 180° prior to MIT and 180° after MIT were compared in CS and NS screws (Figure 4). At each measurement in the 360° arc, there were no significant differences in torque ($p < 0.05$).

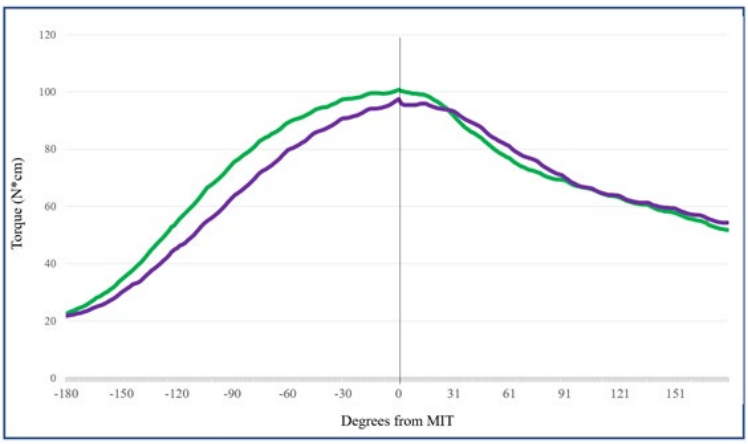

Figure 4. Insertional torque (in N-cm) measured 180° before and 180° after MIT reinserted screws of appropriate length (NS; purple) and for reinserted CS (green).

DISCUSSION

Based on the initial hypothesis, a decrease in MIT after CS reinsertion compared to NS reinsertion was anticipated. Since no statistically significant reduction in MIT was found, this hypothesis must be rejected. The results supported the surgeon's practice of cutting screws which are determined to be too long during osteosynthesis as a cost savings measure, as CS reinsertion did not compromise MIT in either the normal cortical bone or osteoporotic bone models. Based on these data, we believed that surgeons may reintroduce screws which were cut or shortened during fracture fixation without regard to a patient's bone quality.

The health care cost savings resulting from this practice may be substantial as long screws were present in approximately 25% of constructs.[14,15] If an orthopaedic surgeon performs 500 cases per year, then an estimated 125 cases have potential cost savings associated with cutting a screw. For nonlocking cortical screws at $20 per screw, there could be a cost savings of $2,500 per year. For interlock screws like those used in a tibial nail at $240 per screw, there could be a cost savings of up to $30,000. Thus, the financial implication of just a single surgeon adopting the practice of cutting screws would be impactful.

Although there are various parameters to quantify screw purchase, the use of MIT is most appropriate for this study. MIT has been recommended as the preferred method for quantifying compression from the screw head against a compression plate.[8] This compression maintains the stability of the plate-screw construct and has been shown to be a predictor of successful internal fracture fixation.[11,16,17] Lack of stability leads to problems such as screw loosening and cutout, which may require reoperation and result in poor patient outcomes.[18-21] Previous biomechanical studies have demonstrated decreased screw pullout strength after screw reinsertion.[22,23] However, these studies should be interpreted in light of the findings of Ricci et al.[8], who showed that changes in screw design affected MIT but did not correlate with pullout strength.

The findings regarding MIT with screw reinsertion were consistent with previously published studies. For example, Marmor et al.[7] found that screw purchase was not affected adversely until the third reinsertion in a normal cortical bone model. In their osteoporotic cortical bone analog, the 8% decrease in MIT observed with the first reinsertion was not statistically significant. Similarly, this study did not show a significant difference in MIT with screw reinsertion, indicating that the practice of removing a screw which was too long, cutting the tip, then reinserting the CS did not weaken the construct as measured within clinically relevant ranges.

When examining insertional torque in the 180° of screw head rotation leading up to and following MIT, there were no significant differences in torque between NS and CS. As MIT is reached at a single point in time (or turn of the handle), very rarely is MIT achieved in a clinical setting. One study showed that orthopaedic surgeons strip up to 20% of screws that are placed.[24] Thus, it is reassuring that the insertional torque on a CS increases (and decreases) at a rate like a NS.

There were several limitations to this study. One was that the upper limit of MIT was not reached for tests with the normal cortical bone analog which precluded quantitative measure of differences in MIT in the NS and CS test conditions. Another limitation was that only stainless steel screws were studied. Titanium is more malleable than stainless steel and has different mechanical properties. Therefore, cutting a titanium screw may produce more deformation of the distal threads and lead to a different test result. Likewise, cutting screws of different sizes may have an impact on MIT. A final study limitation was that bone analogs were used instead of human cadaver bone. The results, therefore, may not be extrapolated directly to in vivo human bone.

In conclusion, this study showed that cutting a 3.5 mm stainless steel cortical screw did not decrease its purchase as determined by maximal insertion torque in normal cortical bone or osteoporotic cortical bone models. During osteosynthesis, orthopaedists may choose to remove screws which are too long, cut the screw tip to remove excess length, and reinsert the screw without compromising the fracture reconstruction, while at the same time avoiding implant waste and saving health care dollars.

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Keywords: biomechanics, fracture fixation, medical waste, bone screws, torque

KANSAS JOURNAL of MEDICINE

Stacked 1/3 Tubular Plates for Fixation of Pediatric Forearm Fractures: A Biomechanical Study

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ABSTRACT

Introduction. Among operatively treated pediatric forearm fractures, many different fixation constructs are described. The goal of this study was to define the biomechanical properties of a double stacked 1/3 tubular plate construct used by the senior author for some fractures and to review available literature regarding the use of stacked plates.

Methods. Biomechanical testing was performed by 4-point bending of three different plate constructs: 1/3 tubular plate, stacked 1/3 tubular plates, and 2.7 mm LC-DCP plate. Five test specimens were evaluated for each of the three plate constructs. From stress-strain curves, flexural stiffness (N/mm), force to cause plastic deformation (N), and force to cause 10° bend (N) were calculated and compared using standard t-test statistics.

Results. Key outcome parameter means (± SD) for the three plate constructs (1/3 tubular plate, stacked 1/3 tubular plates, and 2.7 mm LC-DCP plate) were reported respectively as follows: flexural stiffness (55.4 ± 3.5 N/mm, 131.7 ± 3.5 N/mm, 113.3 ± 12.1 N/mm), force to cause plastic deformation (113.6 ± 11.0 N, 242.1 ± 13.0 N, 192.2 ± 17.9 N), and force to cause a 10° bend (140.0 ± 8.4 N, 299.4 ± 14.1 N, 265.5 ± 21.2 N). Mean values of all three measures were significantly larger for the stacked 1/3 tubular plates than for the other plate constructs.

Conclusions. The stacked 1/3 tubular plate construct was biomechanically superior to the other plate constructs tested. Stacked plating significantly improved stiffness of the fracture fixation construct supporting the use of this technique in selected trauma cases.

Kans J Med 2022;15:63-66

INTRODUCTION

Forearm fractures are among the most common fractures in pediatric patients. While many of these fractures can be managed nonoperatively, much controversy exists with regards to indications for operative treatment.[1,2] Indications for fixation can include open fractures, inability to achieve adequate reduction, loss of reduction, and limited remaining growth/remodeling. Once operative fixation is chosen, hardware selection for fracture fixation includes numerous different implants and often there is no clear indication to choose one type over another.[3,4] Even when selecting a plate and screw construct, many different geometries, materials, thicknesses, screw types, and other variables are available from numerous vendors. Surgeons must consider characteristics of the fracture being treated along with other patient and treatment factors when selecting the appropriate construct for fixation. Biomechanical research offers some insight into properties of plate and screw selection and provides clinicians objective information to guide clinical practice.

The inspiration for this study was the senior author's use of stacked 1/3 tubular plates in the treatment of pediatric forearm fractures. This work specifically aimed to perform a biomechanical analysis between fixation constructs using two different plates, as well as the stacked plate construct, to define the mechanical properties quantitatively. While the study design was chosen with this clinical application in mind, the results could be applied more generally. The mechanical properties and comparison between various commercially available plates are not well described by industry product guides or in the orthopaedic literature. Anecdotally, a thicker or larger plate, as well as stacking two plates, would increase the stiffness, but quantitative data were lacking.

The goal of this study was to characterize the mechanical properties of three different plate constructs and provide quantitative data which could be used by providers to guide clinical practice decisions. What evidence exists in current literature with regards to stacking plates for fracture fixation? How does quantitative biomechanical performance (flexural stiffness, force to cause plastic deformation, and force to cause 10° bend) by 4-point bending compare between the 1/3 tubular plate, stacked 1/3 tubular plate, and 2.7 mm LC-DCP plate? This study presents and discusses possible applications of the stacked plating construct, as well as limitations and potential for further work.

METHODS

Sawbones® (part #3403-24, cylinder 10 mm OD x 2.5 mm wall thickness) were acquired and used for this fracture model (Pacific Research Company; Vashon, WA, USA). A transverse fracture was created with a saw and plate fixation was applied leaving a 1-mm fracture gap. Plate constructs included three different groups: 6-hole 1/3 tubular plate (Synthes® item # 241.36), double stacked 6-hole 1/3 tubular plates (item # 241.36), and 7-hole 2.7-mm LC-DCP (Synthes® item # 242.207); 2.7-mm cortical screws of appropriate length were used for fixation of all groups (Synthes®; West Chester, PA, USA). The 6-hole 1/3 tubular and 7-hole 2.7-mm LC-DCP plates were chosen due to similarity in overall construct length due to the symmetry of hole spacing in the 2.7-mm plate versus elongated span between central holes on the 1/3 tubular plate (Figure 1).

Figure 1. Plate constructs used in this study included: (A) 2.7-mm LC-DCP plate, (B) 1/3 tubular plate, and (C) stacked 1/3 tubular plates.

Testing was performed at the National Institute for Aviation Research mechanical testing lab (NIAR, Wichita State University, Wichita, KS) on an 810 Material Test System (MTS®, Eden Prairie, MN). The test system is shown in Figure 2. The 4-point bending setup was adapted to fit the specimens from testing specifications of

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the American Society for Testing and Materials (ASTM).[5] Support span was set at 81 mm; load span was set between 25.5 mm and 27 mm based upon screw location to ensure load was applied between screw heads and would not interact with screws during bending (Figure 3). While changing the load span would introduce variability in the results, a change within 1.5 mm over the 81-mm support span would be minimal and allow the benefit of not loading directly onto a screw head, which would lead to slippage during loading. Load rate was 0.015 mm/sec; load and deflection were sampled at 60 Hz. Specimens were tested through elastic and plastic deformation to a deflection of at least 5 mm. A representative plot from testing of a double stacked 1/3 tubular plate is shown in Figure 4.

Figure 2. Test setup on MTS® machine.

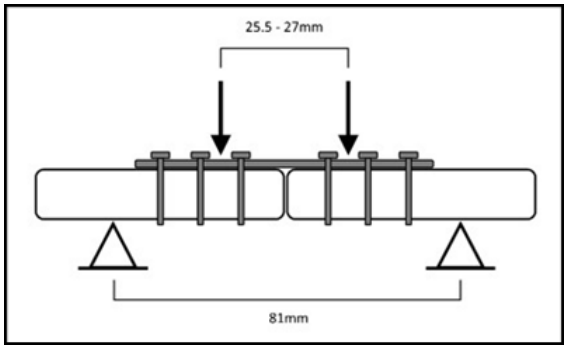

Figure 3. Test setup force diagram.

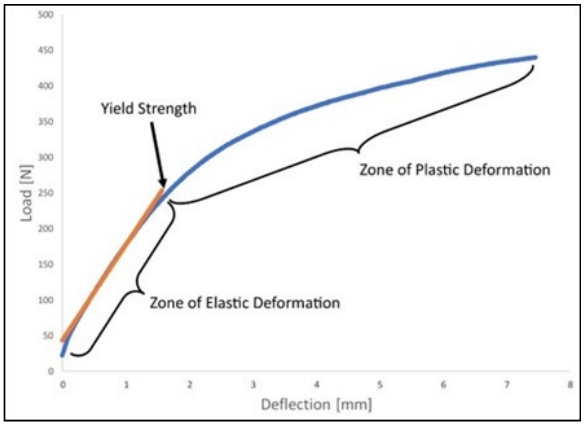

Figure 4. Representative plot from the testing of double stacked 1/3 tubular plate construct showing stress-strain data collected from testing and labeling zones of elastic and plastic deformation as well as yield strength.

Analysis was performed on data to calculate the flexural stiffness (N/mm) based on the linear region of the stress/strain curve. Force to cause a plastic deformation was defined as a deviation of greater than 5% from the linear stress/strain relationship. Force to cause a 10° bend was identified along the stress/strain data based upon the geometry of the test setup, as shown in Figure 2, to provide a clinical corollary of construct strength. Data were compared with standard t-test statistics with a selected significance value of $p = 0.05$. T-tests were run for the following comparisons: 1/3 tubular vs. stacked 1/3 tubular, 1/3 tubular vs. 2.7-mm LC-DCP, stacked 1/3 tubular vs. 2.7-mm LC-DCP.

RESULTS

The three plate constructs (1/3 tubular plate, stacked 1/3 tubular plate, and 2.7-mm LC-DCP plate) were each tested with $n = 5$ and the following results are reported respectively with standard deviations (Table 1): flexural stiffness (55.4 ± 3.5 N/mm, 131.7 ± 3.5 N/mm, 113.3 ± 12.1 N/mm), force to cause plastic deformation (113.6 ± 11.0 N, 242.1 ± 13.0 N, 192.2 ± 17.9 N), and force to cause a 10° bend (140.0 ± 8.4 N, 299.4 ± 14.1 N, 265.5 ± 21.2 N).

Table 1. Results from biomechanical testing.

Construct	Flexural stiffness (N/mm)*	Force to cause plastic deformation (N)*	Force to cause 10° bend (N)*
1/3 tubular plate	55.4 ± 3.5	113.6 ± 11.0	140.0 ± 8.4
Stacked 1/3 tubular plate	131.7 ± 3.5	242.1 ± 13.0	299.4 ± 14.1
2.7 mm LC-DCP plate	113.3 ± 12.1	192.2 ± 17.9	265.5 ± 21.2

*Tabulated values are mean ± standard deviation.

Statistical significance by t-test was performed for each of the three reported results (flexural stiffness, force to cause plastic deformation, and force to cause a 10° bend). When comparing 1/3 tubular plate against stacked 1/3 tubular plate and 1/3 tubular plate against 2.7-mm LC-DCP plate, all were significant at $p < 0.001$. When comparing stacked 1/3 tubular plate versus 2.7-mm LC-DCP plate, flexural stiffness was significant at $p = 0.0114$, force to cause plastic deformation was significant at $p = 0.0010$, and force to cause 10° bend was significant at $p = 0.0177$. Failure analysis of test specimens after bending also was performed, which showed that 2.7-mm LC-DCP plates failed at a single point of bending at the center screw hole overlying the fracture, whereas 1/3 tubular plates (stacked and single) failed by bending at the 2 screw holes adjacent to the fracture (Figure 5).

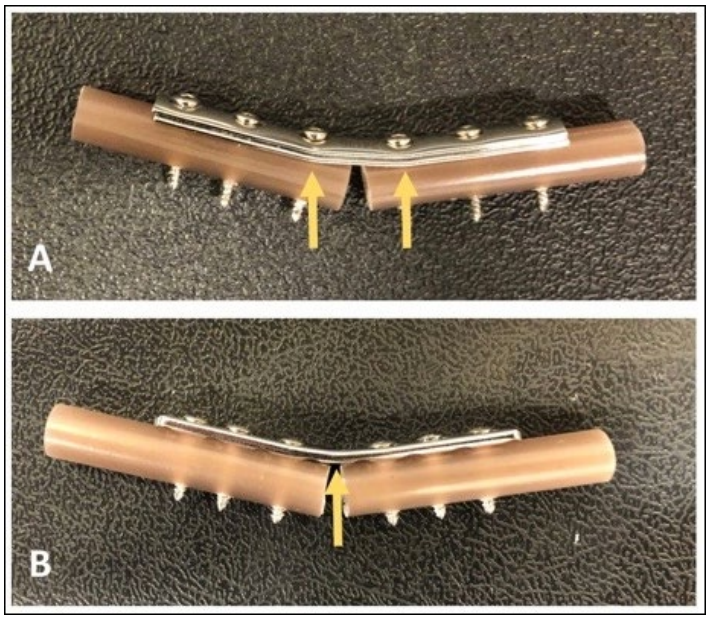

Figure 5. Failure analysis of (A) stacked 1/3 tubular plates and (B) 2.7-mm LC-DCP plate. Arrows show the site(s) of bending in each construct.

DISCUSSION

This study confirmed the hypothesis that stacked 1/3 tubular plates are biomechanically superior to a 2.7-mm LC-DCP plate. Further, it demonstrated that stacked plating provided a better than additive quantitative mechanical improvement in bending. This was true of the three metrics reported in this study of 4-point bending: flexural stiffness, force to cause plastic deformation, and force to cause a 10° bend.

Review of previously published works regarding stacked plating yielded only a few studies. Mudgal and Ring[6] published a technique report about using stacked plating in adult distal radius fractures that had metadiaphyseal extension. They suggested using a combination of a T-plate plus a dynamic compression plate to allow longer extension of the construct to span from the metadiaphyseal fracture to the distal radius continuously. In their work, they presented the technique, as well as two case reports of its use with good outcomes; however, no biomechanical analysis was done. A recently published case report[7] used a similar technique of stacking plates as a method of extending fixation across a metadiaphyseal segmental fracture in a pediatric patient with a good result. Uniquely, their construct combined titanium and stainless-steel plates. While the investigators reported successful fracture union without complication, they offered no biomechanical or construct analysis.

Another study completed in the field of veterinary surgery compared stacked plating for front leg fractures in canines.[8] Biomechanical analysis was performed with axial load cyclic testing to compare single plate versus stacked plates. In their stacked plate constructs they tested 8-hole plate constructs stacked with another plate of either eight holes, four holes, or two holes. This study found that single plate constructs failed and most of the stacked plate constructs did not. However, due to the design of their mechanical testing, they were not able to provide any quantitative data as to the added strength of implementing stacked plating.

When designing our testing model, 4-point bending was chosen as it was judged to be more relevant to the authors' clinical question regarding its use in pediatric forearm fractures. The complexity of the two bones in the forearm and typical fracture mechanism make bending more applicable over torsion. To analyze the difference in the constructs fully, as well as to apply these results to other fractures (such as distal fibula), further work is necessary to test the plates in torsion. Fatigue testing also deserves consideration in future work. However, in fracture fixation of pediatric fractures, perhaps cyclic testing is less clinically relevant since fractures typically achieve bony union quickly and often are treated with supplemental immobilization.

While limited work has been published on stacked plating, numerous studies of other plate and screw constructs populate the literature. Since the advent and popularization of locking plates and screws, their biomechanics and performance have been presented and analyzed.[9] Several studies have looked at how screw configuration, plate positioning, and bone quality impact biomechanical properties.[10-12] Other studies have evaluated biomechanical properties of various plate and screw constructs in the setting of ankle fractures.[13-15] While these works have drawn an array of conclusions with regards to their specific hypotheses, much can be learned and leveraged with regards to study design and methods. The testing design and parameters of the presented study were chosen with an aim to provide quantitative biomechanical data which would help to analyze the hypothesis objectively. Importantly, plastic deformation was achieved in all constructs which, unlike the only previously published biomechanical study on stacked plating,[8] enabled the ability to compare the quantitative stiffness and performance between groups.

The results of this study supported the use of stacked 1/3 tubular plates as a biomechanically superior construct compared to 2.7 mm LC-DCP plating. This is a technique that the senior author has utilized to manage a wide variety of operatively-treated pediatric forearm fractures, including radial shaft fractures in the setting of both bone forearm fractures and ulna fractures in the setting of Monteggia fracture patterns (Figure 6). Benefits for use of stacked 1/3 tubular plates included: (1) tubular plate shape improves bone-plate fit in many patients, (2) availability of implants in a community hospital or surgery center, (3) tubular plates more easily contoured independently with improved strength by stacking, and (4) reduced cost.

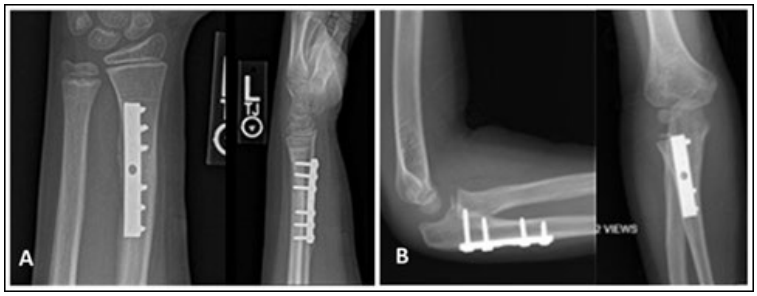

Figure 6. Radiographs showing stacked 1/3 tubular plate constructs used in pediatric patients to treat: (A) distal 1/3 both bone forearm fracture with fixation of the radius and (B) Monteggia fracture with fixation of the ulna.

While the purpose of this work was not to define or explore the use of stacked plating fully, it helped to define the mechanical properties of the stacked plate construct, which could be used to guide clinical decision making, and supported the use of stacked plating in many fractures. The described and tested construct of stacked 1/3 tubular plates offers clinicians another option in fracture fixation.

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Keywords: biomechanics, fracture fixation, bone plates, materials testing, equipment design

KANSAS JOURNAL of MEDICINE

Disseminated Infection Due to *Neocosmospora (Fusarium) falciformis* in a Patient with Acute Myelogenous Leukemia

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INTRODUCTION

Fusarium species are ubiquitous in soil, plants, organic matter, and water; they are important plant pathogens associated with vascular wilt, rots, and damping-off diseases.[1] Some species are animal and opportunistic human pathogens. *Fusarium solani* species complex (FSSC), recently renamed *Neocosmospora*,[2] accounts for half of human infections caused by *Fusarium*. Some of the species are associated with severe infections in transplant recipients and patients with hematological malignancies, persistent neutropenia, or immunosuppression caused by corticosteroid therapy.[3] We present a case of disseminated *Neocosmospora (Fusarium)* infection in a 55-year-old male who developed febrile neutropenia on day four post induction chemotherapy for acute myelogenous leukemia. This case highlighted the clinical presentation and treatment for disseminated *Neocosmospora (Fusarium)* infection and the importance of clinical examination allogenic stem cell transplant recipients.

CASE REPORT

A 55-year-old male presented to his primary care provider with fatigue and diarrhea. Initial work-up showed a white blood cell count (WBC) of 103,600 cells/uL prompting admission. Acute myelogenous leukemia (AML) with monocytic differentiation was diagnosed by bone marrow biopsy and he was started on induction chemotherapy on admission (day one), in addition to prophylactic acyclovir 400 mg twice daily, levofloxacin 500 mg daily, and micafungin 50 mg daily. He became neutropenic on day four. On day 16, he developed febrile neutropenia and a new painful grey lesion was noted between his right fourth and fifth toes (Figure 1); otherwise, examination was unremarkable. WBCs were 200 cells/uL, hemoglobin 6.9 g/dL, and platelets 8,000/uL. Renal and liver function tests were within normal limits. Serum beta-D-glucan and *Aspergillus* galactomannan antigen tests were within normal range.

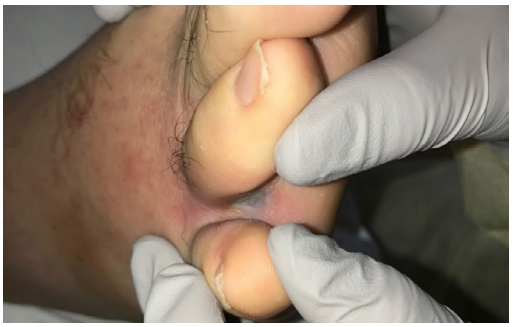

Figure 1. Skin lesion between the right fourth and fifth toes.

The patient was started on liposomal amphotericin B 5 mg/kg daily. Routine blood cultures were positive after four days of incubation. Hyphal elements were reported on the blood culture (Figure 2).

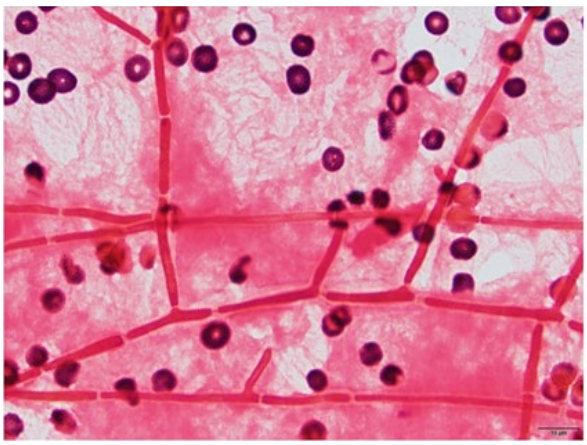

Figure 2. Gram stain of positive blood culture bottle showed septate hyphae (on BD BACTEC Aerobic medium; 20x).

Additionally, the dermatology consult team performed a shave biopsy, which was sent for aerobic, anaerobic, and fungal cultures. Routine culture grew *Staphylococcus epidermidis*. No tissue was sent for histopathology. After three days of incubation, the fungal culture of the tissue grew a mold identified as *Neocosmospora falciformis* by combined morphology and DNA sequencing of the TEF and RPB2 genes at the reference lab (Figure 3). The patient developed acute hypoxic respiratory failure requiring 4 L/min of oxygen by nasal cannula. Chest computed tomography (CT) showed innumerable nodular opacities throughout both lungs, which were greatest in the apices with surrounding ground-glass opacities suggestive of multifocal fungal pneumonia (Figure 4). Two weeks after broad spectrum antifungal therapy, a fungal Grocott's methenamine silver (GMS) stain of bronchioalveolar lavage fluid demonstrated similar looking septate hyphae, but fungal culture remained negative. A transbronchial lung biopsy remained culture negative as well.

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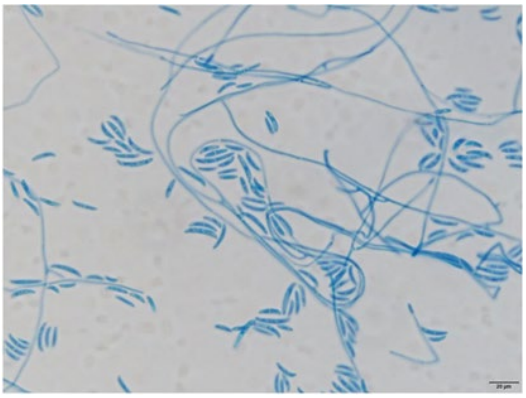

Figure 3. Lactophenol cotton blue stain of the culture prep, 40x.

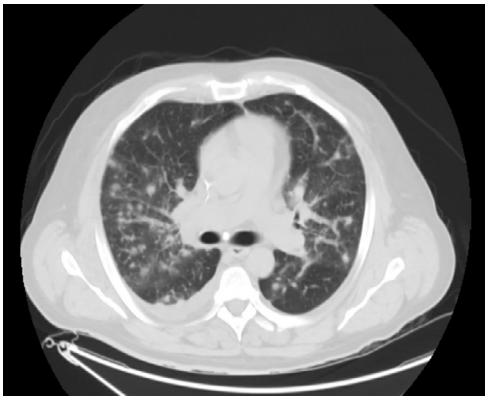

Figure 4. Computed tomography scan of the chest with bilateral multiple nodules.

Repeat CT of the chest two weeks after starting liposomal amphotericin showed slight increase in size of nodules with cavitation, as expected with neutrophil recovery. Antifungal susceptibility testing for the *Neocosmospora (Fusarium) falciformis* recovered showed low minimal inhibitory concentration (MIC) only reported to amphotericin B (amphotericin B MIC 0.5 mcg/mL, voriconazole MIC > 16 mcg/mL, isavuconazole MIC > 16 mcg/mL, posaconazole MIC > 16 mcg/mL, caspofungin MIC > 8 mcg/mL, terbinafine MIC > 2 mcg/mL). The patient was treated with antifungal therapy for a total of five months. At five months, the patient had resolution of symptoms and was breathing well on room air. Repeat CT of the chest showed significant improvement with residual patchy nodular infiltrates throughout both lungs. Eventually, the patient had relapsed AML and transitioned to hospice care as he was no longer a candidate for intensive chemotherapy.

DISCUSSION

The classification of fungi historically was based on morphology of the sexual forms.[4] Many fungi are known to reproduce only asexually, and some have both asexual (anamorph) and sexual (teleomorph) states causing confusion in fungal taxonomy as several were inadvertently given two separate names. Since January 2013, each fungus can have only one name, as the system of permitting separate names to be used for anamorphs ended.[5] However, confusion continues since many medically important fungi still are known by their established anamorph names (i.e., *Candida*). In this case study, the mold from both shave biopsy and blood culture was identified as *Neocosmospora falciformis*. The genus *Neocosmospora*, previously under *Fusarium solani* species complex (FSSC), contains at least 60 species.[2,6] Taxonomy changes to *Fusarium* species have caused scientific opposition,[7] due to the confusion it generated, and clinical laboratories are encouraged to continue to use the term *Fusarium* until conflicting viewpoints are resolved.[2]

Infections with *Fusarium* species may result in a broad spectrum of clinical manifestations, including superficial keratitis and onychomycosis (second most common pathogen after dermatophytes), locally invasive or disseminated disease. Infection severity and location depends on the immune status of patients and the pathogen portal of entry. Invasive and disseminated infections occur almost exclusively in severely immunosuppressed patients, particularly among those with hematological malignancy with prolonged neutropenia.[3] Allogeneic stem cell transplant recipients with graft-versus-host disease on steroid treatment are at particular risk for disseminated or invasive infection. Between 1986 and 1995 the incidence of *Fusarium* species infection was 1.2% among 750 allogeneic and 0.2% among 1,537 autologous marrow transplant recipients at M.D. Anderson Cancer Center in the U.S.[8] *Fusarium* is reported to be the third most common mold infection in hematology patients and organ transplant recipients after *Aspergillus* and Zygomycetes.[9]

The limited diagnostic tools available to diagnose invasive fungal infections lead to a delay in the diagnosis and treatment of these infections. Any clue to the early diagnosis of these infections may lead to changes in antifungal therapy and may be critical for an improved outcome. One of the most frequent, and frequently the only clinical sign, aspect of infections with *Fusarium* species is the development of skin lesions. Recognition of the skin manifestations will lead to early administration of antifungal therapy and obtaining biopsies for histopathology and fungal cultures.

Colonies of *Neocosmospora* (FSSC) grow rapidly within a few days and display aerial white to cream mycelium that turns bluish-brown when sporodochia develop. Curved, fusiform macroconidia with three to five septa (characteristic of *Fusarium* species) develop after four to seven days of incubation, while small, oval, one- or two-celled microconidia are usually abundant (Figure 3).[10] *Fusarium* and *Neocosmospora* species are unique among other commonly identified clinical filamentous molds (e.g., *Aspergillus* and *Zygomycetes* species) in their ability to grow in routine blood cultures.

With unpredictable response to therapy, high virulence seen in case reports and animal models, *Neocosmospora* (FSSC) infections often are associated with poor prognosis in patients.[11] Our patient's specimen displayed significant resistance to antifungals with low MIC only reported to amphotericin B. *Fusarium* and *Neocosmospora* species are relatively resistant to most antifungals,[12] therefore antifungal susceptibility testing is recommended while managing these infections, even though a correlation between MICs and clinical outcomes is not established. Treatment is typically a combination of surgical debridement, source control, and high dose liposomal amphotericin B, voriconazole with or without terbinafine.[3] Novel antifungals like olorofim are being evaluated.[13]

CONCLUSIONS

This case demonstrated the importance of a detailed physical examination for patients especially immunocompromised with fever. It also illustrated the changing fungal nomenclatures and the relatively high degree of antifungal resistance seen in *Neocosmospora (Fusarium)* infections.

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Keywords: Fusarium falciformis, Neocosmospora falciformis, soft tissue infection, acute myelogenous leukemia, febrile neutropenia

KANSAS JOURNAL of MEDICINE

Diabetic Ketoacidosis in Undiagnosed Acromegaly: A Case Report and Literature Review

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INTRODUCTION

Diabetic ketoacidosis (DKA) is both a potentially deadly hyperglycemic crisis and one of the most common causes of diabetes-related hospitalization in the U.S.[1,2] DKA currently is not established as a complication of acromegaly,[3-5] even though many authors have described their association.[6,7] This case reports a middle-aged male patient with a long history of untreated acromegaly who developed DKA.

Acromegaly is a rare endocrinologic disease first mentioned in 1886 by Perrier Marie, characterized by overproduction of growth hormone (GH), and in most cases from a pituitary adenoma.[8,9] It often is diagnosed between 40 and 50 years old,[10] and the common manifestations are acral growth, facial features deformities, soft tissue edema, hyperhidrosis, visual impairment, menstrual disturbances in women, and decreased libido in men.[11,12]

Diabetes mellitus (DM) is a common complication of acromegaly, with a prevalence ranging from 19 - 56%.[3,13] The primary mechanism of DM in acromegaly is growth hormone (GH)-induced insulin resistance,[14] thus hyperosmolar hyperglycemic state (HHS) would be expected as in Type 2 DM complications, instead of DKA.[15]

CASE REPORT

A 41-year-old male presented with a two-week history of polyuria, polydipsia, blurred vision, and dizziness, which progressed to nausea and vomiting for the prior two days. He had a medical history of hypertension, and a family history of Type 2 diabetes mellitus in his mother.

Physical examination was remarkable for a body mass index of 30 kg/m^2, blood pressure of 92/50 mmHg, heart rate of 105 beats/min, dry mucous membranes, a fruity odor to his breath, and physical findings suggestive of acromegaly: coarse facial features, enlarged mandible, enlarged-fleshy nose, increased space between the lower incisors, and bony overgrowth of the hands (Figure 1).

Visual field examination was unremarkable. Initial blood workup showed high anion gap metabolic acidosis (pH 7.27, bicarbonate 13.2mEq/L, and anion gap of 25mEq/L), serum glucose 472 mg/dl, glycosylated hemoglobin (HbA1c) 15.2%, ketones present in blood and urine, and serum osmolality 298 mOsm/kg.

Current 2021 British DKA guidelines for treatment,[16] as well as ADA 2009 latest guidelines for hyperglycemic crisis in adults,[17] recommended that the initial therapy starts with 0.9% sodium chloride solution and regular insulin infusion should be initiated at a rate of 0.1 units/kg/h. Efforts also should be made to maintain potassium in normal range. Hourly reassessments are needed to maintain blood glucose below 200 mg/dL until DKA resolves. This patient responded avidly to therapy and rapidly stabilized with expected ranges of blood glucose, pH, and bicarbonate.

Magnetic resonance imaging (MRI) of the head revealed a sella turcica mass (0.82 x 0.59 inches) with bilateral cavernous sinus invasion and likely mass effect on the optic chiasm (Figure 2).

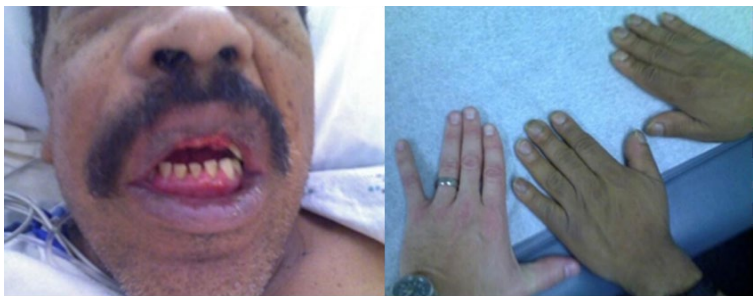

Figure 1. Patient shows coarse facial features, enlarged mandible, enlarged-fleshy nose, increased space between the lower incisors (left image), and bony overgrowth of the hands (right image).

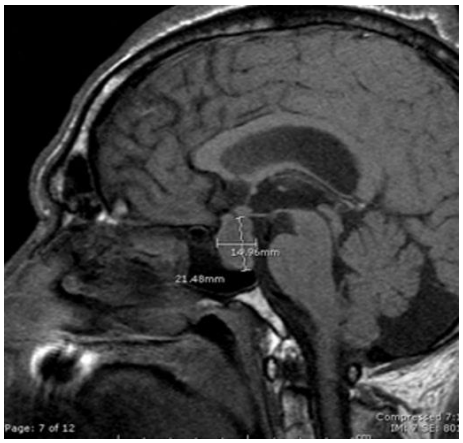

Figure 2. MRI showed a homogeneously enhancing hypointense T1/isointense T2 mass arising from the sella turcica.

An acromegaly laboratory panel confirmed the disease; random GH level was 98.2 ng/ml (normal 0-6 ng/ml) and insulin-like growth factor-1 (IGF-1) was 398 ng/ml (normal 101-267 ng/ml). Additional pituitary hormonal testing was unremarkable. A fasting C-peptide was 1.1 ng/dl (1.1-5 ng/dl), indicating some degree of insulin secretory reserve. Glutamic acid decarboxylase (GAD65) antibodies were negative, ruling out autoimmunity-related diabetes.

The patient underwent trans-nasal, trans-sphenoidal resection of the pituitary mass without complications, and biopsy confirmed pituitary adenoma (Figure 3).

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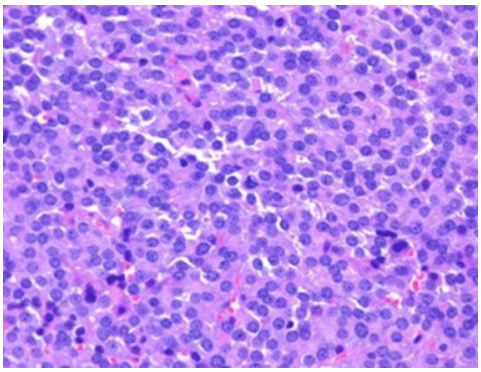

Figure 3. Pituitary adenoma composed of uniform, monomorphic polygonal cells arrayed in cords, with evidence of modest mitotic activity (400X).

Discharged treatment included subcutaneous insulin and metformin. At two-week follow-up, his coarse facial features slightly improved (Figure 4). At two months, the IGF-1 remained elevated at 837 ng/ml (98-261), indicating residual tumor. The patient was scheduled for a second MRI of the sella and consultation for stereotactic radiation therapy. Unfortunately, the patient was lost to follow-up.

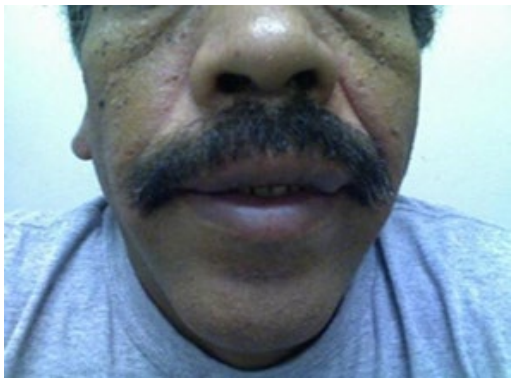

Figure 4. Improvement of coarse facial features two weeks post-surgery.

DISCUSSION

The DKA episode was the initial presentation of the acromegaly in this patient. It was likely due to a combination of severe insulin resistance from acromegaly and impaired insulin secretion (or relative insulin deficiency) from chronic undiagnosed hyperglycemia. Although there are a few reports of DKA as a complication of acromegaly,[6,7] the association was not well established.

Diabetes mellitus is a common complication of GH excess and caused by hepatic and peripheral insulin resistance.[18] At the hepatic level, GH increases gluconeogenesis and glycogenolysis. Peripherally, GH inhibits glycogen synthesis and glucose oxidation.[19] Growth hormone excess also causes increased lipolysis and, as a consequence, an increase in free fatty acid, which may contribute to insulin resistance.[20]

Diabetic ketoacidosis occurs in the presence of insulin deficiency and excess of counterregulatory hormones like GH.[7] The diabetogenic effect of GH initially is compensated by hyperinsulinemia;[21] if GH excess remains, fasting hyperglycemia may develop, often corresponding with a fall in fasting insulin levels. Finally, the insulin response to carbohydrate exposure is decreased,[14] which could result in DKA.[6,7]

Islet cells may undergo progressive changes when exposed to prolonged high levels of GH, which could result in cell degeneration, a reduction in insulin production, and finally DKA.[22] However, this mechanism has been borne out only in animal studies. An autopsy from an acromegalic woman who became diabetic and required insulin showed larger and more abundant islets with hypergranular beta cells,[23] suggesting the initial hyperglycemic state with normal insulin secretion.

Another plausible explanation was that acromegalic patients who develop DKA might have DM independent of their acromegaly.[24] Two important risk factors for DM secondary to acromegaly are hypertension and a positive family history of DM.[13] Both were present in our patient. In these patients, chronic glucose toxicity leads to insulin resistance and contributes to impairment of insulin secretion.[25]

Our patient had characteristics of ketosis prone, antibody-negative diabetes mellitus according to the A β classification system,[26] in which it was hypothesized that chronic hyperglycemia increases susceptibility of the beta cell to desensitization and alters post-insulin receptor signaling.[27]

Endocrine remission occurs in 50% of GH-secreting macroadenomas after surgery.[14] Remission was not seen in this patient, owing to the presence of an unresected tumor in his cavernous sinuses. During follow-up, the IGF-1 level remained elevated, reflecting the presence of residual tumor. In previous case reports of DKA in acromegalic patients, complete discontinuation of insulin therapy was possible after GH level normalization.[7,24,28] In our patient, the clinical scenario indicated that insulin discontinuation would not be possible, presumably due to persistent GH-induced insulin resistance that could yield another DKA episode.

If the patient was not lost to follow-up, further treatment or cure of his acromegaly would have revealed the extent to which his hyperglycemia and DKA were the result of acromegaly.

LIMITATIONS

Our patient had the phenotype for Type 2 DM, with obesity, age greater than 30 years, and a positive family history. This may have led to an atypical presentation of Type 2 DM rather than acromegaly-related DKA.

CONCLUSIONS

Growth hormone excess in acromegaly antagonizes insulin action both at the hepatic level and peripherally, making DKA an unlikely complication. It might be caused by B-cell failure due to chronic hyperglycemia. DKA can be managed with positive results, as well as hyperglycemic state after DKA control, until remission of the secreting-GH pituitary adenoma. This case report suggested that DKA was a possible complication of acromegaly and that it should be recognized as one.

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TABLE OF CONTENTS

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Comparative Analysis of Topical Versus Intravenous Administration of Epsilon-Aminocaproic Acid on Blood Management in Total Knee Arthroplasty

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ABSTRACT

Introduction. Although the use of antifibrinolytics to reduce perioperative blood loss during total knee arthroplasty (TKA) has shown unequivocal benefit in regard to blood conservation, the best route of administration remains in question. This study tested the hypothesis that topical delivery of epsilon-aminocaproic acid (EACA) was superior to intravenous (IV) administration in the setting of primary TKA.

Methods. This cross-sectional study included a six-year retrospective chart review of TKA patients done by a single surgeon. Post-operative hemoglobin levels and the incidence of blood transfusions were compared among three patient subgroups: no EACA, topical EACA, or IV EACA. Key outcome measures included post-operative hemoglobin, need for post-operative transfusion, and length of hospital stay.

Results. Of the 668 patients included in this study, 351 (52.5%) received IV EACA, 298 (44.6%) received topical EACA, and 19 (2.8%) received no EACA. For the three-way comparisons, significant differences were observed for post-operative mean hemoglobin on day one ($p < 0.001$), day two ($p < 0.001$), and day three ($p = 0.004$), with consistently higher means for participants in the topical group. Eight patients required transfusions in the IV EACA group, but none were needed in the topical EACA group ($p = 0.027$). Length of stay was shortest for patients in the topical group, with 66% hospitalized for two days, while 84% of the IV group remained hospitalized for three days ($p < 0.001$).

Conclusions. The topical delivery of EACA is superior to IV administration with respect to blood conservation for patients undergoing primary TKA. ***Kans J Med 2022;15:73-77***

INTRODUCTION

Total knee arthroplasty (TKA) is one of the most common orthopaedic surgery procedures performed today in the United States. The number of arthroplasties is expected to increase by 85%, to 1.26 million procedures, by 2030.[1] Historically, the reported rate of blood transfusion after TKA has been as high as 40%.[2] However, recent blood conservation efforts markedly have decreased this transfusion rate and the associated complications and costs.

The mainstay of blood conservation treatment in the setting of TKA is the administration of antifibrinolytics, such as tranexamic acid (TXA) and epsilon-aminocaproic acid (EACA). The mechanism of action of these medications is through the inhibition of fibrinolysis by blocking the lysine-binding sites of plasmin and plasminogen to fibrin. This prevents the premature dissolution of clots, thereby decreasing perioperative bleeding and the need for blood transfusion. Multiple studies have confirmed the efficacy and safety of these medications in TKA patients.[3-7] Although TXA historically has been used more widely, it has not been shown to be superior to EACA for TKA.[8] Moreover, EACA is more affordable than TXA.[9] For example, Churchill et al.[10] determined that the average cost of EACA for each procedure is $2.23 compared to $39.58 for TXA.

The optimal method of EACA administration has not been determined. Antifibrinolytics may be administered orally, intravenously, topically by intra-articular placement during surgery, or by a combination of these means. Recent studies have shown that topical administration of TXA was associated with more effective blood conservation than intravenous (IV) administration during TKA.[2,11] To the best of our knowledge, no similar study has been done on the more affordable antifibrinolytic alternative EACA.

This study compared topical vs. IV EACA administration, assessing key outcome measures, including post-operative hemoglobin (Hgb), the need for post-operative transfusion, the number of blood units required, and the length of hospital stay after primary TKA. Adverse events such as deep venous thromboses (DVT), pulmonary emboli (PE), or bleeding were recorded. We hypothesized that topical administration of EACA results in higher post-operative hemoglobin levels and fewer blood units transfused compared to intravenous administration. We also expected that fewer adverse events occurred in the topical EACA group compared to the group in which the drug was administered systemically.

METHODS

A retrospective chart review was performed on patients who had primary TKA by one fellowship-trained orthopaedist at a single institution from 2011 to 2016. This study was approved by the local institutional review board. Since this was a retrospective review of medical records, informed consent was waived.

Patient Population. All patients in this cross-sectional study underwent a unilateral cemented TKA through a medial parapatellar approach under tourniquet control. The wound was not drained following surgery. Post-operative pharmacologic DVT prophylaxis varied during the study period, according to the surgeon's preference, which changed over time. Fondaparinux was used in 2011, rivaroxaban from 2012 to 2014, and aspirin from 2015 to 2016. Patients who were on warfarin prophylaxis pre-operatively were bridged to warfarin post-operatively using low-molecular-weight heparins as bridging agents.

Patients were excluded from antifibrinolytic treatment if they had allergy to EACA, disseminated intravascular coagulation, coronary stenting (drug-eluting stent within one year of placement or bare-metal stent within two months of implantation), heart valve replacement,

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atrial fibrillation, current anticoagulation therapy, or documented personal history of DVT, PE, or hematuria.

Treatment Cohorts. Three patient groups were compared. The control group included patients who did not receive antifibrinolytic therapy at any point in the perioperative period during the TKA. The EACA treatment group included patients who received epsilon-aminocaproic acid either intravenously or topically during the TKA. The method of EACA administration varied according to surgeon preference, which evolved during the study period.

In the IV group, the EACA dosing regimen included a loading dose of 5 g intravenously over 30 minutes, followed by a maintenance dose of 10 g over five hours by intravenous infusion. The loading dose was started in the operating room at the beginning of the procedure. Patients in the topical group received an intra-articular administration of EACA after the TKA. A single 5 g dose of EACA in 20 cc of saline was injected into the knee joint after capsular closure and before the tourniquet was deflated.

Outcome Measures. Patient demographic data collected during chart review included age, gender, and body mass index. Key clinical outcome data included the dosage and route of EACA administration, pre-operative hemoglobin level, hemoglobin values on the first three days after TKA, the requirement for blood transfusion, the number of blood units transfused, the length of hospital stay (LOHS), and occurrence of DVT, PE, and post-operative bleeding. The indication for a blood transfusion was any post-operative patient with a Hgb < 8 g/dL. Post-operative hemoglobin values on days one, two, and three served as estimates for operative blood loss.

Statistical Analysis. A power analysis was conducted in a web calculator using data from Wang et al.[2] Results comparing two proportions, IV (81%) vs. topical (71%), showed that 267 patients per group, or 534 total patients, would have 80% power to detect a significant difference between the two groups using an alpha level of 0.05.

Descriptive statistics were used to summarize the data. Continuous data were assessed for normality using the Kolmogorov-Smirnov test. Where the normality assumption was valid, continuous data were reported as means and standard deviations (SD). Otherwise, medians, minimums (min), and maximums (max) were used to characterize the data. Categorical data were summarized as frequencies and percentages.

Bivariable comparisons by groups were conducted using Pearson Chi-square test, Fisher exact test, Mann-Whitney exact test, ANOVA, Tamhane T2 test (equal variances not assumed), or Kruskal-Wallis exact test. Exact tests were used to accommodate sparse data. Generalized Estimating Equation was conducted to assess hemoglobin measures over time by EACA route. Wilcoxon signed-rank test was used for analyzing pre-operative and post-operative paired ordinal data. All statistical tests were two-sided and conducted with IBM® SPSS Statistics, version 26.

RESULTS

The total number of patients receiving TKA during the study period was 748. Eighty patients who did not have unilateral primary TKA were excluded. Of the remaining 668 patients comprising the study cohort, 351 (52.5%) received IV EACA, 298 (44.6%) received topical EACA, and 19 (2.8%) received no EACA (Figure 1). The mean age of those studied was 63.8 years with a SD of 10.8, mean BMI was 34.2 (7.2), and LOHS ranged from one to five days. There were 427 (63.9%) women in the study group.

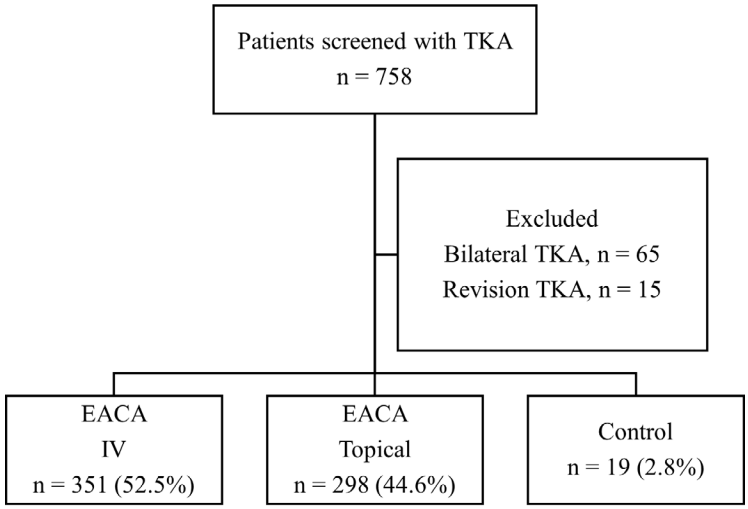

Figure 1. Study population.

Table 1 shows participant comparisons by EACA route of administration: IV, topical, and control. The table shows two sets of p values: the first compared all three groups, while the second compared IV vs. topical. For the three-way comparisons, significant differences were observed for post-operative mean hemoglobin days one, two, and three ($p < 0.001$, $p < 0.001$, and $p = 0.004$, respectively) with consistently higher means for participants in the topical group. The number of transfusions also differed significantly by group ($p = 0.027$), although most patients did not receive one. Regarding the number of blood units transfused, five participants received one unit and three received two units. All transfusions were in the IV group ($p = 0.026$). LOHS was shortest for patients in the topical group, most (66%) incurred two hospital days, while almost all (84%) of the IV group were hospitalized for three days ($p < 0.001$). Apart from mean hemoglobin day three, all results were significant for the two-way comparisons.

Paired comparisons were conducted between mean pre- and post-operative day one hemoglobin measures for all groups (Table 1). All differences were statistically significant ($p < 0.001$). The greatest mean reduction observed over time was in the control group, 13.7 g/dL vs. 10.5 g/dL on day one, followed by the IV group, 14.0 g/dL vs. 11.6 g/dL on day one.

Results from Generalized Estimating Equations showed that mean hemoglobin changes in both IV and topical groups differed significantly as compared to perioperative hemoglobin differences in the control group ($p < 0.001$) as shown in Figure 2. Within group differences by day were also significant as compared to pre-operative hemoglobin ($p < 0.001$ for each comparison).

Table 1. Comparison of participant characteristics by group.

Description	N	IV n = 351 (52.5%)	Topical n = 298 (44.6%)	Control n = 19 (2.8%)	p*	p**
Gender; n (%)	668					
Male		134 (38.2)	104 (34.9)	3 (15.8)	0.115	0.414
Female		217 (61.8)	194 (65.1)	16 (84.2)		
Median age; y (min, max)	649	65 (25, 88)	65 (28, 87)	--	0.519	
Median BMI (min, max)	649	33 (17.2, 73.0)	33.5 (19.2, 54.8)	--	0.344	
Operation side; n (%)	667				0.410	0.375
Left		186 (53.0)	147 (49.5)	12 (63.2)		
Right		165 (47.0)	150 (50.5)	7 (36.8)		
Mean preop hemoglobin; g/dL	668	14.0 ± 1.1[a]	14.0 ± 1.2[a]	13.7 ± 1.1[a]	0.425	--
Mean postop hemoglobin, day 1; g/dL	668	11.6 ± 1.4[a]	12.1 ± 1.3[b]	10.5 ± 1.3[c]	< 0.001	--
Mean postop hemoglobin day 2; g/dL	477	10.8 + 1.5[a]	11.3 + 1.5[b]	9.8 + 1.3[c]	< 0.001	--
Mean postop hemoglobin day 3; g/dL	263	10.1 ± 1.4[a]	10.7 ± 1.4[a]	9.0 ± 10.9[b]	0.004	--
Transfusion number; n (%)	668				0.027	0.009
None		343 (97.7)	298 (100.0)	18 (94.7)		
One		8 (2.3)	0 (0.0)	1 (5.3)		
Blood unit number; n (%)	668				0.026	0.009
None		343 (97.7)	298 (100.0)	18 (94.7)		
One		5 (1.4)	0 (0.0)	0 (0.0)		
Two		3 (0.9)	0 (0.0)	1 (5.3)		
Length of hospital stay in days; n (%)	668				< 0.001	< 0.001
One		0 (0.0)	15 (5.0)	0 (0.0)		
Two		25 (7.1)	197 (66.1)	4 (21.1)		
Three		295 (84.0)	77 (25.8)	12 (63.2)		
Four		29 (8.3)	8 (2.7)	2 (10.5)		
Five		2 (0.6)	1 (0.3)	1 (5.3)		

* Three group comparisons: IV vs. Topical vs. Control
** Two group comparisons: IV vs. Topical
[a,b,c] Tamhane's T2 (equal variances not assumed); letter change indicates significant differences between groups.

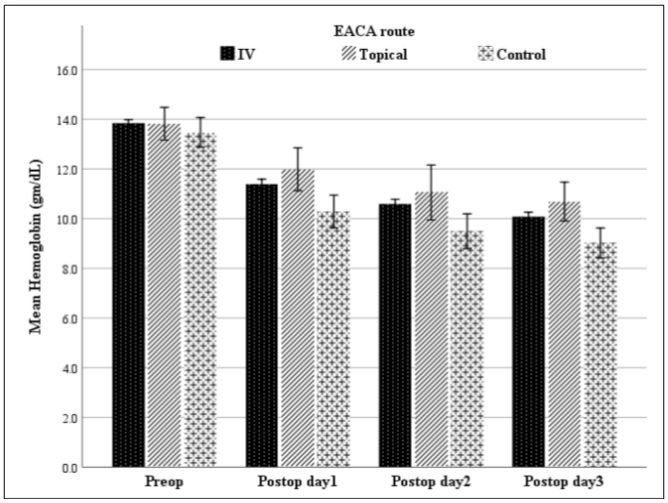

Figure 2. Results from Generalized Estimating Equations. Mean hemoglobin changes in both IV and topical groups differed significantly as compared to perioperative hemoglobin differences in the control group ($p < 0.001$). Within group differences by day were also significant as compared to pre-operative hemoglobin ($p < 0.001$ for each comparison).

Pre- and post-operative day one hemoglobin was measured by gender within each subgroup as hemoglobin tends to differ for males and females (Figure 3). No other time differences were evaluated because data were sparse, and males were absent in the control group for day three hemoglobin. All such comparisons revealed statistically significant differences for both men and women ($p < 0.001$). While post-operative hemoglobin measures were below average ranges for both genders, differences were smallest for those in the topical group at 2.1 g/dL for both males (14.7 vs. 12.6) and females (13.7 vs. 11.6).

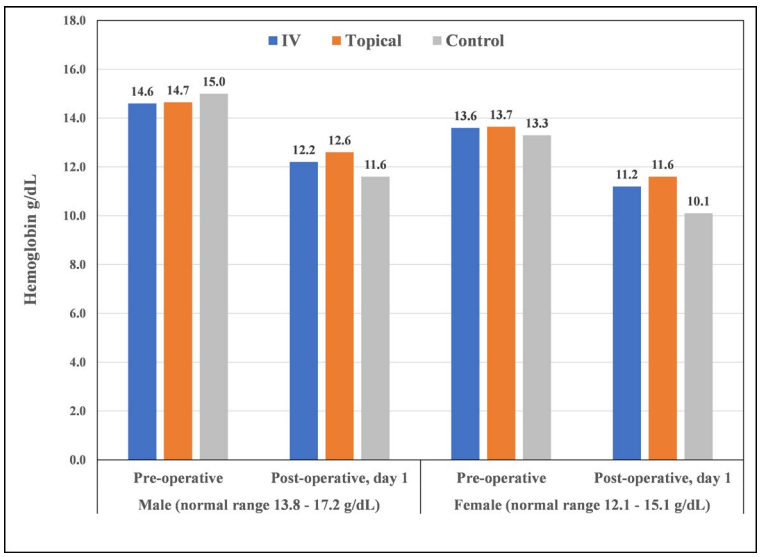

Figure 3. Comparing pre- and post-operative hemoglobin measures (g/dL) by group and gender. Wilcoxon signed-rank tests showed all pre- and post-operative differences were significant ($p < 0.001$).

DISCUSSION

The results of this study indicated the blood conservation effects of EACA were superior when the drug is administered topically rather than intravenously during primary unilateral TKA. The topical EACA group had a statistically higher post-operative day one hemoglobin value compared to both the IV EACA group and the control group. Statistical significance also was observed in the post-operative day two hemoglobin comparison. Furthermore, no patients in the topical group received blood transfusions compared to the IV group in which 1.4% of patients received one unit of blood product and 0.9% received two units. This difference also was statistically significant. Interestingly, the pre-operative hemoglobin values between male and female participants were significantly different, but the efficacy of EACA showed no gender bias regarding its effects on blood conservation.

This study demonstrated a statistically significant shorter LOHS in the topical EACA group. Of the 298 patients in the topical group, 197 (66.1%) were discharged from the hospital on post-operative day two compared to 25 of the 351 patients (7.1%) in the IV group. The majority of patients (84%) in the IV group was discharged from the hospital on post-operative day three.

To the authors' knowledge, there is no published literature comparing outcomes of intravenous EACA to topical administration. However, this comparison has been made for patients treated with TXA in the setting of unilateral primary TKA. For example, Goyal et al.[12] in a randomized trial of 83 patients treated with intra-articular TXA and 85 receiving IV TXA, found that topical administration of TXA was not inferior to intravenous administration. The investigators concluded that a single dose of topical TXA was preferable to IV administration secondary to the ease of administration.

In another randomized trial, Wang et al.[2] analyzed 150 unilateral primary TKA patients evenly divided into three study groups: topical TXA, IV TXA, and no TXA. Their study showed topical administration of TXA significantly reduced total blood loss and drainage volume to a greater degree than IV administration. In a third study, Chen et al.[11] randomized 50 patients to receive IV TXA and 50 patients to receive topical TXA in the setting of primary unilateral TKA. They found no difference in peri-operative blood loss or post-operative lower limb swelling between the two groups. Notably, these two trials utilized intra-articular drains post-operatively which can complicate data comparisons.

A recent meta-analysis showed EACA and TXA to be equally efficacious for blood conservation after TKA,[13] which is consistent with established literature. Comparing the data from similar studies to our own results suggested that topical TXA and topical EACA were both effective means of blood conservation in unilateral primary TKA. Moreover, EACA is the more cost-effective alternative of the two options. Comparable studies evaluating IV and topical TXA have not reported on LOHS.

There were several limitations to our study. First, as is typical in retrospective chart reviews, some data were missing resulting in an incomplete demographic database. Second, all procedures were performed at a specialty hospital without a critical care unit, thus introducing a bias towards patients with fewer comorbid conditions. Third, since patients in the study were not classified according to American Society of Anesthesiology grade, we could not determine if there were significant differences in co-morbidities among the cohorts. Fourth, we did not control for peri-operative anticoagulation, which varied over time according to the surgeon's preference and was a confounding variable. Fifth, EACA was administered intravenously from 2011 to 2014

and topically later in the study to limit the potential adverse effects of systemic administration. Furthermore, this transition period occurred during a trend toward enhanced recovery protocol (ERP) for TKA which incorporates a standardized pre-operative education program, regional anesthesia, post-operative multimodal pain management, and early rehabilitation. Since ERP usually results in earlier hospital discharge, this was also a confounding variable in the study and our LOHS data must be interpreted accordingly.

Strengths of this study included the relatively large number of patients analyzed and the fact that the procedures were all performed by a single surgeon. This large patient population (668) permitted detection of statistical significance among the study groups. However, due to the low incidence of adverse reactions, a larger cohort of patients would be required to detect a significant difference in regard to thromboembolic events. Future research should use randomized controlled methods to delineate the optimum administration of EACA.

CONCLUSIONS

Our results showed that topical administration of EACA outperforms IV treatment. Participants in the topical group required no transfusions and had higher post-operative hemoglobin levels. Furthermore, a single intra-articular introduction of EACA was easier than multiple intravenous dosing and is our preferred method of administration.

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Keywords: antifibrinolytic, blood conservation strategy, epsilon-aminocaproic acid, knee arthroplasty, blood transfusion

KANSAS JOURNAL of MEDICINE

Suture Education with Soft-Embalmed Cadavers: A Cut Above the Rest

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ABSTRACT

Introduction. The efficacy of a surgical skills curriculum was assessed for third-year medical students focused on suturing training on soft embalmed cadavers, which simulate natural tissue more effectively for surgical procedures than traditionally preserved cadavers or surgical practice pads.

Methods. A retrospective cohort study compared pre- and post-survey results at a premier, accredited, nationally ranked academic medical center. Study participants were third-year medical students completing their required surgical clerkship rotation who participated in suturing sessions on both synthetic suture practice pads and soft-embalmed cadavers prior to beginning their operating room experience.

Results. A total of 40 participants were included, with slightly more male participants. The majority of participants (52%) were interested in pursuing a non-surgical career. After participating in Clinical Anatomy Mentorship Program (CAMP), participants felt significantly more confident in their ability to suture in the operating room (median 4 [3-4] vs. 2 [1-3], $p < 0.001$); in their knowledge of basic suturing supplies and instruments (median 4 [4-4] vs. 3 [2-3], $p < 0.001$); and in their ability to determine when different suture techniques are appropriate in the operating room (median 3 [3-4] vs. 1 [1-2], $p < 0.001$). Participants felt more confident in their ability to suture in the operating room after their experience suturing on soft-embalmed cadavers compared to suture practice pads (median 5 [4-5] vs. 4 [4-4], $p = 0.002$).

Conclusions. Medical students' confidence in suturing skills and in the knowledge of important characteristics of suturing practice was improved significantly after a suture training session on soft-embalmed cadavers. ***Kans J Med 2022;15:78-81***

INTRODUCTION

Suturing is a critical skill that physicians need to be able to perform confidently and proficiently. The foundation of this skill is best built early in training, often during medical school.[1] In fact, suturing is one of the most common procedural skills for medical students to perform during their clinical rotations. Yet, medical students often experience a significant amount of anxiety when asked to suture wounds.[2] Formal training sessions for medical students are known to increase both student confidence and skill with suturing.[3-5]

An ideal strategy for developing procedural skills is to practice with material that simulates living tissue as closely as possible. It previously has been demonstrated that medical students' type of practice material has a notable impact on suturing skills acquisition.[6] Cadaveric tissue has been an excellent choice for trainees to learn and practice a wide variety of procedural skills.[6-13] Soft embalmed cadavers, which are cadavers preserved in a more lifelike manner than traditionally preserved cadavers, simulate natural tissue more effectively for surgical procedures than traditionally preserved cadavers.[6-19] With these known benefits of soft-embalmed cadavers in medical trainee procedural skills practice, medical students would benefit greatly from practicing their suturing skills on soft-embalmed cadavers prior to suturing in the operating room.

We hypothesized that medical students will feel more confident in their suturing skills and knowledge of suturing principles after participation in suturing practice on soft-embalmed cadavers. Secondarily, participants will attribute their confidence in suturing more to their experience suturing on soft-embalmed cadavers than their experience suturing on synthetic suture practice pads.

METHODS

Study Design. A retrospective cohort study was performed to evaluate the hypotheses. All aspects of this study were approved by a duly constructed Institutional Review Board at our institution prior to commencement of any study activity. Data utilized for this study were collected via surveys as part of the Clinical Anatomy Mentorship Program (CAMP), a near-peer surgical education program for medical students at our institution. Data collected from CAMP and analyzed in this study were collected from May 2021 to July of 2021. The Institutional Review Board at our institution approved this secondary use of regularly collected CAMP data for use in this study without the need to obtain informed consent from each prior participant in CAMP. Therefore, informed consent for each previous participant in CAMP was not needed nor pursued for study activity.

Surgical Skills Curriculum. During CAMP, the third-year medical students participate in a full-day anatomy and surgical skill workshop prior to their surgery clerkship. Participants are taken through demonstrations of common surgical procedures in general surgery and various surgical subspecialties, practice foundational laparoscopic techniques, and practice suturing on soft-embalmed cadavers. During this suturing practice, participants practice a myriad of methods, including simple interrupted, simple running, interlocking, horizontal mattress, vertical mattress, buried, subcuticular, 1-hand tie, and 2-hand tie techniques. These skills are taught by fourth-year medical students who have received training by expert surgeons on how to teach fundamental suture skills effectively to their peers. This concept is termed near-peer teaching in CAMP at our institution. The same group of students participated in a suture practice session on practice pads earlier that week, where they were introduced to the techniques mentioned above.

Assessing Curriculum Efficacy. A pre-survey was distributed to students before they participated in CAMP, and a post-survey was distributed to participants after participation in CAMP as part of the program. These surveys collected information from students on many topics, ranging from anatomy knowledge to medical student perceptions of surgery, to suturing. The survey responses that focused on suturing were collected for use in this study. These questions were developed in a Likert scale format to assess students' confidence in suturing in the operating room, perceived knowledge of suturing instruments and

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appropriate suture techniques, and the impact of their experiences suturing on both suture practice pads and soft-embalmed cadavers. While not validated, these questions were constructed by CAMP directors, including active surgeons and experts in medical student education. Student responses to these questions were collected for analysis in this study.

Statistical Analysis. Statistical analysis was performed using IBM® SPSS® Statistics software (Version 26.1). Baseline participant characteristics were analyzed as frequencies utilizing medians and interquartile ranges. Comparison of participant responses to Likert scale questions between the pre- and post-survey, as well as a comparison of questions within the same survey, were accomplished via the Wilcoxon Signed Rank test. Statistical significance was set at $p < 0.05$.

RESULTS

Table 1 presents the summary statistics for baseline information describing our study participants. A total of 40 third year medical school participants were included with an average age of 25 years. There were slightly more males than females included (52% male). The majority of participants (52%) were interested in pursuing a non-surgical career.

Table 1. Participant characteristics.

Baseline participant characteristics	n = 40
Age*	25 [24-28]
Gender	
Female	19 (48%)
Male	21 (52%)
Career interest	
Surgical	19 (48%)
Non-surgical	21 (52%)
Prior operating room experiences	
Yes	37 (93%)
No	3 (7%)

*Median [interquartile range]

Selected pre-and post-survey results are displayed in Table 2. After participating in CAMP, participants felt significantly more confident in their ability to suture in the operating room (median 4 [3-4] vs. 2 [1-3], $p < 0.001$), in their knowledge of basic suturing supplies and instruments (median 4 [4-4] vs. 3 [2-3], $p < 0.001$), and in their ability to determine when different suture techniques are appropriate in the operating room (median 3 [3-4] vs. 1 [1-2], $p < 0.001$). Notably, participants responded that they felt more confident they would seek out opportunities to suture in the operating room after participating in this program (median 4 [4-5] vs. 4 [3-4], $p = 0.009$).

Table 3 displays the difference in participants' confidence gained from practicing on both suture pads and soft-embalmed cadavers. Participants felt more confident in their ability to suture in the operating room after their experience suturing on soft-embalmed cadavers compared to suture practice pads (median 5 [4-5] vs. 4 [4-4], $p = 0.002$).

Table 2. Comparison of pre- and post-survey results.

Survey questions	Pre-survey median Likert scale response*	Post-survey median Likert scale response*	p value
I am confident in my ability to suture in the operating room.	2 [1-3]	4 [3-4]	< 0.001**
I am confident in my knowledge of basic suturing instruments and supplies.	3 [2-3]	4 [4-4]	< 0.001**
I am confident in my ability to determine when different suture techniques are appropriate in the operating room.	1 [1-2]	3 [3-4]	< 0.001**
I am confident I will seek out opportunities to suture in the operating room.	4 [3-4]	4 [4-5]	0.009**

* Median [interquartile range]
** $p < 0.05$, statistically significant

Table 3. Comparison of responses in the post-survey.

	Practicing suturing on suture practice pads improved my confidence to suture in the operating room.*	Practicing suturing on soft-embalmed cadaver tissue improved my confidence to suture in the operating room.*	p value
Scores	4 [4-4]	5 [4-5]	0.002**

* Median [interquartile range]
** $p < 0.05$, statistically significant

DISCUSSION

This study evaluated the primary hypothesis that medical students would feel more confident in their suturing skills and knowledge of key suturing principles after utilizing soft-embalmed cadavers compared to synthetic suture practice pads to practice this skill. Additionally, we hypothesized that students who gained confidence in their suturing skills after practicing on both materials would attribute this increase in confidence more to their experience with soft-embalmed cadaver tissue compared to practice on synthetic suture practice pads. The first major finding of this study was that medical student confidence in their suturing skills and their knowledge of vital characteristics of suturing practices improved significantly after a suture training session on soft-embalmed cadavers compared to their confidence and knowledge after practicing suture skills on synthetic suture practice pads. Our medical students attributed their gain in suturing confidence to their experience with soft-embalmed cadavers, as compared to synthetic suture practice pads.

This study added to the numerous examples in the literature of the superiority of soft-embalmed cadaver tissue for education of medical trainees compared to alternatives. While not all focused on suture skills, there has been clear benefit in educating medical students on a variety of procedural skills.[7,8,16-18] These benefits are evident in improving resident procedural skills utilizing soft-embalmed cadavers as well.[7,9-12,15] Gonzalez-Navarro et al.[6] conducted a study focused on determining the ideal suturing model for medical students to practice suture skills.

This investigation determined that medical students preferred practicing suturing on pork fat tissue compared to sponges, oranges, or commercially available suture practice models. While our study did not investigate each of these different materials and the Gonzalez-Navarro et al.[6] study did not include soft-embalmed cadaver tissue, both studies had similar findings in that the true tissue was superior to the synthetic and non-human/animal alternatives.

A notably relevant prior study was conducted by Guler et al.[19] to compare midwifery student confidence in repairing episiotomy with suturing after practicing with both cow tongue tissue and synthetic suture practice models. This investigation determined that students' confidence in their ability to repair an episiotomy was significantly higher after practice with the cow tongue tissue compared to the synthetic model. Our findings that students' confidence in their ability to suture was greatest after practice with and primarily due to their practice with soft-embalmed cadaver tissue was similar with these findings.

The importance of increasing both medical student confidence and proficiency with suturing should not be overlooked. As medical students often are asked to perform suturing in the operating room,[1,2,5] educating them in this skill in the most ideal way is paramount. At our institution, it is common for medical students to close the majority of surgical incisions on many surgical services. While that cannot be generalized to all other healthcare facilities, it is likely that medical students participate in the operating room in some capacity. Importantly, the operating room is likely not the ideal place for a medical student to learn and practice how to suture for the first time. Medical students viewed the operating room as a less ideal place to learn various technical surgical skills initially compared to attending surgeons.[20] Medical students often viewed suturing on patients in the operating room as an anxiety-ridden experience.[2,5,20,21] Clearly, there needs to be greater focus on providing high-quality instruction and practice material for medical students to develop their suturing skills prior to performing suturing on a patient in the operating room. It has been demonstrated previously that early suture training programs for medical students prior to their introduction to the operating room benefits their technical skills and confidence in these abilities.[3-5,22] Combining early acquisition and repetition of suture skills with high quality soft-embalmed cadaver tissue that is far more realistic to patient tissue than synthetic alternatives likely will benefit medical student operating room experience, technical skill in the operating room, and care of the surgical patient.[7-13]

One necessary element to consider with soft-embalmed cadavers is the financial need to secure and properly maintain these cadavers. There are increased costs to procure and maintain soft-embalmed cadavers compared to suture practice pads as various chemicals, deep freeze storage space, and support personnel is required.[14] In our experience, soft embalmed cadavers cost approximately $1,300 per body to obtain and maintain for one year and it was within the capacity of our anatomy laboratory to maintain these bodies with deep freezer capacity. These cadavers were viable for an entire academic year.

Consumer available suturing pad cost varied widely, as did the quality of the pads themselves. Notably, many of these synthetic suture practice pads can be used for years. Some may view this as justification for providing suturing pads as practice, however, our results add to the multi-faceted decision of providing ideal training opportunities for medical students to the need for cost consideration of such ventures. A key point of this decision was that a soft-embalmed cadaver used for medical student suture education can be utilized by different specialties for additional education, thus increasing the utility of each cadaver and making the investment in soft-embalmed cadavers more justifiable.[23] The most important limitation with the pads, in our experience, was the inability for learners effectively to practice buried and subcuticular suture techniques on synthetic suture practice pads. Those techniques are challenging to practice on anything but true tissue. It was the experience of many students at our institution that these were also the two most common suture techniques that they were asked to perform in the operating room. Through the suture practicing on soft-embalmed cadavers during the CAMP sessions, students effectively practiced these techniques that were asked of them most commonly in the operating room.

There were important limitations to discuss with our results. First and foremost, this study was limited by small sample size. While a series of 40 medical students was sufficient to investigate our hypothesis with a significant result, it was possible that our findings may not be consistent with larger samples of medical trainees. Secondly, we were not able to assess our hypothesis using a true control group. Suture education on soft-embalmed cadavers was already the standard educational method at our institution, and as this study was non-interventional, we were limited in this capacity. However, we believed our hypothesis still was assessed adequately by sending the pre-survey prior to student participation in this suturing session. Secondly, the primary aim of this study did not seek to define whether the students' technical skill was improved, but rather their confidence with their suturing skill. As there could be mismatches between participants' confidence in suturing and their suturing skill, our results and conclusions could not assess true skill in suturing.

Notwithstanding these limitations, this study suggested soft-embalmed cadavers provide a benefit to medical student education regarding suture technique and knowledge prior to operating room experience. Further work is required to establish the viability of our results regarding student confidence and understanding of the benefit of utilizing soft-embalmed cadavers in this fashion. A natural progression of this work is to investigate student proficiency with suture technique with the use of soft-embalmed cadavers, stepping beyond just student confidence in their preparedness to suture.

CONCLUSIONS

Although there was increased cost associated with supplying and maintaining soft-embalmed cadavers properly compared to cheaper, more convenient alternatives, such as suture practice pads, improving medical students' confidence in and knowledge of suturing with far more realistic simulation will benefit both the students and their patients. Medical students frequently were called upon to suture, heightening the importance of improving education in this area. While not addressed in this study, investigating the impact of soft-embalmed

cadavers on medical students' technical skills with suturing is a logical next step in addressing this educational need. We also would like to investigate whether our training session impacts the amount of hands-on suturing experience students achieve in the operating room during the surgery clerkship.

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Keywords: medical student, medical education, simulation training, cadaver, surgery

KANSAS JOURNAL of MEDICINE

Activity-Based Checks (ABCs) of Pain: A Functional Pain Scale Used by Surgical Patients

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ABSTRACT

Introduction. Increased rates of surgery, combined with concerns about high-risk pain medications, have highlighted the need for improved methods of meaningfully assessing pain. In response to lack of medical context and functional data in existing scales, the Activity-Based Checks (ABCs) was developed.

Methods. This prospective, cohort study was deployed at a single-institution, academic center. The primary outcome was to correlate the ABCs to the 0 - 10 numeric rating scale (NRS) in post-operative general surgery patients. Secondary outcomes included assessing the impact of patient factors and prescribing patterns on opioid consumption, in milligrams of morphine equivalents (MME), after discharge.

Results. The function that correlated most to the NRS at discharge was "Out of Bed to Chair". Indicators of better mental health were correlated inversely with MME consumption. Interestingly, the largest predictor of MME taken was MME prescribed. Over 40% of prescribed opioids goes unused.

Conclusions. Functional pain scales, like the ABCs, may be useful adjuncts to evaluate pain. Individual functions, such as, "Out of Bed to Chair", may be of particular importance. Clinicians must be aware that the strongest predictor of MMEs taken by patients was MMEs prescribed, highlighting the importance of better pain assessments and opioid stewardship. ***Kans J Med 2022;15:82-85***

INTRODUCTION

In the United States, 48 million surgical inpatient procedures were performed in 2010.[1] Most, if not all, resulted in some form of pain. As the rate of surgical procedures grows annually, postsurgical pain and treatment are increasingly important and there is a need for evidence-based standards for pain management. This includes assessments of clinically relevant pain that can guide treatment to avoid undertreatment, as well as overtreatment, of pain. The latter is critical given the expanding use and availability of analgesics, especially opioids, and associated concerns about their overuse or abuse.

Current proven methods of assessment are lacking, with prior studies showing that clinicians frequently are frustrated by both poor pain assessment and lack of knowledge about pain.[2] There have been numerous efforts to develop better pain scales.[3,4] In addition to the commonly utilized 0 - 10 pain scale, assessments such as the pain visual analog scale (VAS), numeric rating 0 - 10 scale (NRS), and the Wong-Baker (FACES) scale have been studied. These scales are all linear and unidimensional. Their greatest utility is that they allow for quick assessment of pain intensity. However, their applications to clinical care are limited by a lack of medical context and functional data. Without functional indicators or other anchors, pain measurement is highly variable making the connection between pain assessment and prescription patterns unpredictable.[5]

In response to this need for a functionally relevant pain assessment, the Activity Based Checks of Pain - Functional Pain Scale (ABCs) was developed. The ABCs is a novel functional pain scale that links pain to functional activities deemed important in the recovery period. This prospective observational cohort study deployed ABCs in a perioperative setting with patients undergoing general surgical procedures, such as breast/epigastric flap surgeries, laparoscopic abdominal surgeries, lymph node dissections, and head and neck procedures, including thyroidectomies and parathyroidectomies. The primary objective was to compare the ABCs scale to the 0 - 10 NRS. The secondary objective compared the impact of patient and provider factors on medication usage and prescribing patterns.

METHODS

Overview. This study was a prospective, observational study comparing scores for the ABCs of Pain against those of the NRS pain scale. It was approved by the Institutional Review Board at the University of Kansas Medical Center.

Patient Cohort. This study was conducted in an urban, academic hospital. Patients between the ages of 18 and 80, who were scheduled to undergo thyroid/parathyroidectomies, local wide excisions, and other general abdominal surgical procedures, were considered for inclusion in this study. Exclusion criteria consisted of Eastern Cooperative Oncology Group (ECOG) performance status of ≥ 3 at baseline, known pain disorders or history of pain medication abuse, dementia or neurocognitive disorders, diagnosis of depression or anxiety, or if patients were unable or unwilling to provide accurate pill counts of outpatient pain medications used as required by study protocol.

Scale Formation. To establish face validity, a convenience sample of clinical faculty of the general surgery (n = 3), urologic surgery (n = 2), orthopedic surgery (n = 1), and otolaryngology departments (n = 4) assembled to determine post-operative priorities regarding functional recovery. Two authors developed the visual representation of the scale. It then was approved by the surgical faculty (Figure 1). The included functional activities increase in difficulty as the scale descends. Scoring is scaled to reflect the increased functional demands of each activity. Horizontally, a score is recorded for the pain experienced performing the corresponding functional activity, given that they are able to perform that activity. For the purposes of data analysis, the columns are assigned an ordinal number from 0 to 5. For example, "no pain" is scored a zero and "new worst pain" is scored a five. The "old worst pain" column was included to anchor each patient in a previous experience that, to this point, would qualify as the worst pain ever endured. The patient is asked if they need pain medication at that point in time. The patient's edition only includes the table with the images on the left. The colored arrows seen in Figure 1 are present only for clarity for the reader in the study.

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The original ABCs were modified for thyroid/parathyroid surgery to reflect the surgical site and includes functions such as neck movement. Of note, the ABCs scale is strictly experimental at this point in its production and is not used as a tool for guiding prescribing patterns or treatment.

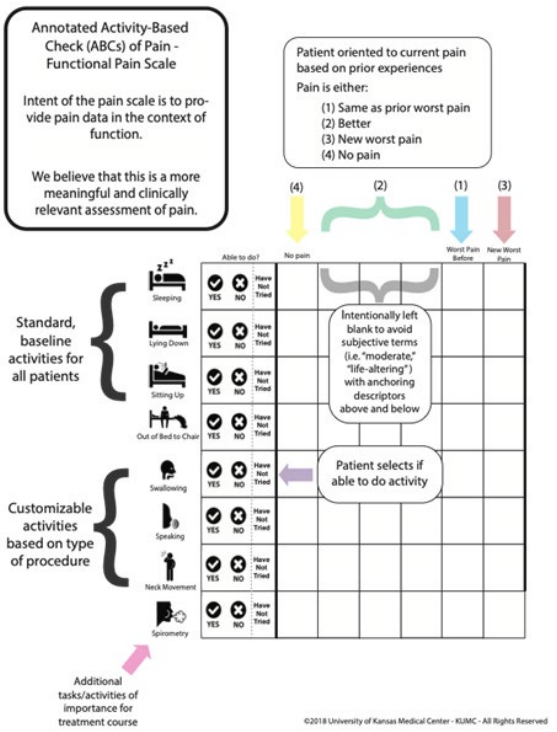

Figure 1. Annotated Activity-Based Check (ABCs) of Pain - Functional Pain Scale.

Enrollment Process. Eligible patients were identified through the pre-anesthesia clinic and enrolled at their pre-operative appointment. At this appointment, a team member would explain and review the ABCs and ensure that the subject was familiar with how to complete it properly. The SF-12 Health Questionnaire, the NRS Pain Scale, and the ABCs then were completed, which served as each patient's "baseline" reference values. The SF-12 was used as a standard marker of overall health while the NRS and ABCs were used to establish a pre-operative baseline to compare scores. Two summary scores are reported from the SF-12, a mental component score (MCS-12) and a physical component score (PCS-12). The United States population average PCS-12 and MCS-12 are both 50 points, with a standard deviation of 10. The SF-12 is intended to measure the impact that a patient's health plays on their everyday life.[6] Our team obtained one SF-12 score pre-operative for each participant. This helped to compare our cohorts baseline quality of life as a reflection of health in comparison to the population.

Hospital Stay. Enrolled patients were entered into the Research Electronic Data Capture (REDCap®) database and followed throughout their post-operative course. The ABCs and 0 - 10 pain levels were collected once daily until discharge. The once daily scales collected during hospitalization for each patient were condensed into single indexes for each activity except for the last scale collected prior to discharge, which served as the value "at discharge". The treating surgical team was blinded to ABCs data to avoid biasing treatment.

Post-Operative Appointment. Patients were scheduled for a post-operative follow-up visit per the treating surgeon's preference. This universally occurred within one to three weeks after discharge. The ABCs and 0 - 10 pain scale were administered and recorded as the "post-operative" value. The following information about pain medications was recorded: medication prescribed, number of pills prescribed, and number of pills taken.

Statistical Analyses. Data were analyzed using SPSS Version 26 (Armonk, NY). Descriptive statistics for scale variables were reported as medians (interquartile range). Spearman's Rho was used to assess correlation between scale variables. Group comparisons were performed using Mann-Whitney U tests. Significance was set at $p < 0.05$.

RESULTS

Forty patients were enrolled to completion in this study. During the period of data collection, there was an estimated 110 patients that met our inclusion criteria. This provided a 12% margin of error at a 95% confidence interval, thus demonstrating that the sample generally represents the population. The mean age was 52 years; 82.5% were white, non-Hispanic, and 47.5% were male (Table 1).

The ABCs demonstrated correlation to the NRS at baseline ($\rho = 0.687$, $p < 0.01$), prior to discharge ($\rho = 0.881$, $p < 0.01$), and at post-operative follow-up visit ($\rho = 0.312$, $p < 0.05$; Table 2). The function that correlated most to the NRS at discharge was "Out of Bed to Chair" ($\rho = 0.691$, $p < 0.01$; Table 3). The function that correlated most with MME prescribed was "Out of Bed to Chair" at discharge ($\rho = 0.471$, $p < 0.01$; Table 4). Post-operative opioid prescription usage was correlated significantly to the amount of MME prescribed ($\rho = 0.559$, $p < 0.01$). Post-operative MME taken correlated to their pain score on the NRS scale ($\rho = 0.344$, $p < 0.05$) and the ABCs ($\rho = 0.303$, $p > 0.05$; Table 5). The function that demonstrated significant correlation with the amount of MME taken was "Out of Bed to Chair" at discharge ($\rho = 0.485$, $p < 0.01$). Indicators of better mental health on SF-12 were correlated inversely with MME consumption ($\rho = -0.35$, $p < 0.05$; Table 6).

Table 1. General patient demographics.

Demographics	N = 40 (%)	Mean [SD]
Age		51.7 [16.4]
Short Form Survey (SF-12)		
Mental Component Score (MCS-12)		51.6 [8.5]
Physical Component Score (PCS-12]		45.5 [10.1]
Gender		
Male	19 (47.5)	
Female	21 (52.5)	
Ethnicity		
White	36 (90)	
Hispanic	2 (5)	
Asian American	1 (2.5)	
African American	1 (2.5)	
Procedure		
General Surgery	26 (65)	
Head & Neck	14 (35)	

Table 2. Correlation of numeric rating scale (NRS) to Activity-Based Checks (ABCs) at varying time points.

Correlation of NRS to ABCs at:	ρ (Rho)	p value
Baseline	0.687	$p < 0.01$
Discharge	0.881	$p < 0.01$
Post-operative	0.312	$p < 0.05$

Table 3. Correlation of numeric rating scale (NRS) to Activity-Based Checks (ABCs) functions at baseline.

Action	ρ (Rho)	p value	Cohort
Out of bed to chair	0.691	$p < 0.01$	
Lying down	0.64	$p < 0.01$	
Sleeping	0.556	$p < 0.01$	
Sitting up	0.521	$p < 0.01$	
Walking up stairs	0.534	$p < 0.01$	General Surgery only
Swallowing pain	0.622	$p < 0.05$	Head & Neck Surgery only

Table 4. Correlation of milligrams of morphine equivalents (MME) prescribed.

	ρ (Rho)	p value	Performed
Numeric Rating Scale (NRS)	0.412	$p < 0.01$	at discharge
Activity-Based Checks (ABCs)	0.401	$p < 0.05$	at discharge
Out of bed to chair	0.471	$p < 0.01$	at discharge
Lying down	0.369	$p < 0.05$	at discharge
Sleeping	0.375	$p < 0.05$	at discharge
Sitting up	0.310	$p > 0.05$	at discharge
Walking up stairs	0.359	$p > 0.05$	at discharge
Swallowing pain	-0.052	$p > 0.05$	at discharge

Table 5. Correlation of milligrams of morphine equivalents (MME) taken.

	ρ (Rho)	p value	Performed
MME prescribed	0.559	$p < 0.01$	
Numeric Rating Scale (NRS)	0.344	$p < 0.05$	at discharge
Activity-Based Checks (ABCs)	0.303	$p > 0.05$	at discharge
Out of bed to chair	0.485	$p < 0.01$	at discharge
Mental Component Score (MCS-12)	-0.35	$p < 0.05$	

Table 6. MME prescribed and taken by procedure type.

MME prescribed and taken	Mean [SD]
General Surgery	
MME prescribed	153.4 [83.6]
MME taken	87.9 [99.2]
Head & Neck	
MME prescribed	126.8 [61.6]
MME taken	21.4 [36.0]

DISCUSSION

This study investigated the efficacy of the Activity-Based Checks of Pain (ABCs) to assess peri-operative pain in comparison to the current standard of care using a 0 - 10 numeric rating scale (NRS). The impetus for this study was the lack of a "gold standard" for measuring the functional impacts of pain in a post-operative setting and the limited clinical utility of the current 0 - 10 NRS.[7] Based on the findings of this study, the ABCs pain scale was comparable to the current standard practice of peri-operative pain assessment using the NRS. The functions on the ABCs scale that demonstrated significant correlation with the amount of MME taken were "Out of Bed to Chair". Interestingly, the factor that was correlated most strongly with opioid MME taken was not pain, but quantity prescribed.

The 0 - 10 NRS gained popularity in the 2000s and has been collected as a vital sign for the past decade, although it was not validated as a screening tool. Unlike vital signs such as heart rate and blood pressure, there is little guidance regarding optimal treatment of pain levels that are outside of what is expected or desired. Correlation of opioids prescribed with pain at discharge varied based on clinical setting. For example, opioid MME prescriptions are correlated inversely with documented NRS pain scores in the emergency department setting.[5]

Using functional markers to assess acute pain helps the provider and patient personalize care towards the patients' goals. This will improve post-operative opioid decision making for pain management, while minimizing the harms that can be associated with opioid analgesics. Pilot testing of this novel, visual, and functional pain scale showed the potential utility a scale such as this could serve in the future.

Determinants of post-operative opioid usage are multifactorial. Our study is consistent with prior literature demonstrating that prescribing patterns drive consumption patterns.[5,8,9] For example, a large retrospective population-based study also found that the quantity of opioid prescribed is associated with higher patient-reported opioid consumption, with 77% of patients taking one-half or less of the prescribed pills.[8] Similarly, the strongest correlation with MMEs taken after discharge was MMEs prescribed. These data also agreed with our findings that over 40% of prescribed opioids goes unused (Table 6). This indicated that, even if patients can avoid overuse of prescribed opioids, an excess remains in circulation at risk for misuse or diversion. This is significant as 75% of those addicted to opioids report prescription drugs as their first opioid exposure.[10]

These data underscored that neither pain scale proved to be the main determinants of opioid analgesic usage, and the need for improved methods of pain assessment that can be incorporated meaningfully into clinical decision making. Ideally, such methodology would address systems barriers to pain assessment and management such as failure to adopt a standardized pain assessment tool beyond the NRS 0 - 10 or other numeric scale and lack of clinician time to document multi-dimensional aspects of pain. Attempts to address these issues have yielded pain scales that attempt to capture pain's impact on function and quality of life.[11,12] However, their rating system can be complex. For example, the Indiana Polyclinic Combined Pain Scale requires a specifically trained clinician to conduct the test.[11] Typically, patients must respond to written prompts on a Likert-scale,

which can be mentally taxing for the participant, especially if recovering from anesthesia or analgesics. These limitations restrict their use in an acute post-operative setting.

In contrast, the ABCs scale was designed to be highly visual in nature. Visual relay of information has been shown to decrease the cognitive effort required to both complete and interpret information.[11] The functions included in the ABCs also can be customized for different procedures and patient populations. Ultimately, the best way to assure that pain is addressed properly is by utilizing an interprofessional team that approaches pain assessment using a multidimensional approach, making the development of a function-based pain scale essential for a progressive step against the opioid epidemic.

LIMITATIONS

This was a pilot study with a relatively small sample size. The study population consisted mainly of patients in a tertiary academic center undergoing parathyroid/thyroidectomy procedures or lymph node dissections, and recovery was typically quick, uncomplicated, and without significant pain burden. However, patients routinely experienced measurable, post-operative pain that the team was able to track over time using the ABCs pain scale.

Despite recognizing that functional pain assessment is important, there are no clear guidelines regarding which functions to assess. Further discussion with physicians and patients will aid in finding specific functional milestones that patients desire to reach.

Although the goal of this study was not to ascertain patient perspectives on the ABCs, confusion for patients while recording their pain levels was noted. Since patients have become accustomed to quantifying their pain through the NRS scale over the last couple decades, it was difficult with some patients to grasp the concept of functional pain instead of numerical pain. It was not believed that this significantly biased the results because of the descriptive anchors provided at the two extremes of the scale.

Future Directions. Given that functional priorities may be individualized, future mixed-methods studies will investigate patient attitudes towards pain assessment, including the ABCs. We also will investigate the utility of the ABCs as a tool to facilitate communication about pain between patients and their care teams. As MMEs prescribed, and not pain levels, were highly correlated to MMEs taken after discharge, future studies will investigate educational interventions (or integrating pain scales into discharge analgesic prescribing decisions) on prescribing patterns.

Lastly, not only did amount of MMEs prescribed have a stronger correlation than the NRS and the ABCs scale with amount of MMEs taken, "Out of Bed to Chair" also had a stronger correlation. This further highlighted the novelty of this research into function-based pain scales. The ABCs scale, although visually appealing and more simple than previously proposed scales, might have potential to be simplified further as more research is done into which activities correlate best with different procedures further streamlining efforts to provide individualized care for patient's pain-control. Continued study into functional methods of pain quantification could prove to be beneficial considering the strong correlation "Out of Bed to Chair" measurement proved to be in relation to amount of MMEs taken.

CONCLUSIONS

The primary purpose of the study was to assess the correlation between a novel, visual, and functional pain scale compared to the current 0 - 10 numeric rating scale. The strongest predictor of MMEs taken by patients was MMEs prescribed. Knowing this should provide health professionals with great pause as we look to provide evidence-based, quality pain-control to each patient. Having more tools available, such as the ABCs pain scale, when making decisions for patients' post-operative pain management can provide more individualized care and aid physicians to practice proper opioid stewardship.

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Psychological State of Camp Counselors with Type 1 Diabetes who Have Attended Diabetes Camp

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ABSTRACT

Introduction. By 2050, more than 580,000 children in the United States will be diagnosed with type 1 diabetes (T1D). Management of T1D requires careful and continuous intervention, and children with T1D experience unique challenges in disease management compared to their adult counterparts. Diabetes camps are designed to help those with T1D learn diabetes management skills while experiencing summer camp. Psychological aspects are not addressed explicitly in diabetes camps located in Kansas. The purpose of this study was to evaluate the psychological state of past campers and camp counselors from one diabetes camp in Kansas.

Methods. Campers and counselors, all of whom had T1D, and attended diabetes camp from 2015 to 2019 in Kansas were recruited to complete a survey about diabetes-related stress, diabetes management self-efficacy, and symptoms of depression. A link to the online survey was distributed to previous campers and counselors by email and through Facebook.

Results. A total of 24 camp counselors and 10 campers were surveyed, 100% of whom reported having T1D and attending camp at least once. One-third of respondents (n = 8) reported having severe diabetes-related stress, and 100% (n = 34) reported high levels of diabetes management self-efficacy. Most participants reported moderate levels of depression, and 9% (n = 3) reported a past suicide attempt. These results suggested a relatively high prevalence in signs of psychological distress from former campers and camp counselors with T1D.

Conclusions. This study suggested that campers and counselors with T1D have high levels of diabetes-related stress, high diabetes management self-efficacy, and many signs of depression.

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INTRODUCTION

Every year in the United States, approximately 18,200 children are diagnosed with type 1 diabetes (T1D).[1] In 2018, 187,000 children had T1D, and by 2050, more than 580,000 children are expected to be diagnosed.[2,3] Annually, healthcare costs and lost income associated with T1D exceeds $16 billion.[4] Despite modern interventions and advances in medicine, there is a strong association between T1D and premature mortality, partially due to complications from poor blood glucose control.[5]

Management of T1D requires careful and continuous intervention, and children with T1D experience unique challenges in disease management than their adult counterparts. Constant changes in growth, puberty, and hormonal development are all factors unique to children that have major impacts on blood sugar control.[6] Additionally, counting carbohydrates, calculating insulin doses, and factoring in blood glucose corrections require math and logic too advanced for some children.[7] Accordingly, children often rely on their parents, caretakers, doctors, nurses, or school supervisors for help.[8] This can be problematic as many of these adults are not trained in proper T1D care, and changing between different caretakers can mean changes in the way a child's T1D is managed.

Adolescents and young adults with diabetes experience higher levels of stress from having a serious medical condition than their peers without diabetes.[9] This diabetes-related stress can occur as a result of multiple factors (e.g., the challenges of management, isolation, fear of adverse reactions) and can lead to poorer outcomes in diabetes management. This can manifest as increased levels of depression and anxiety when compared to their peers without diabetes, which can lead to suboptimal blood sugar control.[10]

Depression is a serious concern among those with T1D. Adolescents and young adults with T1D have a higher prevalence of both depression and anxiety, between 14% and 32%, which is almost double the prevalence of their adolescent counterparts without T1D.[11,12] Increased levels of depression are known to be related directly to poorer diabetes management, leading to higher HbA1c levels and a decreased frequency of blood glucose monitoring.[11]

Self-efficacy is a factor that can play a role in diabetes management. As a principle, self-efficacy encompasses one's belief in oneself to perform necessary tasks to attain a goal. Adolescents and young adults with T1D are in a transition period of gaining more freedom and having less help from parents or caregivers in their diabetes management. This can correlate with changes in self-efficacy.[13] Self-efficacy levels impact young adults' management strategies and their blood glucose control overall, as well as playing a role in mediating the stress levels associated with T1D.[14] All of these factors have a role in a young adult's ability to maintain good diabetes control in order to minimize diabetic complications.

Diabetes camps are designed to help those with T1D experience traditional summer camp, learn diabetes management techniques, and meet others with diabetes.[15] Camps are effective in helping children better manage their T1D. One study suggested that mean HbA1c levels decreased from 10.0 before camp to 8.2 after camp.[16] For this reason, participating in diabetes camp can play an important role for children with T1D. By 2011, more than 30,000 people had attended a diabetes camp in North America.[17] However, there is limited research regarding the psychological state of campers and camp counselors who have T1D and attended diabetes camp, including diabetes-related stress, diabetes management self-efficacy, and symptoms of depression. The purpose of this study was to assess former campers and camp counselors with T1D regarding diabetes-related stress, diabetes management self-efficacy, and signs of depression.

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METHODS

Participants. Eligible participants attended at least one, week-long diabetes camp in Kansas, Camp Discovery, as a camper or camp counselor anytime from 2015 to 2019. Camp Discovery hosts approximately 100 kids with T1D in 4th through 10th grades each summer at Rock Springs 4-H Center in northeast Kansas. All eligible participants had a diagnosis of T1D. Parents of children campers were emailed links for their children to complete, and previous camp counselors were emailed directly. Participants were asked to complete a survey, and if needed, the child's parent/guardian could assist them in completing the survey. No incentive was provided to study participants.

Instrument. A novel survey was developed for this study and included demographics (e.g., age, gender), self-reported health-related variables (e.g., HbA1c levels, duration of disease), and diabetes management strategies (e.g., type of insulin therapy, glucose monitoring). In this study, a HbA1c level of less than or equal to 7 was used as "normal," whereas greater than 7 was considered elevated or "poor control," as established by the American Diabetes Association (ADA) criteria for adolescents with T1D.[18] In addition, standardized assessments were used to measure diabetes-related stress, diabetes management self-efficacy, and signs of depression.

The Problem Areas in Diabetes (PAID) scale was used to measure diabetes-related stress.[19] A total score of 40 or greater indicated high stress levels from diabetes. The Self-Efficacy for Diabetes (SED) scale was used to assess for self-efficacy in: diabetes management (SED-D), medicine (SED-M), and general self-efficacy (SED-G).[20] Respondents' scores for each category were added for a total score. Maximum scores on SED-D, SED-M, and SED-G are 120, 25, and 30, respectively. Scores of 40% or greater of the maximum per category indicated increased self-efficacy in that scale. The Patient Health Questionnaire-9 Modified (PHQ-9M) was used to assess for signs of depression. PHQ-9M scores of 10 or greater had high sensitivity and specificity for major depressive disorder.[21]

Procedures. This project was approved by the Institutional Review Board at the University of Kansas Medical Center. Eligible participants were identified through three channels. On June 23, 2020, the Director of Youth and Family Initiatives for the Central Territory of the American Diabetes Association, which hosted the camp, e-mailed the online survey link to former campers' parents from the summers of 2018 and 2019. The ADA sent a second e-mail on July 5, 2020 to campers' parents from 2015 through 2019. On July 2, 2020, a research team member e-mailed the survey link to former camp counselors from the summers of 2015 through 2019 (the list of which was provided by ADA), and the camp's private Facebook page displayed a request for former campers or counselors to complete the survey.

Surveys were electronically administered in Research Electronic Data Capture (REDCap®).[22] Depending on the age of the potential participant, the survey was accompanied by parent/guardian consent and child assent forms, or just an adult consent form. These forms described that the survey was voluntary and parental assistance was allowed, and potentially complex terms were defined, especially for those younger than 18 years. Participants were given two weeks to complete the survey once open.

Statistical Analysis. SAS 9.4 (SAS/STAT Inst., Cary NC) was used for data analysis. The socio-demographic characteristics were summarized using descriptive statistics. Means and standard deviations, or medians and interquartile ranges, were reported for continuous variables; counts and percentages were reported for categorical variables. Likelihood ratio chi-square and Fisher's exact tests were used for 2*2 and r*c contingency tables to test the association between the categorical and nominal variables. Phi coefficient was used to quantify the strength of association between categorical variables. Further, the Cochran-Mantel-Haenszel test was used to reveal associations between categorical/nominal variables after controlling for the strata variables in a multiway table. Prior to the analyses, continuous outcomes were tested for normal distribution using the Shapiro-Wilk test. For normally distributed variables, an independent t-test with Welch corrected t-test was used to compare the mean difference between groups. In the case of non-normal distribution with appropriate transformation operations on the response variables in group lists, Mann-Whitney U test was conducted to test differences between groups. The test results of Mann-Whitney U were justified with the Savage Two-Sample Test. All statistical tests at $p \leq 0.05$ were considered significant.

RESULTS

A total of 34 surveys were completed. Most respondents (79%, n = 27) reported being female, and 71% (n = 24) reported having been a camp counselor (Table 1). Ages of respondents ranged from 13 to 48 years, with an average of 31 years. The reported average time since their diabetes diagnosis was 23 years (SD = 11). Their mean (self-reported) current HbA1c level was 7.25 (SD = 0.96), with 55% (18) reporting a HbA1c of greater than 7.0. Most (82%, n = 28) respondents reported using a continuous glucose monitor, and 18% (n = 6) reported using a traditional glucose meter. Most participants (79%, n = 27) reported they were more likely to have an insulin pump for infusion therapy, and 21% (n = 7) reported using multiple daily injections.

Among the 34 respondents, 91% (n = 31) self-reported feeling that they had their diabetes "under control". However, 55% (n = 18) of all respondents reported HbA1c levels greater than 7.0. PAID scores ranged from 19 to 87, with an average of 39.8 (SD = 17.8). One third (33%, n = 8) reported severe diabetes-related stress. Respondents' SED-D scores ranged from 76 to 120, with an average score of 109 (SD = 10). SED-M scores ranged from 15 to 25, with a mean score of 23 (SD = 3). SED-G scores ranged from 10 to 30, with a mean of 26 (SD = 5). Overall, 100% (n = 34) reported high levels of self-efficacy in every category: SED-D, SED-M, SED-G. The PHQ-9M scores ranged from 9 to 35, and the mean score was 15 (SD = 6.2). In total, 95% (n = 21) of participants completing the PHQ-9M had scores of 10 or greater, indicating a high risk of major depressive disorder. Three respondents (8.8%) indicated a history of suicide attempts. Amongst these three, two had high HbA1c levels (greater than 7.0), and all three had PHQ-9M scores that indicated risk of depression. Two of the three had been counselors at the camp. Regardless of age, gender, counselor

status, or years of attending diabetes camp, these results for HbA1c, PAID score, SED score, and PHQ-9M were not different.

Table 1. Participant characteristics.

	Percent	Total
Gender		
Female	79%	27
Male	21%	7
Age in years		
13 to 18	6%	2
19 to 25	27%	9
26 to 35	38%	13
> 35	29%	10
Years with diabetes		
< 10	9%	3
10 to 15	9%	3
16 to 25	41%	14
> 25	41%	14
Years of camp attendance		
1 to 5	29%	10
6 to 10	35%	12
11 to 15	18%	6
> 15	18%	6
Participation status		
Previous camp counselor	71%	24
Previous camper only	29%	10
Insulin therapy		
Insulin pump	79%	27
Injections	21%	7
Blood glucose monitoring		
Continuous glucose monitor	82%	28
Glucometer	18%	6
HbA1c		
< 7.0	38%	13
7.0 to 7.9	35%	12
8.0 to 8.9	21%	7
> 8.9	6%	2

DISCUSSION

The current study suggested poor diabetes control, regardless of age, among more than half of respondents with T1D (n = 18). This was consistent with past research on people with T1D, although not studied on past diabetes camp attendants.[23] Approximately 25% of young adults (18 to 25 years) with T1D and 50% of those older than 25 years with T1D have a HbA1c of less than 7.0 for optimal diabetes control.[24] The current study's average age was 31 years, and typically there is an increase in HbA1c levels after adolescence, which potentially is attributed to less help from parents or caretakers than when they were younger.[13,25]

The current study suggested that the number of years attending diabetes camp was unrelated to depression, stress, and self-efficacy levels among those with T1D. Few studies have discussed these outcomes specifically; nonetheless, of the available literature, these findings were concerning, especially because diabetes camps can build self-efficacy through educational activities.[15,26] Through our results of poor diabetes control, yet high levels of self-efficacy, we also saw this inconsistency. This may be due to a variety of factors including, but not limited to, a misunderstanding of diabetes control, limitation of resources, or even extenuating circumstances not elicited in this study. Additionally, previous studies have associated lower stress levels with camp, as participants demonstrate improved attitudes toward their chronic disease due to friendships made at camp.[27,28] Therefore, attending camp more often should help to improve stress levels, which may be inconsistent with our study results. This finding was surprising given the past research of diabetes camps and their effects on participants; however, with little historical data on camp counselors, this could be one reason why we see different results among our study participants specifically.

The current study suggested that children and young adults with T1D who have attended or worked at a diabetes camp reported high levels of diabetes-related stress, which was consistent with research on adults with T1D who have not attended camp.[24] As diabetes camp should improve diabetes-related stress levels, this may suggest an inconsistency; however, many other factors contributed to one's diabetes-related stress levels.[28] Research in this field is important as diabetes-specific stress and depression were associated with higher HbA1c levels and poor self-management strategies.[9,29] Our study suggested that one-third (33%, n = 8) of respondents scored high enough to indicate severe diabetes distress. This was in line with another study that suggested that 36% of participants with T1D who had not attended camp scored in the high diabetes stress range on PAID,[30] whereas another study suggested that 14% of those with T1D scored high enough to indicate diabetes-related stress.[31] In one study of Korean children with T1D from a diabetes camp consistently reported high stress and depression levels.[32] These inconsistencies in the literature lead to a need for further studies evaluating the diabetes-related stress levels among this vulnerable population.

All study respondents reported high scores of self-efficacies across all three categories of the SED scale. As our study did not include young children, this was consistent with previous research stating self-efficacy improves during adolescence.[33] This is thought to be due to an increase in autonomy during adolescence when patients become more responsible for their diabetes care. Additionally, one study documented improvements in self-efficacy after attending a diabetes camp; this was likely a factor associated with the high levels of diabetes self-efficacy reported amongst respondents.[26] In the study of Korean children from a T1D camp, participants consistently reported low levels of T1D self-efficacy which further suggested that younger age groups may have lower levels of self-efficacy in their diabetes management.[32]

The current study suggested that 9% had previously attempted suicide, and all participants reported some level of depression.

This was consistent with research that young adults with T1D are at higher risk for depression and suicide when compared to their same-age counterpart without diabetes.[34] This unique population is known to be at high risk for psychological problems. In fact, a meta-analysis suggested that suicide is an increased cause of mortality amongst those with T1D, with approximately 16% having a previous suicide attempt.[35] This is much greater than adolescent populations without diabetes, where approximately 9% have attempted suicide.[36] With such elevated prevalence of depression and suicide, research with this high-risk population is warranted, especially to identify how to best support these young adults in coping with their chronic disease.

Future Research. Further research is needed to understand the impact diabetes camp has on people with T1D. The current study has been a preliminary look into the psychological traits of both campers and camp counselors alike. Many factors must be considered when evaluating the psychological state of adolescents and young adults. Diabetes camp may be one factor that could be associated with varying levels of stress, depression, and self-efficacy. However, socioeconomic status, race, and family dynamics have a large and consistent impact on mental health and need to be considered in further studies.[37,38]

A pre- and post-camp study could provide insight as to the impact of such a camp on diabetes-related stress, management self-efficacy, and signs of depression. A prospective study comparing a diabetes camp control group to a group that offers a psychological counselor at camp could provide new information to the field of psychology and diabetes camps. By evaluating the effect of psychological support at diabetes camp, we may uncover if the psychological state of campers and camp counselors truly is affected by the activities of diabetes camp.

Due to the high amount of stress, depression, and suicidal attempts among this small sample size, it warrants further investigation into how we can serve this vulnerable population. This gives a steppingstone to improve the psychological supports offered to improve the lives of those with T1D. Diabetes camp is just one part of a larger life for people with T1D but offering some type of psychological support at camp may be one way to increase quality of life for these individuals.

Limitations. There were multiple limitations to the study. First, this was a small study including 34 respondents with T1D. Due to the barrier of parents needing to act as a liaison between our survey and their children, the average age of participants was high, as most participants were of age to access the survey themselves. Future work must include larger sample sizes to illustrate more accurately the uniqueness of this group. Additionally, this study was cross-sectional, which only allowed for a baseline look at this population. In the future, studies with a longitudinal design may enumerate relationships between variables better, such as HbA1c and depression. Moreover, due to the nature of self-reported data, the current study may suffer from both recall and non-response bias.

The SED scale for measuring self-efficacy, especially among people with T1D, has been controversial. Although it is used widely, it does not have sufficient data to prove its reliability; in fact, there was limited support for its validity.[20] Future research would benefit from a more reliable scale to measure self-efficacy among persons with diabetes.

This research was conducted during the COVID-19 pandemic, and psychological states may not have reflected accurately non-pandemic psychological states. However, due to the lack of research on this population, we proceeded with this study. Of particular note, no research with T1D camp counselors has been conducted prior to this study, and there appeared to be a clear need to provide support and interventions to camp counselors with T1D in addition to the campers.

CONCLUSIONS

Campers and counselors with T1D have high levels of diabetes-related stress, high diabetes management self-efficacy, and many signs of depression. Future research must evaluate the psychological distress experienced by people with T1D further, and how interventions are needed to decrease diabetes-related stress, improve diabetes management self-efficacy, and prevent and treat depression.

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Keywords: diabetes mellitus, camping, self-efficacy, psychological stress, depression

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Assessing Provider Utilization of COVID-19 Inflammatory Marker Trends in Hospitalized Patients and Implications in Optimizing Value-Based Care During a Pandemic

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ABSTRACT

Introduction. Numerous inflammatory markers may serve a role in prognostication of patients hospitalized with COVID-19 infection. Early in the pandemic, our health system created an admission order set which included daily d-dimer, c-reactive protein (CRP), lactate dehydrogenase (LDH), and ferritin. Given more available outcomes data, limiting standing order of labs that do not affect daily management could result in significant cost savings to the health system without adverse patient outcomes. The purpose of this study was to determine ordering and utilization patterns of inflammatory markers by physicians caring for patients hospitalized with COVID-19 infection.

Methods. An anonymous 10-question survey was distributed to 125 physicians (Infectious Disease, Hospitalist, Pulmonary and Critical Care faculty). Responses were tallied and values greater than 50% were identified as the majority of the surveyed group.

Results. Of the 125 physicians surveyed, 77 (62%) responded. A total of 57.1% (44/77) of physicians reported ordering daily inflammatory markers for 3 - 10 days from admission. Another 31.2% (24/77) ordered markers until clinical improvement or hospital discharge. D-dimer was used for care decisions by 83.1% (64/77) of respondents; 93.8% (60/64) of those reported utilizing it in determining anticoagulation dose. CRP was used by 61% (47/77) of physicians to help identify a secondary infection or determine steroid dose or duration. LDH and ferritin were not used for management decisions by the majority of physicians. Inflammatory markers were not used routinely after isolation precautions had been discontinued, even when ongoing care required mechanical ventilation.

Conclusions. Of the markers studied, both d-dimer and CRP were considered useful by most respondents. LDH and ferritin were used less frequently and were not considered as useful in guiding medical decision making. Discontinuation of standing daily LDH and ferritin orders is believed to have potential to result in cost savings to the health care system with no adverse patient outcomes.

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INTRODUCTION

In December 2019, a novel coronavirus was described in Wuhan, China and quickly spread throughout the world. By the end of January 2020, the World Health Organization declared the outbreak a Public Health Emergency of International Concern.[1] According to the Johns Hopkins Coronavirus Resource Center, there have been a total 397 million cases worldwide, including 5.75 million deaths as of February 8, 2022.[2] Early in the pandemic, risk factors for progression to severe disease were identified by analyzing trends in hospitalized patients including age, hypertension, diabetes, body mass index (BMI), and race. In addition, elevations in numerous inflammatory markers were found to be risk factors for disease severity.[3] Laboratory markers associated with critical illness included lymphocytopenia, thrombocytopenia, elevated c-reactive protein (CRP), elevated transaminases, decreased creatinine clearance, elevated ferritin, elevated lactate dehydrogenase (LDH), elevated serum amyloid A, and elevated d-dimer.[4,5]

Using a retrospective cohort analysis published in September 2020, researchers at Johns Hopkins developed a COVID-19 Inpatient Risk Calculator.[3] When laboratory results and patient data are applied to the calculator, death and progression to severe disease can be predicted. Two predominant risk factors have direct implications in therapy, d-dimer and a requirement for supplemental oxygen. The RECOVERY Trial demonstrated improved 28-day mortality when administering dexamethasone to COVID-19 patients requiring supplemental oxygen compared to placebo.[6] Patients with elevated d-dimer plus a sepsis-induced coagulopathy score ≥ 4 have improved 28-day mortality when given low molecular weight heparin versus no heparin product.[7] In a randomized, controlled, open-label trial, the RECOVERY Collaborative Group identified tocilizumab as having improved 28-day mortality in patients with hypoxia and CRP > 7.5 mg/dL.[8] Clear evidence regarding the roles of ferritin and LDH in guiding COVID-19 therapy were not available.

At The University of Kansas Health System (TUKHS; Kansas City, KS), CRP, ferritin, LDH, and d-dimer were added to the inaugural COVID-19 admission order set as inflammatory markers of interest based on information related to clinical outcomes in patients with COVID-19 available at the time. This order set was designed specifically for admitting patients with SARS-CoV-2 positive polymerase chain reaction (PCR) to guide initial monitoring and management. The order set included options for daily monitoring of CRP, ferritin, LDH, and d-dimer but had no expiration date based on clinical status (indefinite until death or hospital discharge). If a physician felt there was no longer need for inflammatory marker trending, they would have to discontinue the orders manually. TUKHS operates with a closed ICU model where intensivists act as the primary physician for patients meeting ICU admission criteria. Hospitalists acted as the primary physician for most general internal medicine COVID-19 patients admitted to telemetry and general medicine wards. Consultation with Infectious Diseases or Pulmonary services was at the discretion of the primary

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service and not a requirement. While there are implications for patient management with d-dimer results, the roles of the other markers, outside of risk stratification, are less clear.

From March 1, 2020 to February 6, 2021, TUKHS admitted 2,369 patients with COVID-19 with an average length of stay of 7.7 days resulting in a total of 18,241 patient days. The cost for reagent and labor on average per test for d-dimer, CRP, LDH, and ferritin is $7.55 at our institution. This represented approximately $551,000 spent on inflammatory markers for COVID-19 patients since the beginning of the pandemic at TUKHS.

The study aim was to use survey responses from physicians most frequently assigned to care for patients with COVID-19 to determine if daily trends in d-dimer, LDH, ferritin, and CRP guided daily management in patients hospitalized with COVID-19. Of particular interest were steroid duration and dose, level of anticoagulation (therapeutic versus prophylactic), and workup of potential secondary infection. Secondarily, we aimed to see if "recovered" status as determined by Infection Prevention and Control (IPAC) professionals altered the perceived frequency of COVID-19 inflammatory marker ordering. Finally, we sought to determine if there were potential laboratory cost savings to be obtained by comparing the self-reported ordering patterns of the tests in question to the self-perceived utility of these tests in patient care.

METHODS

An anonymous and voluntary 10 question yes/no/open-ended response survey utilizing SurveyMonkey®, an online survey development cloud-based software, was distributed to faculty within infectious diseases, intensive care, and hospital medicine who practiced at TUKHS in December 2020 (Figure 1). This staff was selected given they provided the majority of daily care to patients admitted with COVID-19 infection. The survey was closed after one month. The results of the survey were tabulated for each question. An open-ended response that qualified for multiple preselected categories was split accordingly. For example, for a respondent who used c-reactive protein for both steroid dosing and workup of a secondary infection, 0.5 votes were added to each category. In the case that an open response qualified for three categories, 0.33 votes were added to each category. Votes then were converted to percentages of all respondents. For purposes of evaluation of responses, options selected by greater than 50% of the surveyed population were considered to represent the majority of the respondents. This quality improvement project was approved by the University of Kansas Medical Center Human Subjects Committee prior to the distribution of the survey. The nature of the study and associated survey was exploratory. Patients were not involved directly in this study.

RESULTS

Of the 125 physicians surveyed, 14 were Infectious Disease faculty, 28 were Intensivists/Pulmonary consultants, and 83 were Hospitalists. Of those invited to participate, 62% (77/125) completed the survey (Table 1). The faculty responding were not required to document which division they represented. Most physicians checked inflammatory markers for at least three to five days of hospitalization; 30% (23/77) checked for 6 - 10 days and 18% (14/77) monitored until discharge (Figure 2). In total, 57.1% (44/77) of respondents obtained inflammatory markers daily (Figure 3).

How often do you check COVID-19 inflammatory markers?	
How many days do you check COVID-19 inflammatory markers?	
Do you check COVID-19 Inflammatory markers on "recovered" patients who are actively requiring mechanical ventilation?	
Do you check COVID-19 Inflammatory markers on "recovered" patients who are actively requiring Heated High Flow Nasal Canula?	
Do you check COVID-19 inflammatory markers on "recovered" patients who are requiring supplemental oxygen via traditional nasal canula?	
Do you use d-dimer to change management of	
	Steroid duration or dose
	Anticoagulation
	Workup of secondary infection
	Other (please explain)
Do you use ferritin to change management of	
	Steroid duration or dose
	Anticoagulation
	Workup of secondary infection
	Other (please explain)
Do you use c-reactive protein to change management of	
	Steroid duration or dose
	Anticoagulation
	Workup of secondary infection
	Other (please explain)
Do you use LDH to change management of	
	Steroid duration or dose
	Anticoagulation
	Workup of secondary infection
	Other (please explain)
Do you think that removing the check-boxes for standing COVID-19 inflammatory markers (essentially requiring a provider to place the order on an as needed basis) will negatively impact patient care?	
The survey was distributed via an email link to 125 physicians who actively participated in the care of patients infected with COVID-19. Preceding the survey was a short disclaimer. "The following is a 10 question multiple choice survey. Please assume that all questions are regarding patients who have a positive COVID-19 PCR and symptoms on admission unless explicitly stating otherwise. COVID-19 inflammatory markers include d-dimer, ferritin, lactate dehydrogenase (LDH), and c-reactive protein (CRP). "Recovered" is the designation that Infection Prevention and Control gives to patients who no longer need isolation."	

Figure 1. COVID-19 Inflammatory Marker Usage Survey.

Table 1. Survey demographics.

Faculty division	Number of physicians
Infectious Disease faculty	14
Critical Care faculty	28
Hospitalist	83
Total	**125**
Surveys completed	**77**
% Surveys completed	**62**

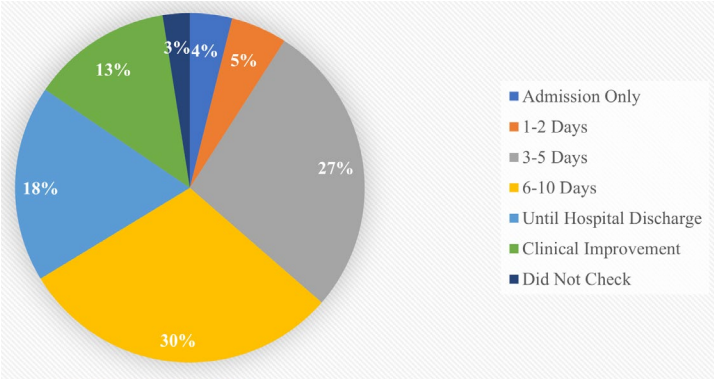

Figure 2. Duration of COVID-19 Inflammatory marker monitoring.

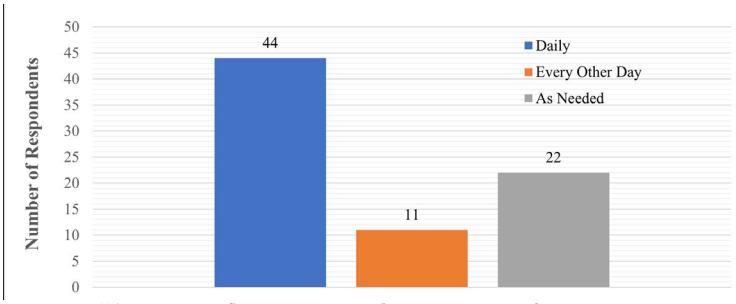

Figure 3. COVID-19 inflammatory marker monitoring frequency.

D-dimer was utilized by 83.1% (64/77) of respondents for medical management decisions. Of the 83%, 93.8% (60/64) used d-dimer to determine dose of anticoagulation. Ferritin was not used regularly by 49.4% (38/77) respondents and used only for trending purposes in 2.6% (2/77). Of the remaining 46.8% (36/77) of providers who answered, 62% (22.33/36) used the ferritin level to determine steroid duration or dose and 31.5% (11.33/36) utilized ferritin in the workup of a secondary infection, respectively. Most providers (61%; 47/77) used CRP to make medical decisions, with 57.1% (26.83/47) of respondents using CRP to determine steroid duration or dose and 35.8% (16.83/47) reporting use in the workup of a secondary infection. Most physicians (59.7%; 46/77) did not use LDH to guide any therapy. One respondent deferred to answer how each inflammatory marker was utilized (Table 2).

Of the 77 survey respondents, 32 reported managing mechanically ventilated patients as part of their practice. Of those 32, 56.3% (18/32) did not check the aforementioned COVID-19 inflammatory markers in patients requiring mechanical ventilation and determined to be "recovering" by IPAC. Of the respondents managing patients requiring heated high flow nasal canula (53/77), 56.6% (30/53) reported checking inflammatory markers. In addition, 61% (47/77) of all respondents did not check inflammatory markers on "recovered" patients requiring supplemental oxygen by nasal cannula (Table 3).

When asked if changing the current COVID-19 admission order set would affect patient care negatively, 62.3% (48/77) reported that it would not, while 37.7% (29/77) felt that it was possible or that they were unsure. The concern that inadequate dosing of anticoagulation would be a result of not obtaining d-dimer leading to increased thromboembolic events was reported most frequently.

DISCUSSION

The COVID-19 pandemic has presented numerous challenges related to diagnostic testing, therapeutic development and implementation, vaccine development, and management of complications, amongst other issues. Through worldwide efforts, these processes have been expedited and improved in all areas. There is still a significant burden on hospital systems to manage hospitalized patients with severe symptoms from COVID-19. The abundance of case series, retrospective analyses, and prospective studies have helped to identify markers of inflammation and their association with prognosis.[3-5] A meta-analysis regarding the association of inflammatory markers in COVID-19 could not conclude that ferritin was correlated with severe disease.[9] While there is evidence supporting use of d-dimer to guide anticoagulation and CRP for tocilizumab administration, there is a limited role outside of prognostication for other markers.[8] Our survey suggested that most providers at our institution measure inflammatory markers on a daily basis for at least three to five days, with many checking for six to ten days or until discharge. Additionally, the survey suggested that physicians used inflammatory markers for trending inflammation, steroid dosing or duration, anticoagulation dosing, and workup of a secondary infection. In other responses, they were not being used at all. For respondents who felt there was a need to monitor multiple inflammatory markers, there was not a specific question to inquire about why they believed this practice was beneficial.

Most providers checked inflammatory markers daily for at least three to five days. This supported the practice of using the institution's COVID-19 admission order set via the electronic medical record, particularly given that most respondents (93.8%; 60/64) used d-dimer to assist in dosing of anticoagulation. Our institution adopted an algorithm that included d-dimer levels among other factors to determine anticoagulation dosage based on the published literature at the time.[7] Prior analysis showed that up to 25% of patients with COVID-19 requiring intensive care unit (ICU) level of care were diagnosed with venous thromboembolism (VTE).[10] Sequential autopsies on 26 COVID-19 patients performed at Mount Sinai Health System revealed that 42% of patients had either pulmonary embolism or VTE without clinical suspicion prior to their deaths. In addition, four of the 26 who had autopsies performed required therapeutic anticoagulation prior to admission for another condition. Although none of the patients previously on therapeutic anticoagulation had VTE on autopsy, there was evidence of microthrombi in two of the four.[11] Given the evidence supporting d-dimer's utility in anticoagulation dosing and mortality benefit with prophylactic anticoagulation, one could argue against checking d-dimer in the population who required therapeutic anticoagulation prior to admission. Our results suggested that physicians find utility in frequent monitoring of d-dimer. Although there is significant evidence of VTE being problematic in COVID-19, the exact role of d-dimer testing frequency as it relates to VTE and patient outcomes is unclear.

The majority of respondents utilized CRP in clinical care to either aid in steroid dose or duration or workup a secondary infection. A decrease in the CRP was thought to be the best marker of improvement by some of the providers surveyed. In a review of over 4,000 patients, only 3.6% had a secondary bacterial or fungal infection.[12] Over 71% of the entire cohort received broad spectrum antibiotics and 65% were admitted to the ICU. On average, a secondary bacterial or fungal infection was correlated with a maximum CRP of greater than 20 mg/dL. Interestingly, 95% of the respiratory coinfections occurred in intubated patients and only 6% had a positive bacterial culture prior to or on the same day of a positive SARS-CoV-2 PCR, suggesting a potential nosocomial source. Thus, while CRP use was not as frequent as d-dimer use, targeted use when a secondary infection is suspected may be useful. Whether this requires daily monitoring is less clear.

There is not compelling evidence in the literature regarding the use of CRP to guide corticosteroid therapy. The *CoDEX* clinical trial

Table 2. Physician utilizations of various COVID-19 inflammatory markers.*

	Method of utilization	Physician response (%)	Steroid dose/ duration (%)	Anticoagulation (%)	Secondary infection (%)
d-dimer	Change in management	83.1	0.0	93.8	6.3
	Trending inflammation	1.3			
	Not using	14.3			
	No response	1.3			
Ferritin	Change in management	46.8	62.0	6.5	31.5
	Trending inflammation	2.6			
	Not using	49.4			
	No response	1.3			
CRP**	Change in management	61.0	57.1	7.1	35.8
	Trending inflammation	3.9			
	Not using	33.8			
	No response	1.3			
LDH***	Change in management	39.0	50.0	13.3	36.7
	Trending inflammation	0.0			
	Not using	59.7			
	No response	1.3			

*Depicting the method of utilization for d-dimer, ferritin, CRP, and LDH as a percentage of the total number of physicians surveyed. Change in management was split further into steroid dosing/duration, dosing of anticoagulation, and workup of a secondary infection. This is a percent of the group who utilized the lab value for change in management only.
**CRP = c-reactive protein.
***LDH = lactate dehydrogenase.

Table 3. Obtaining inflammatory markers in "recovered" COVID-19 patients.*

Level of support	Obtaining markers		Response (%)
Mechanical ventilation	Yes	14	43.8
	No	18	56.3
	N/A	45	
Heated high flow nasal canula	Yes	30	56.6
	No	23	43.4
	N/A	24	
Nasal canula	Yes	30	39.0
	No	47	61.0
	N/A	0	

*"Recovered" is designated to patients with a prior positive SARS-CoV-2 Polymerase Chain Reaction assay who no longer require isolation. Selections under N/A represent that a provider does not manage patient requiring that level of support. The percent response does not include the N/A group.

evaluated ARDS dosed dexamethasone (20 mg for five days followed by 10 mg for five days) against routine care (no steroid).[13] The study was terminated early for ethical reasons after findings of RECOVERY were published. A metanalysis of seven trials did not show evidence that higher dose corticosteroid improved mortality over a lower dose in critically ill patients.[14] None of these studies, however, provided any evidence regarding guiding corticosteroid therapy by CRP as was reported to be done frequently by our surveyed physicians.

There was no consensus in how LDH or ferritin was utilized among the physicians surveyed in our study. Though ferritin level on admission is helpful in determining severity of disease, there is no evidence to suggest utility of serial monitoring to guide therapeutic decision making.[3,9] The split in responses may be a reflection of the lack of literature, suggesting its use as a general marker of inflammation.[9]

Similar to ferritin, the literature was lacking in regard to the role of LDH outside of prognostication on initial presentation. Most providers did not feel that measuring LDH was beneficial to patient care.

The institution's IPAC group designated patients who no longer require isolation as "recovering". At TUKHS, this "recovered" status is defined for immunocompetent patients as 10 days from a positive test result. Most physicians did not order inflammatory markers on "recovering" patients requiring supplemental oxygen via nasal cannula or even mechanical ventilation. A third survey question was presented considering heated high flow nasal cannula (HHFNC). The data were disregarded as institutional policy was changed two weeks after the survey had been distributed. Prior to distribution, HHNFC required ICU status. The change allowed floor patients meeting certain criteria to use HHFNC. Majority of providers checked inflammatory markers on these patients. This may reflect a level of comfort with the clinical status of the patient or some confusion regarding the differences in HHFNC and high flow nasal cannula, which was previously available for floor status patients. Most survey respondents valued the inflammatory markers in the first 10 days of hospitalization.

Based on the results of the survey and the current available evidence, it may be reasonable to implement three changes to the current standard of practice at our institution. It is practical to obtain ferritin and LDH on admission for prognostication purposes, but frequent monitoring is of unclear importance and does not have a significant effect on patient management. Second, discontinuation of d-dimer monitoring on patients requiring therapeutic anticoagulation prior to admission for an underlying condition such as atrial fibrillation, deep vein thrombosis, pulmonary embolism, mechanical heart valve, or left ventricular assist device. Finally, a limitation for daily orders for CRP and d-dimer to 10 days via the order set with an alternative selection to monitor less frequently could be considered. Inflammatory markers orders outside of these parameters would not be restricted but would require the provider to order the marker as a stand-alone test when it is felt to be necessary.

By eliminating both LDH and ferritin from the standardized order set, our hospital system could save over $15 per patient day. This represents $10,570 savings to our health system during an average week based upon a COVID-19 inpatient census of around 100 if admitting physicians do not extend LDH and ferritin outside of the order set.

A strength of this study was the collection of data from the first year of the pandemic including 2,369 patients at a large tertiary care center in the Midwest, in addition to physician feedback and financial analysis that were used to modify the existing algorithm for our healthcare system. This information was timely, when no available guidance for physicians regarding utility of these inflammatory markers in the management in COVID-19.

The primary limitations to this study were the relatively small sample size and response rate. Only 125 physicians were surveyed (focusing on physicians who cared for the majority of admitted COVID-19 patients) and of that group only 77 completed the survey. As a result, there was increased risk for selection bias from practitioners who cared for fewer COVID-19 patients overall. Two of the groups of surveyed physicians were also specialists in the fields of Infectious Diseases and Pulmonary and Critical Care medicine and may have been more aware of research in the area of COVID-19 related diagnostic and prognostic markers. Furthermore, this was a single institution which limited practice variability given a single electronic medical record, a single supervisory COVID-19 management taskforce, and single specialist group of Infectious Diseases and Pulmonary and Critical Care consultants. Surveying multiple institutions and limiting the surveys to providers immediately after completing a service block managing COVID-19 patients may limit some bias, as would have opening the survey to all physicians at the institution with admitting privileges. Additionally, correlating the survey data with true usage information would inform true use patterns better as they relate to therapeutic changes and patient outcomes. Opening the survey for a more prolonged period may have recruited more responses from the intended survey group (125 physicians) but was intended to be brief given the rapid changing climate of COVID-19 related admissions.

If the changes described above are implemented, additional data related to ICD-10 codes for secondary infections, total length of stay, ICU length of stay, and mortality before and after an order-set change intervention could be carried out to monitor for possible effects of those changes. A cost-savings analysis comparing the number of tests both directly and indirectly (e.g., computed tomography angiography, lower extremity ultrasound doppler, sputum culture, blood culture) related to this study before and after the proposed order set changes also could be considered.

In conclusion, physicians within our institution who primarily were managing patients with COVID-19 favored checking d-dimer and CRP daily for at least three to five days. Most physicians did not utilize ferritin or LDH routinely for inpatient management decisions. Therefore, as a diagnostic stewardship initiative, the institutional algorithm was changed after analyzing the ordering pattern through physician survey responses. Future studies could assess safety outcomes by comparing one-month mortality and length of hospital stay in the preintervention and postintervention groups.

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KANSAS JOURNAL of MEDICINE

Improving Electronic Patient Handoff in an Orthopaedic Residency using the Listrunner© Application

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ABSTRACT

Introduction. Miscommunication during shift change and other handoff events is a common source of malpractice claims and patient-care errors. An efficient patient handoff system is imperative to prevent miscommunication. Owning to limitations with our current handoff system and to an ever-increasing reliance on electronic health information, our residency program sought to modernize our handoff method.

Methods. To improve handoff communication, the HIPAA-compliant application Listrunner© was adopted. Members of the orthopaedic trauma team were oriented to the new application. Change-of-shift patient handoff was transitioned from the current email system to Listrunner©. After three months of using the new application, a web-based questionnaire was administered to all members of the care team to assess their experiences, including perceived benefits and limitations of the Listrunner© application.

Results. Seventeen orthopaedic resident physicians and three orthopaedic trauma attending physicians completed the survey. While almost half of the respondents were satisfied using email as a checkout tool, more than half of study participants indicated that it lacked security and several users believed there was a need for improvement. Most indicated that Listrunner© was easy to use, improved clinical efficiency, and improved patient care and safety. Seventeen of 20 respondents reported that they would like to continue using Listrunner© as a checkout tool.

Conclusions. The Listrunner© application was adopted quickly by our orthopaedic trauma team, whose members opined that the application increased the efficiency and accuracy of handoff when compared to the previous secure email system. ***Kans J Med 2022;15:97-100***

INTRODUCTION

Inaccurate communication at shift change continues to be identified as a common source of medical errors. Errors in communication account for 60 - 70% of all sentinel events within a hospital.[1] Furthermore, miscommunication is a leading cause of malpractice claims.[2]

Since many providers are responsible for the care of a single patient, having an efficient patient handoff system to communicate patient information is vital. It is the opinion of these authors that an effective handoff system should contain accurate and up-to-date information about a patient's current condition, care plan, and any anticipated changes in clinical status. With increasing reliance on electronic information sharing, the need for secure electronic patient information sharing has become a top demand among healthcare providers.

Despite their shortcomings, which include user distraction, potential transmission of patient protected health information on unsecure networks and risk of misusing confidential information, smartphone use for patient care is increasing. A recent survey conducted in France documented that approximately 75 - 95% of medical students and residents are using their personal smartphones for clinical work, commonly to utilize applications (apps) or to communicate with the care team via email, text messages, or phone calls.[3] Another survey of American neurology trainees and attending physicians regarding their cell phone use in the clinical setting demonstrated that both groups used their personal smartphones for their physical exams, clinical work, and communications, with the majority of respondents reporting their smartphones as "very useful" or "essential" for patient care.[4] In a systematic review, Gurses et al.[5] showed that information tools, which include electronic devices such as personal digital assistants, wireless tablets and mobile computers, improved situational awareness of multidisciplinary care providers, efficiency of multidisciplinary rounds, and length of hospital stay.

To date, mobile technologies have been used mainly to support coordination of care through text messaging and email among care team members in an informal way, but their use in structured rounding and handoff processes has been limited. However, using computerized rounding and patient handoff tools have been shown to increase efficiency within inpatient medical services.[6] Furthermore, there are stand-alone applications serving as electronic handoff tools and mobile applications associated directly with hospital electronic medical records (EMRs).

In our orthopaedic residency program, a secure email system has been the primary tool used for patient handoff. This consists of a daily email, sent at 0500, providing a summary list of patients who were seen overnight. There are many aspects of the email system that make it less than ideal for patient handoff. Lack of real-time viewing or updating and no capability to input clinical photographs or patient radiographs are two reasons that our program sought a digital upgrade. The objective of this quality improvement (QI) study was to improve communication among care team members using an application, compliant with the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule, which would allow electronic patient handoffs of overnight patient care at two tertiary health care centers.[7]

METHODS

This intervention was performed within the University of Kansas School of Medicine-Wichita orthopaedic surgery residency program, where trauma call at two tertiary care centers was covered by residents on the orthopaedic trauma surgery service. In an effort to improve accuracy and provide real-time updates to attending staff, residents, and other orthopaedic trauma healthcare team members, the HIPAA-compliant application Listrunner© was adopted. The project design was adapted from a publication on the use of mobile devices for inpatient rounding and handoffs.[8]

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During the study period, handoff communication was transitioned from a secure email system to the Listrunner© application. The application has patient list features that are customizable to the preferences of the attending staff. This app can be installed on a mobile device or accessed through the Listrunner© website. Training of the on-call junior residents on proper use of the app was provided by upper-level residents and attending staff members. At our institution, like many other residency programs, junior residents were responsible for managing the orthopaedic trauma service overnight.

After appropriate training and standardized implementation of the Listrunner© app, the overnight junior residents assumed the responsibility of adding patients to predetermined lists that reflected the reason for referral to our orthopaedic service: surgery add-ons, admits, consults, and phone calls. The application allowed for accurate short-form text documentation including medical record number, date of birth, age, history of present illness, discussion, clinical treatment and planning, imaging, clinical photographs, and a to-do section for pending tasks. Team members had the option to allow notifications when a new patient was added to a list, which allowed real-time patient care updates. The application was used only for handoff communication and was not linked formally to the hospital EMR. Patient lists were cleared or updated daily after review by the daytime trauma team.

After three months of consistent use, a web-based questionnaire was created to evaluate the Listrunner© application compared to the previous email system (Appendix available online only at journals.ku.edu/kjm). Specifically, usage patterns, user experiences, and perceived benefits and drawbacks to the Listrunner© app were assessed. The survey consisted of 23 multiple choice items and 4 free-response items. The multiple-choice questions utilized the Likert scale. A draft or pilot survey was used to assess survey validity and readability. After minor modifications, the final survey was distributed via email to all members of the orthopaedic trauma service, including attending physicians, resident physicians, advanced practitioners, nurses, and office scheduling personnel.

Study data were collected and managed using REDCap® (Research Electronic Data Capture) electronic data capture tools hosted at University of Kansas Medical Center.[9,10] REDCap® is a secure, web-based software platform designed to support data capture for research studies by providing 1) an intuitive interface for validated data capture; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for data integration and interoperability with external sources. In an effort to report our findings in a standard fashion, the Revised Standards for Quality Improvement Reporting Excellence (SQUIRE 2.0) guided the preparation of this manuscript.[11]

RESULTS

Our inpatient orthopaedic trauma services at two level one trauma centers began using the Listrunner© patient handoff application in September 2020. We used the application consistently for approximately three months before conducting a one-time survey to compare the Listrunner© application to the previously used email handoff system and to examine user experience, satisfaction, and suggestions for improvement regarding the use of Listrunner©.

The survey was offered to 31 orthopaedic trauma team members including medical assistants, nurses, advanced practitioners, resident physicians, and attending physicians. The initial email solicitation was sent on January 26, 2021. A reminder email was sent on February 18, 2021. Twenty-six team members began the survey and 23 members completed the survey. Only completed surveys of individuals who identified as Listrunner© users were compiled for analysis, with incomplete surveys and non-users being excluded. The survey took an average of 17 minutes to complete.

User characteristics are outlined in Table 1. Seventeen of the 20 residents in our program completed the survey. Sixteen described themselves as continued users of the application and one was self-described as an episodic user. Three of four attending physicians completed the survey. One advanced practitioner, one office staff member, and one nurse also completed the survey. Users universally reported accessing the application using the mobile app, with no respondents reporting routine use of the desktop website.

Table 1. Characteristics of users studied.

Characteristics	Respondents
How would you describe your role?	
Attending physician	3
Resident physician	17
APRN[1]/PA[2]	1
Nurse	1
Office staff/MA[3]	1
Student/other	0
Total respondents	23
Describe your experience using Listrunner©	
Continued user[4]	22
Episodic user[5]	1
Total respondents	23
Which version of the checkout tool do you commonly use?	
Webpage	0
Mobile app	23
Total respondents	23

[1]Advanced Practice Registered Nurse
[2]Physician Assistant
[3]Medical Assistant
[4]Application use for eight weeks or longer
[5]Stopped using application within eight weeks

Multiple choice responses regarding the email system are characterized in Figure 1. About half of respondents agreed or strongly agreed that they were satisfied using the email system as a checkout tool and most felt that the system was efficient and easy to use. However, 10 of the 23 (43.5%) respondents indicated that the email system was inadequate or in need of improvements and 14 respondents (60.9%) indicated that the email system lacked security.

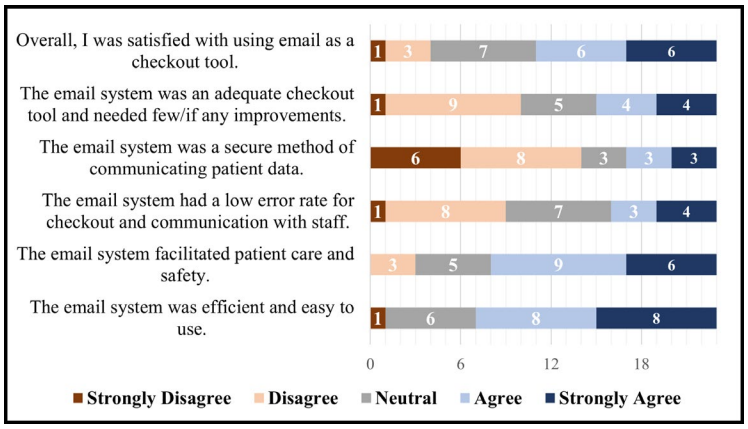

Figure 1. User responses regarding the email system.

Multiple choice responses regarding the Listrunner© application are characterized in Figure 2. The majority of users agreed or strongly agreed that the Listrunner© application was easy to use, improved clinical efficiency, and improved patient care and safety. Eighteen of 23 respondents found the application to be more useful as they became more familiar with it. Fifteen respondents disagreed or strongly disagreed that Listrunner© had significant drawbacks that should prevent its continued use. Seventeen respondents reported that they would like to continue using Listrunner© as a checkout tool.

Free response questions were included in the survey to determine specific likes, dislikes, and suggestions for improvement regarding the email system and the Listrunner© application. Specific likes regarding the email system included the brevity, simplicity, and format of the system. Users found it helpful having all the checkout information in one document, which decreased the amount of time needed to review the entire shift checkout. One specific dislike regarding the email system included a lack of perceived security, specifically when some users were not university employees and did not have access secure email accounts and used their personal email accounts. Other dislikes regarding the email system included difficulty in finding patients from previous shift checkouts, lack of functionality, and a lack of live updates.

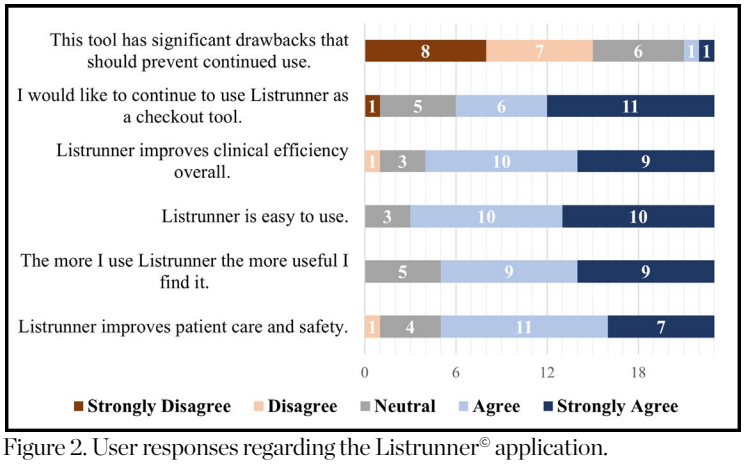

Figure 2. User responses regarding the Listrunner© application.

There were multiple aspects of the Listrunner© application that users liked, including real-time updates, added functionality (e.g., uploading radiographic images and clinical photographs, searching lists for patients, and to do lists), application security, ease of use, and easier coordination of clinical follow up. There were also aspects of the new system that some users disliked, including longer time spent to read through the entire handoff, having to sign into the application multiple times on a single shift, more time spent to enter patient information, and the need to update patient lists continually.

There were numerous suggestions from users to improve the new Listrunner© system. Many commented on the inability to upload groups of pictures at one time. The application required that the user upload one picture at a time, which added significantly more time over the course of a shift, particularly if it was necessary to upload multiple clinical pictures and/or radiographs per patient. Other suggestions for improvement included more consistent daily updating of patient lists and adding indicator tabs to highlight new patients and new tasks added.

Other respondents suggested that use of the application should be standardized on the two trauma services. At one hospital, in addition to being used as a handoff tool, the application also was used as a running inpatient list. At the other hospital, the orthopaedic trauma service utilized the application only as a handoff tool, using the hospital EMR for a running inpatient list. Standardized use of the app on both services would, in the opinion of some users, decrease potential communication errors and make it easier on the resident responsible for entering patients into the application.

DISCUSSION

This QI project showed that the Listrunner© patient handoff application was well received by our orthopaedic residency program and, in the opinion of the users, increased the accuracy and efficiency of patient handoff when compared to a secure email system. A strength of this study was that it clearly showed there was a viable electronic handoff system that can be more efficient and more interactive than a simple email system. Similar to the study on which our QI project was based[8], the results showed that a handoff tool can be adopted quickly, lead to improved patient care, and increase the accuracy of patient handoff. Another unexpected benefit that this project had on our trauma service was improving the efficiency of follow-up scheduling by the office staff, which was an unanticipated benefit of the Listrunner© application.

There were significant limitations to our study. Our small sample size decreased the overall power of the statistical analysis. There were three team members who did not complete the survey, which further limited our sample size. Another weakness of this study was enforcement of the use of the Listrunner© application, and while all handoffs were done using the Listrunner© application, some users may not have been utilizing it throughout their shift. Due to the unique nature of our call system requiring the coverage of two level one trauma centers, the results may not be generalizable to other orthopaedic trauma services. Future QI projects regarding patient handoff tools should include not only other medical and surgical specialties at our institution, but also orthopaedic trauma services at other institutions. In addition to expanding the study to include a more specialties and services, the methodology of future studies should include objective measures of improved efficiency

and patient care. These could include time spent by the on-call resident updating the handoff tool or email, as well as safety outcomes resulting from any miscommunication.

This project partly was inspired by the COVID-19 pandemic, during which the need for an accurate electronic patient handoff system to replace an in-person meeting became a top priority for our orthopaedic trauma service. Now, more familiar in-person interactions and verbal communication has resumed as the primary checkout modality. However, having a real-time, electronic handoff system that was convenient for trauma team members to use remains desirable.

At the time the application was adopted, Listrunner© was a free application. Users were able to download and use the program without a subscription or annual fee. After this survey was completed, Listrunner© notified users that the program would no longer be offered free of charge as of June 1, 2021. The app requires an organizational-based contract requiring an initial set-up fee of $5,000 and an ongoing cost of $25 per user per month. As our residency program did not have the budgetary means to enter into a contract with Listrunner©, the application was abandoned, and the residency program returned to using secure email for patient handoff.

At this time, the orthopaedic residency program had no plans to purchase a subscription for the Listrunner© application. Our residency program continued to search for a cost-effective, efficient, and secure alternative to our current secure email system. Given that our two trauma centers use different EMRs, a secure mobile application, separate from a specific hospital EMR, would be an ideal solution for an efficient electronic patient handoff system.

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Academic Impact of COVID-19 in Collegiate Athletes

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ABSTRACT

Introduction. The COVID-19 pandemic caused a pause to nearly all sporting activities in the spring of 2020, and collegiate athletes at the National Collegiate Athletic Association (NCAA)-affiliated universities whose sporting seasons were affected by the pandemic were granted an extra year of athletic eligibility. This study was conducted to determine how collegiate athletes planned to use an additional year of eligibility granted by the NCAA.

Methods. The authors conducted a cross-sectional survey of 632 athletes from two universities in the Midwestern United States, between August and September 2021. The athletes completed an anonymous, nine-item survey to assess the effect of the pandemic on the athletic season, athletic eligibility, and potential change in an academic or professional career. Chi-square tests, generalized linear mixed models, and adjusted odds ratio were used for the analyses.

Results. The participation rate was 74.5% (471 of 632). Nearly 63% (290 of 461) of the athletes received an additional year of eligibility because of the pandemic, with 193 (66.6%) planned to use their extra year for scholastic development. Male athletes (65.3% vs. 34.7%; $\chi^2[1, n = 290] = 11.66$, $p < 0.001$, $\Phi = 0.20$), Division II athletes (59.6% vs. 40.4%; $\chi^2[1, n = 290] = 13.93$, $p < 0.001$, $\Phi = 0.22$), and athletes who had not previously used redshirt (73.1% vs. 26.9%; $\chi^2[1, n = 290] = 4.79$, $p = 0.029$, $\Phi = 0.32$) where more likely to use their extra year of eligibility academically.

Conclusions. Our findings suggested that most of the athletes planned to use their extra year of eligibility to pursue further scholastic or professional development, highlighting the positive part of the COVID-19 pandemic. Future studies should investigate how these findings relate to athletes from universities in different geographical locations and intra-division schools. ***Kans J Med 2022;15:101-105***

INTRODUCTION

Since its introduction into the human population in late 2019, the novel coronavirus infectious disease (COVID-19) has caused significant international and domestic morbidity and mortality.[1] In 2020 especially, the COVID-19 pandemic disrupted many common rhythms of life; communities and families were distanced, professionals began working from home, and schools transitioned to virtual education.[2] In addition, the COVID-19 pandemic caused significant changes in the collegiate athletic world.[2,3] College athletes' learning and athletic environments were disrupted dramatically.[2,3] Many college sports' seasons and events were delayed or canceled completely.[3] Prior to the COVID-19 pandemic, the National Collegiate Athletic Association (NCAA) general administrative authority of Division I, II, and III sports allowed Division I athletes five calendar years to play four seasons of competition in a given sport and Division II and III athletes 10 semesters or 15 quarters to play a given sport.[4] This ruling changed with the COVID-19 pandemic; current athletes during the 2020 Spring through Winter seasons were allowed an additional year of eligibility in all division classifications.[5] The NCAA eligibility change created unique academic and athletic opportunities for college athletes including more sports involvement and pursuit of further education. This study aimed to determine how collegiate athletes planned to use an additional year of eligibility granted by the NCAA. We hypothesized that the athletes would use their extra year of eligibility for scholastic development.

METHODS

Study Design and Participants. The study was a cross-sectional survey of a convenience sample of 632 collegiate athletes from two universities in the Midwestern United States. Between August and September 2021, the athletes were asked to complete a short-written survey during required pre-participation physical evaluations at their respective institutions. The University of Kansas School of Medicine-Wichita (KUSM-W) Institutional Review Board granted exemption for the study as non-Human Subjects Research.

Study Measure. Survey measures (see Appendix) were developed using a multi-stage process, including an expert review, cognitive interviews, and a pretest. The measure assessed the number of athletes whose season was affected by the COVID-19 pandemic, the athletes who were granted an extra year of eligibility, how the athletes planned to use their extra year of eligibility, and how previous use of a redshirt year affected their extra year of eligibility. A redshirt year is where a player and a coach decide to "save" a year of athletic eligibility by not competing in formal events but the athlete practices with the team all year to improve. A redshirt year also can be used for a medical reason where an injured athlete receives an extra year to recover.

Statistical Analyses. Standard descriptive statistics were used to create a demographic profile and to describe how the athletes planned to use their extra year of eligibility academically. Chi-square tests, generalized linear mixed models, and adjusted odds ratios (aOR) were used to evaluate the data. Covariates included the athletes' biological sex at birth, academic standing, and institution (NCAA Division I or Division II). Adequate power (> 0.85) to detect significant relations among the variables with one degree of freedom, $p < 0.05$, and 0.5 effect size requires a sample size of 100 participants.[6,7] All analyses were two-sided with alpha of 0.05. The IBM® SPSS (Statistical Package for Social Sciences; Armonk, NY), version 26, was used for these analyses.

RESULTS

Participants Characteristics. Of the 632 eligible collegiate athletes, 471 agreed to participate in the study for a participation rate of 74.5%. As Table 1 shows, about 52% of the athletes were male, nearly 26% were freshmen, and over 64% attended a NCAA Division II program. Fourteen different sports were represented, with the largest

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group from baseball (17.0% of 483).

Planned to Use Extra Year of Eligibility Academically. Table 2 represents the athletes' responses to how they planned to use their extra year of eligibility. Overall, 63.0% (290 of 461) of the athletes received an additional year of eligibility because of the COVID-19 pandemic. Ten of the athletes who completed the survey did not respond to this question, hence the use of 461 as a denominator for the preceding analysis. Of the 290 athletes who were granted an additional year of eligibility, 193 (66.6%) planned to use their extra year academically by taking additional classes and/or pursuing some type of professional development. Extra year of eligibility differed by biological sex at birth, with 65.3% (126 of 193) of male athletes versus 34.7% (67 of 193) of female athletes planned to use the extra year of eligibility academically (χ^2[1, n = 290] = 11.66, p < 0.001, Φ = 0.20). Extra year of eligibility varied by academic institution as 40.4% (78 of 193) of Division I athletes compared with 59.6% (115 of 193) of Division II athletes planned to use their extra year of eligibility academically (χ^2[1, n = 290] = 13.93, p < 0.001, Φ = 0.22). In addition, extra year of eligibility varied by previous use of redshirt, as 26.9% (52 of 193) of the athletes who had previously used redshirt compared with 73.1% (141 of 193) who had not previously used redshirt planned to use their extra year of eligibility academically (χ^2[1, n = 290] = 4.79, p = 0.029, Φ = 0.32).

Nearly 68.7% (320 of 466) of the athletes reported that their season was affected by the COVID-19 pandemic. Findings of the mixed model analyses indicated that there was a negative association between the athletes whose season was affected by the COVID-19 pandemic and those who received additional year of eligibility (OR = 16.67; 95% confidence interval [CI]: 10.20-27.03; p < 0.001). This association remained significant after adjusting for the covariates of the athletes' biological sex at birth, academic standing, and institution (aOR = 7.52; 95% CI: 4.13-13.70; p < 0.001).

Previous Use of a Redshirt Year. Slightly more than 83.0% (388 of 466) of the athletes previously had not used a redshirt year and were more likely to use their extra year of eligibility academically (63.2% vs. 36.8%: χ^2[1, n = 290] = 4.79, p = 0.029, Φ = 0.13; Table 3). Findings of the mixed model analyses indicated that there was a significant positive association between no previous use of redshirt year and provision of additional year of eligibility due to the COVID-19 pandemic (OR = 4.37; 95% CI: 2.24-8.53; p < 0.001). This association remained significant after adjusting for the covariates (aOR = 2.50; 95% CI: 1.09-5.72; p = 0.03).

No previous use of redshirt year positively associated with season being affected by the COVID-19 pandemic (OR = 2.14; 95% CI: 1.17-3.91; p = 0.013) and plans to use extra year academically (OR = 2.02; 95% CI: 1.07-3.81; p = 0.031). These associations were not significant after adjusting for the covariates.

Table 1. Demographic characteristics of participating athletes (N = 471).

Characteristics	No. (%)
Biological sex at birth	
Male	243 (51.6)
Female	224 (47.6)
Missing*	4 (0.8)
Academic standing	
Freshman	121 (25.7)
Sophomore	102 (21.7)
Junior	117 (24.8)
Senior	101 (21.4)
Graduate students	26 (5.5)
Missing*	4 (0.8)
Institution	
NCAA division I	164 (34.8)
NCAA division II	303 (64.3)
Missing*	4 (0.8)
Type of sports¥	**n = 483**
Baseball	82 (17.0)
Soccer	56 (11.6)
Track and field	55 (11.4)
Softball	46 (9.5)
Basketball	45 (9.3)
Bowling	31 (6.4)
Dance	29 (6.0)
Golf	28 (5.8)
Cross country	27 (5.6)
Cheer	26 (5.4)
Tennis	23 (4.8)
Volleyball	18 (3.7)
Wrestling	10 (2.1)
Triathlon	7 (1.4)

*The number of participants who completed the survey but did not provide an answer to this specific question.
¥Total responses; some athletes played in more than one sport at the NCAA level.

Table 2. How the athletes planned to use their extra of eligibility academically (N = 237).

Activities	No. (%)
Additional classes/minor degree	91 (38.4)
Graduate school	86 (36.3)
Double major	34 (14.3)
Internship or part-time work in intended career field	26 (11.0)

Table 3. Relationship of redshirt year with the use of extra year of eligibility for academic work among the athletes.

	Use extra year academically?					
Measures	**Yes N (%)**	**No N (%)**	**Total**	**χ^2**	**p value**	**Phi**
Previous use of a redshirt year?				4.79	0.029	0.128
Yes	52 (77.6)	15 (22.4)	67			
No	141 (63.2)	82 (36.8)	223			
Total	193 (66.6)	97 (33.4)	290			

DISCUSSION

The study demonstrated that collegiate athletes in the Midwestern United States used their additional year of eligibility granted by the NCAA to pursue a greater variety of academic interests. A significantly high proportion (67%) of the 290 athletes who received an additional year of eligibility planned to use it for scholastic development. The use of extra year of eligibility academically varied by sex with male athletes twice as more likely to use the extra year for scholastic development. This finding is inconsistent with reported results.[8] Compared to their female counterparts, male athletes are typically more motivated to play sports than pursue academic development because there are more opportunities available in professional sports. It has been reported that the NCAA spends more money on male athletes than female counterparts.[9] This financial support may incentivize the male athletes to take an extra year of eligibility for scholastic development while also playing sports. Thus, an extra year of academic eligibility theoretically may be more appealing to a male athlete playing in revenue generating sports, as this time might allow them to focus on their career path.

The data also showed that Division II athletes were more likely to use their extra year of eligibility academically. The NCAA has reported that athletes from Division I institutions are more likely to be drafted to play at a professional sport,[10] suggesting that athletes from the non-Division I institutions tend to concentrate more on education. Another explanation to the findings is that Division I athletes may not have been inclined to use another year of eligibility because of a lack of scholarship money. If COVID-19 affected an athlete's season and the athlete was eligible for an extra year, their scholarship would carry over to the next year. However, the university might not have the financial resources to fund the athlete's scholarship.[5] The NCAA allowed universities to provide more scholarships over the maximum limit per sport but did not supply any funding to the universities.[5] Smaller Division I universities may have struggled to fund the additional student-athletes. Therefore, athletes may want to graduate and pursue a career rather than acquiring debt to continue playing their sport.

Interestingly, the data showed that athletes whose season was affected by the COVID-19 pandemic were eight times less likely to receive an additional year of eligibility. While the reasons for this finding are not clear, the findings may have been influenced by the intercollegiate athletic seasons and time the study was conducted. Data for the study were collected in the fall of 2021, a full year and a half following the start of the COVID-19 pandemic. The first intercollegiate athletic seasons that were affected was the spring of 2020. All spring sport athletes in NCAA Divisions I and II in the academic year 2019-2020 were eligible for an extra year.[5] Additionally, collegiate athletes who participated in fall or winter sports during the 2020-2021 academic year were also eligible, but athletics in the spring of 2020-2021 did not fall into the window of eligibility. This is important to address because for the academic year of 2020-2021, if the collegiate athlete was a freshman participating in a spring sport, they would not have been eligible for an extra year. Similarly, freshmen, regardless of their season of participation, in the 2021-2022 academic year were not eligible for an extension.

This eligibility information could explain the negative association because even though the COVID-19 pandemic may have affected these athletes, they were not eligible for the extra year of academic eligibility. Additionally, the athletes may have thought that their season was affected by new policy procedures, such as having to wear a mask at practice, but not to the extent that the season was so altered that the NCAA offered an extension (such as in the case of spring sports in 2021 and all sports in the 2021-2022 academic year as stated above). It is also possible that some participants may have answered that they were not offered an extra year out of misinformation, not realizing they had been offered an extra year.

Regarding previous use of a redshirt year and the possibility of an athlete receiving an extra year of eligibility, our study showed that the athletes who previously had not used a redshirt year were three times more likely to have received an additional year of eligibility, even after adjusting for the respondents' sex at birth, academic standing, and institution. These findings suggested that the athletes who previously had used a redshirt year might have achieved their goals on the field and in the classroom, and thus taking an extra year of eligibility would postpone graduation and future pursuits. Future studies could investigate if the timing of a redshirt, earlier in a collegiate career (i.e., as a freshman) or closer to graduation, would affect the athlete's desire to take the pandemic extension year, even if eligible.

Study Limitations. This study has several limitations. The results of this study were limited to collegiate athletes from two universities in the Midwestern United States and therefore the findings may not be generalizable to athletes in other regions of the country. Although the response rate of 74.5% is large, responses of the nonparticipant athletes could have changed the results of the study. Second, the data set was not comprehensive throughout all intercollegiate athletics as several important sports sanctioned by the NCAA, such as football, fencing, gymnastics, lacrosse, ice hockey, water polo, swimming, rifle, and soccer, were not played by the participating universities, therefore not represented in this study. This lack of representatives could affect generalizability of the study. Third, as this is a nonexperimental study, a causal relationship between extra year of eligibility and the use of the extra time academically could not be established, nor can it be known whether one preceded the other. Additional interventional research is

warranted. Finally, the survey was conducted during the athletes' pre-participation physical evaluations. It is possible that the desire or need for more attention from the trainers could have biased the responses.

CONCLUSIONS

Overall, these data highlighted a positive effect of the COVID-19 pandemic. Nestled within all the negativity of COVID-19, having more educational opportunities was likely beneficial for many of the student athletes who took an extra year. The extra year could make collegiate athletes more competitive in the job market. More academic opportunities could also allow collegiate athletes to pursue a degree or classes that were previously unattainable due to the rigors of intercollegiate athletics. Further research is needed to determine the effects extra years of eligibility have on the career prospects of the athletes.

Future comparison studies could explore collegiate athletes that were offered an extra year and those that were not and how this affected their ability to achieve and maintain a job in their desired career field. It would also be interesting to see if collegiate athletes who took an extra year of eligibility were more competitive for job opportunities during this pandemic where jobs are limited. Studies could be conducted to explore the effects of the extra year on the performance of individual sports and their recruiting endeavors. Finally, further research should be conducted including universities in different geographical locations, more intra-division programs (Division I and Division II institutions) and inter-division universities (i.e., Division III and the National Association of Intercollegiate Athletics).

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Keywords: COVID-19, academic performances, athletes, Midwestern United States

APPENDIX

Survey of Academic Impact of COVID-19 in Collegiate Athletes

1. What was your biological sex at birth?
   - A. Male
   - B. Female

2. Which school do you attend?
   - A. NCAA Division I
   - B. NCAA Division II

3. What is your current academic standing?
   - A. Freshman
   - B. Sophomore
   - C. Junior
   - D. Senior
   - E. Graduate student

4. What sport do you participate in? (Select all that apply)

A. Basketball	B. Baseball	C. Bawling	D. Cheer	E. Cross country
F. Dance	G. Golf	H. Soccer	I. Softball	J. Tennis
K. Track and field	L. Triathlon	M. Volleyball	N. Wrestling	

5. Have you previously used a redshirt year?
   - A. Yes
   - B. No

6. Was your season affected by the COVID-19 pandemic?
   - A. Yes
   - B. No

7. Were you provided an additional year of eligibility due to the COVID-19 pandemic?
   - A. Yes
   - B. No

8. Do you plan to use your extra year academically?
   - A. Yes (If yes, then go to Question 9)
   - B. No

9. How do you plan to use your extra year of eligibility academically? (Select all that apply)
   - A. Additional classes/minor degree
   - B. Double major
   - C. Graduate school
   - D. Internship or part-time work in intended career field

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Ludwig's Angina in a Centenarian Patient

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INTRODUCTION

Ludwig's angina was described first by physician Wilhem Friedrich von Ludwig in 1836 as a rapidly progressive, potentially fatal spread of bilateral cellulitis of the submandibular space associated with elevation and posterior displacement of the tongue.[1] The most frequent source of infection are the molars, particularly the second and third mandibular molars.[2,3] It is important for medical providers to recognize this condition promptly and initiate proper treatment before the cellulitis progresses to airway obstruction. Before the era of antibiotics, especially penicillin, this disease had a mortality rate greater than 50%. Following the advent of antibiotics, improved dental care, and aggressive surgical treatment, the mortality rate was estimated to be approximately 8%.[1,4] Ludwig's angina is most seen between ages 20 and 60 years, but has been reported in patients as young as 12 days and as old as 84 years.[5,6] The incidence in males is three to four times that in females.[3]

This case study presents a novel report of a centenarian who presented for surgical drainage of Ludwig's angina. Older patients with peritonsillar and parapharyngeal abscesses present in a subtle fashion with few of the classic symptoms such as fever, in addition to a delayed presentation.[7] This tendency made diagnosis challenging. Whether these results can be extrapolated to a patient with Ludwig's angina remains to be seen.

Managing older patients can be difficult due to multiple comorbidities, as seen in our patient, and because of poorer functional status and frailty. A multi-disciplinary team approach was necessary for this complex case, as it presented the dual challenges of an anticipated difficult airway and perioperative considerations of a centenarian.

CASE REPORT

Informed and written consent was obtained from the patient prior to the preparation of this case report. A 100-year-old male was referred to the emergency department by an ear, nose, and throat physician with a chief complaint of anterior neck swelling, dysphagia, and muffled voice. Two weeks prior, the patient had presented to the emergency department with similar symptoms and was given an oral steroid for presumed lymphadenitis; his symptoms, however, did not abate with the steroids. Most of his history was obtained from his family because the patient had muffled speech secondary to extensive soft tissue edema. The patient was unable to wear his dentures for two weeks and only could swallow liquids at the time of presentation. His past medical history included hyperlipidemia, benign prostatic hyperplasia, and hypertension. He had no history of alcohol, tobacco, or illicit drug use.

On the physical exam, the patient did not exhibit respiratory distress but expressed discomfort secondary to pain. His heart rate was 89 beats/min, blood pressure was 131/81 mmHg, oxygen saturation was 94% on room air, and the respiratory rate was 18 breaths/min. His airway exam revealed a severely limited mouth-opening with an interincisor gap of 1 cm. The patient could not extend his neck with effort, which likely was due to both diffuse neck swelling and pain.

Laboratory evaluation revealed the white blood count at 28,000/μL, hemoglobin at 12.1 g/dL, and platelet count at 225,000/μL. A computerized tomography neck scan with contrast was obtained which revealed a large, peripherally enhanced loculated fluid collection at the base of the tongue with surrounding soft tissue edema and resilient mass effect with narrowing of oropharynx. No significant lymphadenopathy was noted, but dental caries in the remaining three mandibular teeth with lucency suggested a dental abscess was prominent.

An oral and maxillofacial surgeon was notified of the above findings and the patient subsequently was scheduled for surgical drainage of his abscess. Secondary to the patient's physical exam findings, his airway was secured with awake fiberoptic intubation.

The patient was denitrogenated with 100% oxygen and administered glycopyrrolate (0.2 mg) via intramuscular injection to dry secretions. Nasal decongestant oxymetazoline 0.05% was administered as well as topical lidocaine to anesthetize the nasal mucosa.

The patient was positioned in the seated position to improve ventilation and ketamine was administered for light sedation to advance the fiberoptic scope through the patient's nares. Some difficulty was noted with visualization of the patient's vocal cords secondary to edema and fogging of the scope; however, tracheal intubation was successful with placement of a 7.5 mm cuffed endotracheal tube. Following confirmation of endotracheal intubation with direct visualization, fentanyl (50 mcg) and propofol (50 mg) were administered through injection. Muscle relaxant was not administered, and the patient's breathing was spontaneous on the ventilator, with sevoflurane as the anesthetic gas for maintenance. Additionally, dexamethasone (10 mg) was administered by injection. The surgical procedure was completed with successful incision and drainage of abscess, and collection of cultures. The patient was shifted to the intensive care unit on an endotracheal tube for elective postoperative ventilation and was extubated successfully the following day.

Postoperatively, the patient did well throughout the remainder of his hospital course. Surgical cultures revealed Streptococcus viridans and Streptococcus intermedius.

DISCUSSION

Ludwig's angina is a potentially life-threatening emergency that requires a rapid diagnosis and aggressive treatment plan that is characterized by airway soft tissue swelling and edema.[8] While the most common patient population is adult males between the ages of 20 and 60 years old,[1] there have been case series where deep neck space infections have been noted in patients from 11 months to 91 years old.[9] However, these case series have not specified the type of deep neck space infection by age group. The confirmed oldest reported case of Ludwig's angina was in a 76-year-old man.[6] Predisposing factors included poor dental hygiene, recent dental extractions, trauma

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including mandibular fractures and oral lacerations, smoking, alcoholism, and systemic illnesses including diabetes mellitus, hypertension, and certain autoimmune conditions such as systemic lupus erythematosus and HIV.[1,10]

Analysis of the microbiology showed the organisms were usually polymicrobial and generally characteristic of oral mucosa flora.[11] The most common organisms included Streptococcus and Peptostreptococcus species, particularly Streptococcus viridans, Bacteroides species, and other anaerobes. Treatment options included an antibiotic regimen of penicillin G with metronidazole, ampicillin-sulbactam, clindamycin, or cefoxitin.[3] The definitive management with abscess formation was with incision and drainage.

Several airway management options can be utilized to secure the airway, with three of the most common techniques being elective tracheostomy, awake blind nasal intubation, and flexible fiberoptic nasal (oral) intubation.[12] While the "gold standard" is a surgical airway, the less invasive methods can be attempted depending on the individual patient and according to their surgical plan, medical comorbidities, and clinical exam.[13] The risk-benefit ratio of each method, with the formation of an airway management plan, should be discussed in detail with the patient and a multi-disciplinary team.

After careful consideration, awake fiberoptic intubation was used on the patient. One major advantage to performing this procedure was the decreased risk of airway collapse from loss of muscle tone from general anesthesia.[2,14] The patient was seated upright with the head in the sniffing position for intubation, as it allowed for maximal opening of the pharyngeal airway for passage of the nasal endotracheal tube. It also allowed for a more accurate assessment of the airway when planning for extubation. Some of the other benefits over direct laryngoscopy included immediate confirmation of placement of the tube following procedure, less sympathetic stimulation, and less risk for airway trauma.[2]

In a case of Ludwig's angina, one of the most important anesthetic concerns while securing the airway is the risk for abscess rupture into the hypopharynx with the potential for aspiration pneumonia.[2] Neff et al.[15] reported an abscess rupture while trying to manipulate an oropharyngeal airway, resulting in the oral cavity filling with pus, consequently causing difficulty when securing the airway. Additional life-threatening complications that have been discussed in the literature include necrotizing fasciitis, descending mediastinitis, pleural effusion, and complications of sepsis resulting in death.[11]

While a traditionally described technique was used to secure the patient's airway successfully, it is worthwhile to note that the patient was a centenarian. According to projections, the population of elderly patients is expected to double from 8% to 16% between 2010 and 2050,[16] with Irwin et al.[17] listing some of the important age-related changes in the geriatric population. In the cardiovascular system of older adults, these changes could include undiagnosed diastolic heart failure, impaired heart rate response and myocardial contractility, and an increased level and activity of inflammatory mediators. The respiratory system is affected by decreased muscle strength and impaired cough mechanism, decreased ventilatory response to hypoxia and hypercarbia, and decreased pulmonary reserve. An increased autonomic dysfunction, impaired autoregulation, and malnutrition also are seen commonly.

There are numerous anatomic changes that occur and should be considered for airway management in the geriatric population. There is a tendency for the airway to collapse and obstruct, increased difficulty to form a proper seal with a bag-valve-mask device due to edentulousness, decreased compliance of the submandibular space, and decreased neck mobility.[18] All these changes lead to increased difficulty in ventilation and intubation in an elderly patient.

Irwin et al.[17] has recommended that every institution have a protocol in place that targets patients undergoing surgery at extreme ages, as well as including perioperative neurocognitive dysfunction as a part of informed consent in elderly patients that require anesthesia. Some of the recommendations include a robust assessment of comorbidities, risk stratification for each person, identification of modifiable factors for preoperative optimization, rehabilitation, and discharge planning. Models such as the anesthesiologist-led "high risk" clinics with an appropriately trained specialist and the geriatric-led "comprehensive geriatric assessment" have both shown a positive impact on postoperative outcomes for elderly patients.[17]

Vigilant management of Ludwig's angina should be employed with rapid diagnosis and aggressive treatment, with airway management and surgical methods if applicable, and appropriate antibiotic treatment. For elderly patients, special consideration for the approach to anesthesia and intubation techniques should be discussed with a multi-disciplinary team. The patient, due to his age, presented an anatomically and physiologically difficult airway that was considered when choosing the procedure plan. In conclusion, life-threatening complications, such as necrotizing fasciitis, mediastinitis, and sepsis should be monitored rigorously, with action plans implemented through multidisciplinary teams to meet the needs of the patient.

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Keywords: Ludwigs angina, centenarians, abscess, drainage, airway obstruction

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Lamotrigine Drug Interactions: Ignorance is not Bliss

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INTRODUCTION

Lamotrigine (LMG) and valproic acid and derivatives (VPA) are antiepileptics commonly used for primary generalized or unclear type seizures.[1,2] The U.S. Food and Drug Administration (FDA) approved LMG as monotherapy for bipolar disorder and adjunctive treatment in generalized seizures (primary and Lennox-Gastaut syndrome) and focal onset seizures, while VPA is FDA-approved for monotherapy in bipolar disorder acute mania and adjunctive therapy for simple and complex partial seizures (including absence), as well as migraine prophylaxis.[3,4] Drug interactions with antiepileptics arise from a variety of mechanisms, especially alterations in drug metabolism through the cytochrome p450 (P450) and uridine glucuronyl transferase (UGT) enzymes.[5] VPA is metabolized through a variety of pathways (P450 and UGT) and inhibits P450 enzymes 2C9 and UGT 1A4, 1A9, 2B7, and 2B15.[6] LMG is metabolized principally by UGT 1A4, which is inhibited by VPA. This interaction increases total LMG level by decreasing clearance and increasing half-life.[7] Inhibition of UGT and shunting LMG metabolism towards the P450 system results in production of toxic metabolites that may be related to cutaneous reactions as an adverse effect of LMG.[8]

Antiepileptic drug-induced hypersensitivity syndrome consists of Steven-Johnson syndrome, toxic epidermal necrolysis, and anticonvulsant hypersensitivity syndrome,[9] for which LMG received a black box warning from the FDA.[4] These reactions are dose dependent,[9,10] and highest incidence occurs within the first two months with a rate of 0.08% in adults when titrated appropriately.[9,11] Factors that are known to increase the risk of rash are use in pediatric patients, simultaneous use with VPA, and rapid escalation of dose.[4] The mechanism behind these reactions is poorly understood, though formation of reactive arene oxide metabolites from the P450 system, susceptibility due to human leukocyte antigen allele associations, and proliferation of T cells have been implicated.[9,12] In addition to severe cutaneous reactions, LMG can precipitate delirium, especially when used concomitantly with VPA.[13-16]

CASE REPORT

The patient was an 82-year-old female with history of major neurocognitive disorder (MNCD), type II diabetes mellitus, atrial fibrillation, hypertension, coronary artery disease, history of COVID-19 infection, and an unknown type of seizure disorder who was admitted to inpatient geriatric psychiatry after being transferred from the medical floor. She had a substance use history of smoking one pack of cigarettes per day for nearly 40 years until she was diagnosed, and she was treated successfully for lung cancer 20 years prior. The patient was admitted for a change of baseline with agitated behaviors towards family caretakers, scoring 2/30 on St. Louis University mental status examination (SLUMS) at the time of admission.

Home medications of amiodarone 100 mg daily, amlodipine 10 mg daily, diltiazem extended release 120 mg daily, lamotrigine 200 mg twice daily, and levetiracetam 500 mg twice daily were continued on the medical floor. In addition, she was given intravenous fluids for management of acute on chronic renal failure, and intravenous potassium for hypokalemia. Vital signs, complete blood count and complete metabolic panel, and serial troponins otherwise were found to be unremarkable. Immediately prior to transfer to geriatric psychiatry, the patient sustained a fall that resulted in a subdural hematoma. Of note, a close family member later reported the patient had not been compliant with home medications for at least two weeks prior to admission.

On arrival to geriatric psychiatry, the patient was oriented to self and location, was conversational though disorganized, and no psychomotor agitation was noted. Geriatric psychiatric admission workup was within normal limits (complete blood count, comprehensive metabolic panel, thyroid-stimulating hormone, urinalysis, drug screen, vitamin B12 and folate, syphilis antibody, human immunodeficiency virus antibody, and hepatitis panel). Serial computed tomography head imaging without contrast showed stable right frontal subdural hematoma, global volume loss, and chronic microvascular changes in areas of the subcortical and periventricular white matter.

Due to possible neuropsychiatric side effects of levetiracetam,[17] the decision was made to change antiepileptic medication by titrating off levetiracetam and starting divalproex. Divalproex extended release was started and titrated (up to 1000 mg daily over five days) to target serum level of about 80 mcg/mL before titrating off levetiracetam, while LMG was continued at 200 mg twice daily. On day nine, the patient began to be titrated off levetiracetam over seven days. Bedside electroencephalogram revealed no epileptogenic activity. In this period, patient behavior worsened resulting in psychomotor agitation, aggression, and three falls. She also exhibited delusions, auditory and visual hallucinations, and a declining oral intake. Due to refusal to take oral medications, VPA briefly was trialed via intravenously before switching to divalproex sprinkles.

On hospital day 17, the patient was concurrently on VPA 1000 mg daily and LMG 200 mg twice daily. Due to interaction between these medications, LMG was held until the next day and dose was quartered and continued thereafter (100 mg daily). By day 22, the patient began to improve and was no longer displaying agitated behaviors, and low dose mirtazapine was started for appetite stimulation. Though she was not reassessed with a SLUMS exam, clinically she continued to have dramatic behavioral improvement and resumed oral intake. Over the next several days, she was noted to be oriented (i.e., self, location, time), ambulating with steady gait, talking pleasantly, and listening to music (Figure 1).

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Day Number	Significant Event
0	Emergency department visit for agitation and admission to hospital
1	Psychiatry consult determined lack of capacity
2	Patient exhibits aggressive behaviors inpatient, sustained a fall
3	Stable right sided SDH on repeat CT. Family desired hospice upon discharge
5	Transferred to geriatric psychiatry for stabilization
6	Valproic acid started at 125 mg at bedtime
7-10	Valproic acid increased to 250 mg at bedtime, increased by 250 mg daily until 1000 mg at bedtime
14	Valproic acid level 0.78 mcg/mL; levetiracetam halved to 250 mg twice daily
17	Levetiracetam halved to 250 mg at bedtime; no epileptogenic activity on EEG
20	Levetiracetam halved to 125 mg at bedtime
21	Lamotrigine stopped
22	Lamotrigine continued at 100 mg at bedtime; Mirtazapine 7.5 mg at bedtime started; no further agitated behaviors
25	Levetiracetam discontinued
25-28	Dramatic behavioral improvement
34	Discharge to nursing home

Figure 1. Timeline of case events.

DISCUSSION

This case illustrated a common, but often missed, pharmacologic interaction that has the possibility for adverse outcomes and medicolegal implications. This patient was admitted for MNCD with behavioral disturbance of unknown etiology and developed a delirium after sustaining many deliriogenic insults (inaccurate medication reconciliation on admission, multiple falls with subdural hematoma, hypokalemia, acute kidney injury, and starting VPA in setting of LMG). Though development of this patient's delirium may have been multifactorial, the most glaring, and preventable, risk factor was the well-documented, but often overlooked, pharmacologic interaction between VPA and LMG. Discontinuation of levetiracetam may have led to this patient's improvement, though she had been stable on this medication as an outpatient and her rapid decline as an inpatient and subsequent improvement was not related temporally to levetiracetam.

Lamotrigine and VPA are common antiepileptics[1,2] and mood stabilizers indicated for use in bipolar affective disorder.[18,19] Side effects of LMG appear to be dose-dependent, prompting a recommended titration schedule in the package insert to minimize adverse effects. Titration schedules and dosing for LMG monotherapy and adjustments for multidrug therapy with known pharmacokinetic interactions (i.e., VPA, carbamazepine, phenytoin, phenobarbital, primidone, rifampin) for each FDA-approved indication are delineated in the package insert to lower risk of adverse events (Table 1).[4]

If a patient misses five half-lives of LMG during titration or maintenance, it is recommended to restart initial titration ($t_{1/2}$ 25.4 hours = approximately five days).[4] Valproic acid's inhibition of LMG metabolism is rapid and profound, leading to increased levels of lamotrigine that can precipitate adverse events. Over half of cases (60%) of LMG hypersensitivity occur in patients concurrently taking VPA.[20] Therapeutic drug monitoring can be useful to determine if serum drug concentrations are at an effective level, which is used commonly for VPA. Serum drug levels should be measured at trough levels after drug has reached steady state, with reference ranges of 50-100 mcg/mL and 50-125 mcg/mL, for use as AED and mood stabilizer, respectively. VPA is highly protein-bound (> 90%), which should be taken into consideration when levels are checked. In addition to the VPA level, complete blood count and complete metabolic panel should be monitored, particularly to monitor liver enzymes, leukocyte, and thrombocyte levels.[3,21-23]

Table 1. Escalation regimen for lamotrigine in patients with bipolar affective disorder.

Escalation timeline	For patients taking Valproate	In patients not taking Carbamazepine, Phenytoin, Phenobarbital, Primidone, or Valproate	In patients taking Carbamazepine, Phenytoin, Phenobarbital, or Primidone, and not taking Valproate
Weeks 1 and 2	25 mg every other day	25 mg daily	50 mg daily
Weeks 3 and 4	25 mg daily	50 mg daily	100 mg daily, in divided doses
Weeks 5	50 mg daily	100 mg daily	200 mg daily, in divided doses
Week 6	100 mg daily	200 mg daily	300 mg daily, in divided doses
Week 7	100 mg daily	200 mg daily	Up to 400 mg daily, in divided doses

The above case illustrated that delirium and an increased risk for other adverse effects likely were caused by restarting LMG at home dose after extended noncompliance and adding VPA to LMG without adjusting LMG dose. This case underscored the importance of performing a careful and diligent medication reconciliation and consideration of black box warnings. These processes are critical for both patient safety (nonmaleficence) and obtaining full informed consent with knowledge of black box warnings (autonomy), in accordance with ethical and legal obligations in the patient-physician relationship.

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Keywords: drug hypersensitivity, drug interaction, valproic acid, lamotrigine, anticonvulsants

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WHAT'S INSIDE: ORIGINAL RESEARCH • CASE REPORT

KANSAS JOURNAL of MEDICINE

TABLE OF CONTENTS

KANSAS JOURNAL of MEDICINE

The Emergent General Surgical Patient: Evaluation Patterns in the Emergency Department

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ABSTRACT

Introduction. Emergency general surgery patients represent a growing segment of general surgical admissions and national healthcare burden. A paucity of literature exists evaluating the work-up of these patients presenting to the Emergency Department (ED), particularly possible evaluation differentials between emergency physicians and physician assistants or advanced practice registered nurses (PA/APRNs). The purpose of this study was to evaluate differences in ED work-up of general surgical patients between emergency physicians and PA/APRNs.

Methods. A retrospective review was conducted of patients presenting to the ED with the chief complaint of abdominal pain. Demographic data, evaluating provider, laboratory and imaging tests, diagnostic data, and disposition were obtained.

Results. Patient median age was 53.5 years, with 49% male and 81.6% Caucasian. Emergency physicians saw the majority (61.2%) of patients. Emergency physicians saw older patients (62.0 vs. 45.5 years; p = 0.017), and more patients that were anemic (28.3% vs. 14.3%) or with elevated creatinine levels (46.7% vs. 25.7%). There was no significant difference between groups for time in the ED (6.1 ± 2.4 vs. 5.7 ± 2.6 hours; p = 0.519), time to surgical consult (3.4 vs. 3.3 hours; p = 0.298), or time to the operating room (29.5 vs. 12.0 hours; p = 0.075). Patients seen by emergency physicians had a longer length of hospital stay (4.5 vs. 2 days; p = 0.002).

Conclusions. Time in the ED and time to surgical consult did not vary between groups although patients first seen by emergency physicians had potentially higher acuity. Decreased hospital length of stay in patients seen by PA/APRNs may reflect disease-specific differences.
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INTRODUCTION

Emergency general surgery (EGS) comprises a significant portion of all general surgery admissions and procedures, and represents a growing portion of national healthcare financial burden.[1,2] Evidence suggested that these admissions comprise over 7% of all hospital admissions and that the annual rate of EGS cases is higher than the rate of new cancer diagnoses.[2,3] Although early recognition of EGS conditions may play a role in outcomes, there was little research that described the process of patient evaluation in the emergency department (ED) prior to initiation of surgical consult or admission with an EGS diagnosis.[4-7]

Furthermore, physician assistants and advanced practice registered nurses (PA/APRNs) play a growing role in health care delivery, particularly in the emergency department,[8,9] as patients presenting with EGS conditions may be first evaluated either by a PA/APRN or an emergency physician. The selection of which type of provider initially will evaluate a patient can be driven by many factors, including perceived level of visit severity assessed at time of triage.[8,9] This may represent an important branch point in patient care. It was unknown if initial provider type had any impact upon the work-up required to diagnose an EGS condition or upon the time from initial evaluation to recognition of an EGS condition or surgical consult. Furthermore, it was unknown whether these variables have any impact on final patient outcomes such as hospital length of stay or mortality.

There were other studies evaluating ED outcomes between patients evaluated by a PA/APRN or emergency physician in some medical patient sub-groups.[10,11] For example, Tsai et al.[11] demonstrated a lower guideline concordance score for PA/APRNs than for emergency physicians when evaluating asthma patients. Although there were data regarding the presentation and evaluation of the EGS patient in the ED, there was a paucity of data regarding PA/APRN-specific involvement and how that altered evaluation and outcomes in the ED within this specific population.[12] The purpose of this study was to compare the characteristics and outcomes between those patients presenting with abdominal pain who were first evaluated by a PA/APRN compared to those that were first evaluated by an emergency physician.

METHODS

This study was approved for implementation by the Institutional Review Board of Ascension Via Christi Hospitals Wichita, Inc.

Study Setting and Population. A retrospective review was conducted of all patients presenting to the ED of a Level 1 trauma center, tertiary-care hospital seeing 60,000 patients annually with the chief complaint of abdominal pain between October 1, 2018 and December 31, 2018. Patients under the age of 18 and prisoners were excluded.

Study Protocol, Measurements, and Key Outcomes. Data were obtained from patients electronic medical records. Demographic data (e.g., age, sex, and race), body mass index (BMI), initial vitals (e.g., heart rate, blood pressure, and temperature), initial laboratory values (e.g., white blood cell count, hemoglobin, creatinine, carbon dioxide, and total bilirubin), and Emergency Severity Index were collected.

Emergency Severity Index is a five-level emergency department triage algorithm. The five levels correspond to patient condition as follows: 1 = immediate, life-saving interventions are required for conditions such as cardiac arrest or massive bleeding; 2 = emergent conditions with high risk of patient deterioration such as cardiac-related chest pain or asthma attack, 3 = patient is stable, but needs urgent care requiring multiple resources, for conditions such as abdominal pain or high fever with cough, 4 = less urgent patients needing only one type of resource for conditions such as simple laceration or pain on urination, 5 = nonurgent conditions such as rash or prescription refill. Type of initial provider was recorded as emergency physician or PA/APRN. The number and types of laboratory tests ordered by the providers were recorded: complete blood count (CBC), comprehensive metabolic panel (CMP), lactic acid,

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and a category of 'other laboratory tests' (which included urine pregnancy test, rapid fingerstick glucose, urine drug screen, B natriuretic peptide, and lipase). The number and type of radiographic studies also was recorded. The patient's disposition was obtained: discharge home, admission to the hospital under a surgical service, admission under a non-surgical service, or in ED death. The total length of time in the ED from admission to final disposition and the time from admission to surgical consult were obtained. Length of hospital stay also was collected. If the patient required general surgical operative intervention, the time from presentation to the ED to arrival to the operating room was ascertained. The ED provider's diagnosis at time of discharge from the ED was obtained from the ED provider's note and final diagnosis at time of surgical discharge was obtained from the surgeon's notes.

Data Analysis. The data were compiled, evaluated, and summarized by calculating means and standard deviations for continuous data and proportions for discrete data. Primary comparisons were conducted comparing patients first evaluated by an emergency physician and those first evaluated by a PA/APRN. An independent samples t-test was used to compare continuous data when normally distributed. Variables that were not distributed normally were reported with medians and interquartile ranges, then compared using the Mann-Whitney U-Test. Chi-square analysis was used for comparison of categorical data. All analyses were run as two-tailed tests and results of analyses were considered significant if the resultant p value was less than or equal to 0.05. Analyses were performed using SPSS 19.0 (2010. IBM Corp, Armonk, NY).

RESULTS

Of the patients presenting to the ED during the study period, 654 presented with a chief complaint of abdominal pain. One hundred thirteen of these patients presenting with abdominal pain (17.3%) required a consult from a general surgeon, either as a documented over the phone consultation between the ED provider and the surgeon or as an in-person evaluation. Four patients were excluded because they were below the age of 18 or prisoners and eleven patients were excluded due to incomplete documentation, leaving 98 patients as the focus of this investigation.

Table 1 lists the demographic, physical characteristics, laboratory values, and final diagnoses in the groups seen by either an emergency physician or a PA/APRN. The majority (61.2%) of patients initially were evaluated by an emergency physician and self-identified as white (81.6%) with one person declining to answer. The median age of these patients was 53.5 years. The majority (63.3%) were obese/overweight. Overall, there was not a significant difference in sex, race, or vitals between the two groups; however, patients first seen by an emergency physician were older (62.0 vs. 45.5 years of age; p = 0.017), more often had elevated creatinine levels (46.7% vs. 25.7%; p = 0.043), and were more often anemic (28.3% vs. 14.3%; p = 0.008). There was no statistically significant difference (p = 0.073) in blood pressure between the two groups; however, all the hypotensive patients in this study were seen by emergency physicians (five patients). While the median emergency severity index score was 3 for both groups, the distribution of scores indicated that patients with scores indicitive of more critical issues were seen more often by an emergency physician. Emergency physicians saw more patients with a score of 1 or 2 (21.6% of patients) compared to those seen by a PA/APRN (5.3% of patients; p = 0.014).

There was a high rate of use of laboratory evaluation (98%; Table 2). There was a trend for increased ordering of CBCs by emergency physicians (100% vs. 94.7%; p = 0.073). Emergency physicians were found to order both lactic acid (33.3% vs. 13.2%; p = 0.026) and comprehensive metabolic panels (CMPs; 100% vs. 92.1%; p = 0.027) more often than PA/APRNs. There was also a high rate of radiographic evaluation, although there was not a significant difference between total number of studies ordered by either group. Emergency physicians ordered significantly more computed tomography (CT) scans than PA/APRNs (88.3% vs. 68.4%; p = 0.015), while PA/APRNs ordered a higher percentage of CT scans with intravenous contrast (88.5% vs. 60.4%; p = 0.011).

Table 3 demonstrates the difference in outcomes between the two groups. There was no significant difference in disposition from the ED, hours in the ED (6.1 vs. 5.7 hours; p = 0.519), or hours to in-ED surgical consult (3.4 vs. 3.3 hours; p = 0.298) between those first seen by emergency physicians or PA/APRNs, respectively. There was also no significant difference between time to consult (12.4 vs. 55.7 hours; p = 0.237) for patients who were admitted to a non-surgical service and subsequently required a general surgery consult. While there was no significant difference between initial provider and proportion going to the operating room, there was a trend for longer time to the operating room for those patients first seen by an emergency physician (29.5 vs. 12.0 hours; p = 0.075). This difference was not seen when evaluating time to surgical consult either for patients who received in-ED surgical consult or for those admitted to a non-surgical service who subsequently received a post-ED surgical consult (99.8 vs. 39.5 hours; p = 0.245). There was general concordance between ED provider diagnosis and final surgical diagnosis, with 81.7% of those seen by an emergency physician in concordance compared to 73.7% of those seen by a PA/APRN (p = 0.348). Hospital length of stay was significantly longer for those patients first seen by an emergency physician compared to those first seen by a PA/APRN (four days vs. one day; p = 0.001). This included those who were discharged from the ED, which was 10.0% of patients seen by a emergency physician and 23.7% of patients seen by a PA/APRN; although this did not reach statistical significance, it showed a trend toward significance (p = 0.067). This difference in hospital length of stay remained higher for patients first seen by an emergency physician for those patients that were admitted to the hospital, excluding those discharged home from the ED (4.5 vs. 2.0 days; p = 0.002).

Finally, there was a difference in the number and type of diagnoses seen in each group (Table 4). PA/APRNs did not see any patients with perforated viscera or organ space infections, whereas perforated viscus was one of the more frequent diagnoses seen by emergency physicians (nine patients). Emergency physicians also treated all the patients with superficial or deep infections (four patients). Overall, emergency physicians also saw more patients with hernias (seven vs. two patients) while PA/APRNs saw more patients diagnosed with bowel obstructions (12 vs. 9 patients).

Table 1. Comparison of patient demographics, initial vitals, and initial laboratory values between patients first evaluated by an emergency physician versus those first evaluated by a physician assistant (PA) or advanced practice registered nurse (APRN).

Variable	All Patients	Study Group		p Value
		PA/APRN	Emergency Physician	
Number of patients	98 (100%)	38 (39.8%)	60 (61.2%)	---
Age (years)	53.5 (40.0 - 66.0)	45.5 (40.0 - 58.3)	62.0 (40.3 - 72.0)	0.017
Gender†				0.800
Male	48 (49.0%)	18 (47.4%)	30 (50.0%)	
Female	50 (51.0%)	20 (52.6%)	30 (50.0%)	
White race	80 (81.6%)	31 (81.6%)	49 (83.1%)	0.852
Body mass index (BMI) (kg/m^2)‡				0.260
Underweight (BMI < 18.5)	2 (2.5%)	1 (3.7%)	1 (1.9%)	
Normal weight (BMI 18.5 - 24.9)	27 (34.2%)	6 (22.2%)	21 (40.4%)	
Overweight or obese (BMI > 24.9)	50 (63.3%)	20 (74.1%)	30 (57.7%)	
Heart rate (HR)				0.733
Bradycardia (HR < 60)	4 (4.1%)	1 (2.6%)	3 (5.0%)	
Normal HR (HR 60 – 90)	54 (55.1%)	20 (52.6%)	34 (56.7%)	
Tachycardia (HR > 90)	40 (40.8%)	17 (44.7%)	23 (38.3%)	
Temperature (°C)				0.959
Hypothermic (< 35.8)	3 (3.1%)	1 (2.6%)	2 (3.4%)	
Normothermic (35.8 - 37.3)	87 (89.7%)	34 (89.5%)	53 (89.8%)	
Hyperthermic (> 37.3)	7 (7.2%)	3 (7.9%)	4 (6.8%)	
Systolic blood pressure (SBP) (mmHg)				0.073
Hypotensive (SBP < 90)	5 (5.1%)	0 (0.0%)	5 (8.3%)	
Normotensive (SBP 90 - 140)	59 (60.2%)	21 (55.3%)	38 (63.3%)	
Hypertensive (SBP > 140)	34 (34.7%)	17 (44.7%)	17 (28.3%)	
White Blood Cell Count (WBC) (cells x 10^3/uL)				0.643
Lymphopenia (< 4.8)	5 (5.3%)	1 (2.9%)	4 (6.8%)	
Normal WBC (4.8 - 10.8)	42 (44.7%)	15 (42.9%)	27 (45.8%)	
Leukocytosis (> 10.8)	47 (50.0%)	19 (54.3%)	28 (47.5%)	
Creatinine (mg/dL)				0.043
Normal Creatinine (< 1.03)	58 (61.1%)	26 (74.3%)	32 (53.3%)	
Elevated Creatinine (≥ 1.03)	37 (38.9%)	9 (25.7%)	28 (46.7%)	
Carbon dioxide (mEq/L)				0.108
Hypocarbia (< 22)	23 (24.2%)	5 (14.3%)	18 (30.0%)	
Normal (22 - 32)	71 (74.7%)	29 (82.9%)	42 (70.0%)	
Hypercarbia (> 32)	1 (1.1%)	1 (2.9%)	0 (0.0%)	
Hemoglobin (gm/dL)				0.008
Anemia (< 12)	22 (23.2%)	5 (14.3%)	17 (28.3%)	
Normal (12 - 16)	61 (64.2%)	21 (60.0%)	40 (66.7%)	
Elevated hemoglobin (> 16)	12 (12.6%)	9 (25.7%)	3 (5.0%)	
Bilirubin (mg/dL)				0.164
Normal bilirubin (< 1.2)	71 (74.7%)	29 (82.9%)	42 (70.0%)	
Hyperbilirubinemia (> 1.2)	24 (25.3%)	6 (17.1%)	18 (30.0%)	

Table 1. Comparison of patient demographics, initial vitals, and initial laboratory values between patients first evaluated by an emergency physician versus those first evaluated by a physician assistant (PA) or advanced practice registered nurse (APRN). *cont.*

Variable	All Patients	Study Group		p Value
		PA/APRN	Emergency Physician	
ED Emergency Severity Index Score	3 (3 - 3)	3 (3 - 3)	3 (3 - 3)	0.014
1	5 (5.1%)	0 (0.0%)	5 (8.3%)	
2	10 (10.2%)	2 (5.3%)	8 (13.3%)	
3	82 (83.7%)	35 (92.1%)	47(78.3%)	
4	1 (1.0%)	1 (2.6%)	0 (0.0%)	

**Presented as n (%) or median (interquartile range).
†One patient did not have a race listed.
‡Nineteen patients did not have a height or weight listed.

Table 2. Comparison of laboratory test and imaging ordering patterns between patients first evaluated by an emergency physician versus those first evaluated by a physician assistant (PA) or advanced practice registered nurse (APRN).*

Variable	All Patients	Study Group		p Value
		PA/APRN	Emergency Physician	
Number of patients	98 (100.0%)	38 (38.8%)	60 (61.2%)	---
Complete blood count	96 (98.0%)	36 (94.7%)	60 (100%)	0.073
CMPs	95 (96.9%)	35 (92.1%)	60 (100%)	0.027
Lactic acid	25 (25.5%)	5 (13.2%)	20 (33.3%)	0.026
Total labs	4 (4 - 5)	4 (4 - 5)	5 (4 - 6)	0.122
Ultrasound	20 (20.4%)	10 (26.3%)	10 (16.7%)	0.248
CT	79 (80.6%)	26 (68.4%)	53 (88.3%)	0.015
CT with contrast	55 (69.6%)	23 (88.5%)	32 (60.4%)	0.011
CT and Ultrasound	10 (10.2%)	5 (13.2%)	5 (8.3%)	0.442
Number of in-ED imaging studies ordered by ED provider	1 (1 - 1)	1 (1 - 1)	1 (1 - 2)	---
0	12 (12.2%)	8 (21.1%)	4 (6.7%)	0.062
1	64 (65.3%)	24 (63.2%)	40 (66.7%)	
2	17 (17.3%)	3 (7.9%)	14 (23.3%)	
3	4 (4.1%)	2 (5.3%)	2 (3.3%)	
4	1 (1.0%)	1 (2.6%)	0 (0.0%)	
Total number of in-ED studies ordered by non-ED provider	0 (1 - 1)	0 (0 - 0)	0 (0 - 0)	0.560
0	92 (93.9%)	35 (92.1%)	57 (95.0%)	
1	6 (6.1%)	3 (7.9%)	3 (5.0%)	

*Presented as n (%) or median (IQR).
CT = computed tomography; ED = emergency department; CMP = complete metabolic panel

Table 3. Comparison of hospital outcomes and diagnostic concordance between patients first evaluated by an emergency physician versus those first evaluated by a physician assistant (PA) or advanced practice registered nurse (APRN).*

Variable	All Patients		Study Group				p Value
			PA/APRN		Emergency Physician		
Number of patients	98	100%	38	38.8%	60	61.2%	---
Disposition from ED							0.170
Discharged home	98	14 (14.3%)	38	8 (21.1%)	60	6 (10.0%)	
Admitted to surgery	98	58 (59.2%)	38	23 (60.5%)	60	35 (58.3%)	
Admitted to other service	98	26 (26.5%)	38	7 (18.4%)	60	19 (31.7%)	
Death in ED	98	0 (0.0%)	38	0 (0.0%)	60	0 (0.0%)	
Time in ED (hours)	98	5.9 ± 2.5	38	5.7 ± 2.6	60	6.1 ± 2.4	0.519
Time to surgical consult (hours)	97	3.3 (2.5 - 4.6)	37	3.3 (1.9 - 4.4)	60	3.4 (2.5 - 5.3)	0.298
Time to surgical consult (hours) for in-ED consults	86	3.3 (2.3 - 4.2)	35	3.3 (1.9 - 4.1)	51	3.2 (2.4 - 4.3)	0.571
Time to surgical consult (hours) for post-ED consults	11	12.4 (6.5 - 22.5)	2	55.7 (12.4 - 99.0)	9	12.4 (6.3 - 20.3)	0.237
Operative intervention	97	47 (48.5%)	38	15 (39.5%)	59	32 (54.2%)	0.156
Time to OR (hours)	47	24.4 (10.2 - 85.5)	15	12.0 (8.0 - 79.1)	32	29.5 (11.2 - 113.1)	0.075
Time to OR (hours) for in-ED consults	40	18.7 (10.2 - 76.6)	13	12.0 (8.4 - 56.6)	27	23.4 (10.2 - 113.1)	0.220
Time to OR (hours) for post-ED consults	7	79.1 (24.7 - 113.1)	2	39.5 (0 - 79.1)	5	99.8 (50.4 - 127.7)	0.245
Hospital LOS (days)	96	2.0 (1.0 - 5.8)	38	1 (0.8 - 2.5)	58	4 (1.0 - 8.3)	0.001
Hospital LOS (days) for those not discharged home from the ED	84	3.0 (1.0 - 6.8)	30	2.0 (1.0 - 4.3)	54	4.5 (2.0 - 9.0)	0.002
Diagnostic concordance	98	77 (78.6%)	38	28 (73.7%)	60	49 (81.7%)	0.348

*Presented as n (%), median (IQR), or mean ± standard deviation.
ED = emergency department; OR = operative intervention; LOS = length of stay

Table 4. Concordance of ED and hospital discharge diagnosis between patients first evaluated by an emergency physician versus those first evaluated by a physician assistant (PA) or advanced practice registered nurse (APRN).*

Diagnosis	Number at ED Discharge	Study Group	
		PA/APRN	Emergency Physician
Number of patients	98 (100%)	38 (38.8%)	60 (61.2%)
Bowel Obstruction	21 (21.4%)	12 (31.6%)	9 (15.0%)
Concordant with final diagnosis	16 (76.2%)	8 (66.7%)	8 (88.9%)
Appendicitis	11 (11.2%)	5 (13.2%)	6 (10.0%)
Concordant with final diagnosis	9 (81.8%)	4 (80%)	5 (83.3%)
Benign Biliary	9 (9.2%)	3 (7.9%)	6 (10.0%)
Concordant with final diagnosis	8 (88.9%)	3 (100%)	5 (83.3%)
Hernia	9 (9.2%)	2 (5.3%)	7 (11.7%)
Concordant with final diagnosis	7 (77.8%)	2 (100%)	5 (71.4%)
Perforated Viscus	9 (9.2%)	0 (0.0%)	9 (15.0%)
Concordant with final diagnosis	8 (88.9%)	-	8 (88.9%)
Cholecystitis	7 (7.1%)	4 (10.5%)	3 (5.0%)
Concordant with final diagnosis	6 (85.7%)	3 (75.0%)	3 (100%)
Benign Bowel Complaint	5 (5.1%)	2 (5.3%)	3 (5.0%)
Concordant with final diagnosis	2 (40.0%)	1 (50.0%)	1 (33.3%)
Post-Operative Problem	5 (5.1%)	2 (5.3%)	3 (5.0%)
Concordant with final diagnosis	5 (100%)	2 (100%)	3 (100%)
Skin or Organ Space Infection	4 (4.1%)	0 (0.0%)	4 (6.7%)
Concordant with final diagnosis	4 (100%)	-	4 (100%)

Table 4. Concordance of ED and hospital discharge diagnosis between patients first evaluated by an emergency physician versus those first evaluated by a physician assistant (PA) or advanced practice registered nurse (APRN).* *cont.*

Diagnosis	Number at ED Discharge	Study Group	
		PA/APRN	Emergency Physician
Pancreatitis	3 (3.1%)	2 (5.3%)	1 (1.7%)
Concordant with final diagnosis	3 (100%)	2 (100%)	1 (100%)
Other	15 (15.3%)	6 (15.8%)	9 (15.0%)
Concordant with final diagnosis	9 (60.0%)	3 (50.0%)	6 (66.7%)

*Presented as n (%).

DISCUSSION

This study demonstrated that the majority of patients presenting to this ED with abdominal pain who receive a surgical consult will be admitted to the hospital (85.7%), although most will not require operative intervention. The rate of operative intervention (48.5%) was somewhat higher than the rate of 28.8% found by Gale et al.[1] in their analysis of the Nationwide Inpatient Sample. Our patient population had a comparable average age (53.5 years) to their national data (58 years), and the most common diagnoses of bowel obstruction, appendicitis, hernia, perforated viscus, and benign biliary complaint in our study were compatible with the most common procedures performed nationally (cholecystectomy, appendectomy, laparotomy, partial small bowel resection, partial colectomy, and operative management of peptic ulcer disease).[13] Our higher operative rate may be accounted for by the data of the study, as Gale et al.[1] found an increase in operations by 32.3% from 2001 to 2010; furthermore, our study population was restricted to patients with abdominal pain, whereas their study population was derived from the National Inpatient Sample.

This study demonstrated widespread use of laboratory and radiographic evaluation of patients prior to and in conjunction with surgical consult among emergency physicians and PA/APRNs. There was a statistically significant difference in the rate of CT usage between emergency physicians and PA/APRNs, with emergency physicians having a higher use of CT scans and CT scans without contrast. This finding differed compared to other studies that have demonstrated modest increase in resources by PA/APRNs compared to emergency physicians.[14,15] For example, Aledheim et al.[15] demonstrated 4.5 more radiographs and 1.7 more CTs ordered by PA/APRNs than emergency physicians; however, this was adjusted for patient acuity, annual volume, and attending hours. The older population had a higher proportion of patients with elevated creatinine, which could be a marker of renal failure, as well as the higher rate of perforated viscus as an underlying diagnosis seen by emergency physicians in our study and may account for the higher use of CT scans and particularly CT scans without contrast by emergency physicians. When looking at the rate of obtaining both an ultrasound and a CT, PA/APRNs had a higher percentage of ordering both (13.2%) than emergency physicians (8.2%), although this was not statistically significant ($p = 0.442$). PA/APRNs also tended to order more in-ED imaging studies with higher percentages ordering more than two in-ED imaging studies than emergency physicians (7.8% vs. 3.3%), although this was not statistically significant ($p = 0.062$).

While there was no statistically significant difference in the number of radiographic studies ordered per patient in the ED between the two groups, the institution may have a high rate of CT usage (80.6%). In comparison, a study by Ijaz et al.[16] demonstrated a rate of CT usage in 55% of patients with abdominal pain and a review of CT usage by Larson et al.[17] demonstrated a rate of 12.8% in 2007. However, our population consisted of patients with abdominal pain who went on to receive a surgical consult, which likely affected the use of CT ordering in the patient population.

There was no difference between the two groups in terms of disposition from the ED, time in the ED, or time to surgical consult. While this study did not evaluate the odds ratio (OR) of surgical consultation in the ED population, Ulloa et al.[18] reported a lower rate of general surgical consultation from physicians compared to PA/APRNs in the outpatient setting (adjusted OR 0.66). Our total rate of surgical consultation request for patients presenting with abdominal pain as a chief complaint was 17.3% (113/654 patients). The evaluation of time to surgical consult specifically in the ED between physicians and PA/APRNs represented a novel area of inquiry in the literature.

Similarly, there was a paucity of data regarding diagnosis from the ED and final surgical diagnosis. This study overall demonstrated a concordance between diagnosis in the ED and final diagnosis (78.6%). This can assure the surgical consultant being called by ED colleagues that the need for surgical evaluation is legitimate. While just under one-half of this study population (48.5%) required operative intervention, this was reflective of underlying diagnoses in this population. Of those that required operative intervention, the variability of time to the operating room was also likely reflective of underlying diagnoses as well as systemic factors. For example, Davis et al.[19] saw a decrease in time from 48.4 to 16.6 hours from radiographic diagnosis to the operating room with the development of a specific emergency general surgery service, and Smith et al.[20] showed an increased likelihood of mortality in those receiving an urgent surgery after a weekend admission compared to a weekday (OR 1.27; CI 1.08 - 1.49). Delaying operative intervention for those needing emergency surgery has been associated with a higher mortality rate, as McIsaac et al.[21] demonstrated with an OR of 1.59 (CI 1.30 - 1.93) in a 2017 study, and as Nawijn et al.[22] demonstrated with improved survival for those with operative intervention in under 12 hours from presentation with an OR of 0.41 (CI 0.27 - 0.61). Out of

ED mortality was not evaluated in our study. However, there was wide variability in time to the operating room for patients for whom surgical consults were placed after admission.

The longer hospital length of stay seen in those patients first evaluated by an emergency physician likely is reflective of the higher rate of perforated viscus and deep organ space infection seen by the emergency physician cohort, whereas PA/APRNs did not see any patients with perforated viscus. The emergency physicians also saw more patients with Severity Index scores of 1 or 2, reflecting that they cared for patients with more urgent and life-threatening issues. The older age of the patient population seen by emergency physicians also likely was associated with longer length of stay as a marker of increased frailty and a higher American Society of Anesthesiologists score as seen by Eamer et al.[23] who found increased hospital length of stay with an adjusted ratio of 1.24.

Limitations. This study was limited by its retrospective nature as well as the population size. The institution has 24-hour general surgical coverage with in-house residents, which may increase the use of general surgical consult compared to a facility without in-house coverage.

CONCLUSIONS

This study highlighted the rapid and extensive work-up that patients with abdominal pain who receive a surgical consult receive prior to ED disposition. There were some differences in imaging and laboratory use between PA/APRNs and emergency physicians, but hospital length of stay likely more was impacted by underlying patient diagnosis. Although PA/APRNs saw younger patients with lower rates of hypotension, anemia, and elevated creatinine, there was minimal effect on time in the ED or time to surgical consult. Further research is needed to determine appropriate initial evaluation of these surgical patients prior to and in conjunction with surgical consult.

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Pre-Hospital Spinal Immobilization: Neurological Outcomes for Spinal Motion Restriction Versus Spinal Immobilization

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ABSTRACT

Introduction. New recommendations for emergency medical services spinal precautions limit long spinal board use to extrication purposes only and are to be removed immediately. Outcomes for spinal motion restriction against spinal immobilization were studied.

Methods. A retrospective chart review of trauma patients was conducted over a six-month period at a level I trauma center. Injury severity details and neurologic assessments were collected on 277 patients.

Results. Upon arrival, 25 (9.0%) patients had a spine board in place. Patients placed on spine boards were more likely to be moderately or severely injured [injury severity score (ISS) > 15: 36.0% vs. 9.9%, p = 0.001] and more likely to have neurological deficits documented by emergency medical services (EMS; 30.4% vs. 8.8%, p = 0.01) and the trauma team (29.2% vs. 10.9%, p = 0.02).

Conclusions. This study suggested that the long spine board was being used properly for more critically injured patients. Further research is needed to compare neurological outcomes using a larger sample size and more consistent documentation. ***Kans J Med 2022;15:119-122***

INTRODUCTION

Spinal column injuries can be catastrophic events if missed. To prevent such an occurrence, pre-hospital spine immobilization (SI) has been the gold-standard for patients with suspected spine injuries after trauma for decades until the National Association of Emergency Medical Services (EMS) Physicians and the American College of Surgeons Committee on Trauma published a change in protocol.[1,2] The rationale behind the practice of SI was to prevent motion of the spinal column to prevent injury to the spinal cord. Interestingly, with so much importance placed on total SI, only 0.5% of the reported one million blunt traumas each year in the U.S. resulted in spinal cord injury.[3]

Adequate spinal immobilization involves securely strapping a patient to a long spine board (LSB), thereby limiting thoracolumbar movement.[4] This is not without risk, as prolonged immobilization can lead to increased risk for pressure ulcers, shortness of breath, respiratory compromise, increased intracranial pressures, tissue breakdown, pain, and anxiety or combativeness.[4-7] Furthermore, these patients are subjected to unnecessary radiation and healthcare costs, because of needless LSB or cervical collar usage.[5,6,8,9] In a study by Tello et al.[4], additional imaging costs occurred when emergency departments (ED) initiated SI, even when EMS deemed it unnecessary. In their study examining 101 blunt force trauma patients that presented to the ED without cervical SI, none had true acute injuries, but 94 received CT scans and 9 received cervical spinal radiographs.

After recognizing these risks and costs, there was a change in SI protocol in 2013 by the National Association of EMS Physicians and the American College of Surgeons Committee on Trauma (later endorsed by the American College of Emergency Physicians and many other national organizations), providing more autonomy to prehospital personnel.[2] It distinguished between the previous traditional method of SI and what now is called spinal motion restriction (SMR). According to this protocol statement, one should have judicious use of LSB during transport weighing risks against potential benefits; however, cervical collar use and maintenance of the spine in a neutral position were to be continued for patients who met criteria. Previously, selective SI protocols have been shown to decrease spine immobilization in trauma patients by 40%.[10,11] This new recommendation limits LSB use to extrication purposes only, with LSB to be removed immediately after, including patients with known spinal fractures or injuries. The Medical Society of Sedgwick County has been working to implement the protocol change for all trauma patients in the county. This study aimed to determine neurological outcomes for SMR and SI patients using LSB under the revised protocol guidelines. A comparison was made between LSB and SI patients to see if implementation of the revised protocol was being used correctly. It was hypothesized that the SI is being implemented correctly and that its implementation has not impacted patient outcomes negatively.

METHODS

Patients and Settings. The Institutional Review Board of Ascension Via Christi Hospitals Wichita, Inc. approved this study for implementation. A retrospective chart review was conducted of all trauma patients with a documented spinal injury, under the care of the multi-disciplinary trauma team at an American College of Surgeons Committee on Trauma (ACSCOT) verified level I trauma center between January 1, 2014 to August 31, 2014. The trauma registry was queried to obtain a list of trauma patients with documented spinal injuries within the specified time frame. The resulting list was filtered by age, EMS provider, and trauma activation level.

Neurologic Examination Protocol. The EMS conducted a brief neurologic examination in the field both before and after injury victim extraction. In the trauma bay, the trauma team conducted an in-depth examination of the patient upon arrival evaluating both sensory and motor function to all limbs.

Data Collection. Data collected included: patient demographics (i.e., age, gender, race); trauma activation level; past medical history; spinal injury details; if the patient was placed on an LSB; any significant neurological medical history (i.e., paraplegia, neuromuscular diseases, neurological injury, ligament injury, disc injury, Parkinson's); motor and sensory assessments conducted at pre-extrication, post-extrication, and in the trauma bay; injury severity score (ISS) on admission; Glasgow Coma Scale (GCS) score on admission; vital signs (i.e., blood pressure, heart rate, respiratory rate); blood alcohol level; intensive

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care unit (ICU) admission and length of stay; the use of mechanical ventilation and number of days on a ventilator; procedures performed [i.e., tracheostomy, gastrostomy or percutaneous endoscopic gastrostomy (PEG) placement, and nasogastric or Dobhoff tube placement]; any delays in diagnosis; do not resuscitate and/or code status; comfort care; hospital length of stay; disposition status (i.e., home, rehabilitation, acute care hospital, skilled nursing facility); and mortality.

Data Analysis. Continuous data were reported as the mean ± the standard deviation of the mean or median (interquartile range) when continuous data were not distributed normally. Frequencies were reported for categorical data. Continuous variables were compared using t-tests and categorical data were compared using chi-square analysis or the Fisher's exact tests when appropriate. McNemar's tests were used to compare the concordance of neurological assessments done by EMS and emergency department staff. All tests were two-tailed and a $p \leq 0.05$ was considered statistically significant. All statistical analyses were conducted using SPSS software, version 19.0 (IBM® Corp., Somers, New York).

RESULTS

Records from 330 trauma patients initially were included based upon the registry search. Of these, 53 were excluded as these patients did not have adequate documentation in the chart to include in the study, leaving 277 (83.9%) patients in the study. Upon arrival to the trauma bay, 25 patients (9.0%) had an LSB in place. Patients placed on an LSB were, on average, younger than those not placed on an LSB (35.2 ± 21.5 vs. 46.9 ± 22.9 years; $p = 0.015$). Patients placed on an LSB were comparable to those not on an LSB regarding gender (male: 68.0% vs. 65.1%, $p = 0.770$) and race (Caucasian: 84.0% vs. 85.7%; $p = 0.768$). Patients placed on an LSB were more likely to be moderately or severely injured (ISS > 15, 36.0% vs. 9.9%; $p = 0.001$) and tended to have a GCS score of eight or less (12.0% vs. 2.8%), but this was not statistically significant ($p = 0.052$; Table 1). As expected per protocol, many patients who presented on LSB tested positive for ethyl alcohol (ETOH; 43.5%, n = 10). Interestingly, 26.4% (n = 61) of patients without SI also had a positive ETOH finding. There was no difference in proportion of patients with spinal injury between the groups and no patient in either group suffered spinal paralysis.

Thirty-five patients (12.6%) had a documented pre-injury history of a neurologic deficit/diagnosis (Table 2). Patients that were placed on an LSB were more likely to have a neurological deficit documented pre-extrication; however, the documentation of pre-extrication neurological assessments was inconsistent in the EMS run sheets. An increase in neurologic and motor deficits pre-extrication to post-extrication were seen for both patients not on an LSB (3-fold, 7 patients to 22 patients) and for those on an LSB (almost 2-fold, 4 patients to 7 patients). However, an in-depth chart review was completed, which revealed poor, inconsistent documentation in pre-extrication to post-extrication evaluation and patients with peripheral nerve injury from fractures were documented as worsening nerve injury. No central neurologic progression of injury was identified in any patient. Patients placed on an LSB were more likely to have neurological post-extrication deficits documented by EMS (30.4% vs. 8.8%; $p = 0.006$) and the trauma team (29.2% vs. 10.9%; $p = 0.018$) compared to those not on LSB.

Table 1. Injury severity and characteristics for patients who arrived on a spine board or without spinal immobilization.

Parameter	Treatment Group		p Value
	No Spine Board N (%)	Spine Board N (%)	
Number of observations	252 (91.0%)	25 (9.0%)	---
Glasgow Coma Scale (GCS) score group			0.052
≤ 8	7 (2.8%)	3 (12.0%)	
> 8	244 (97.2%)	22 (88.0%)	
Injury Severity Score (ISS) group			0.001
≤ 15	227 (90.1%)	16 (64.0%)	
≥ 16	25 (9.9%)	9 (36.0%)	
Positive alcohol test	61/231 (26.4%)	10/23 (43.5%)	0.082
Spine injury	50/252 (19.8%)	5/24 (20.8%)	1.000
Spine paralysis	0 (0.0%)	0 (0.0%)	---

Table 2. Neurological deficits for patients who arrived on a spine board or without spinal immobilization.

Parameter	Overall N (%)	Treatment Group		p Value
		No Spine Board N (%)	Spine Board N (%)	
Significant history	35 (12.6%)	33 (13.1%)	2 (8.0%)	0.752
Pre-extrication deficit[1]	11 (4.0%)	7 (2.8%)	4 (16.0%)	0.011
Post-extrication deficit (any)	29 (10.7%)	22 (8.8%)	7 (30.4%)	0.006
Post-extrication motor	18 (6.5%)	11 (4.4%)	7 (29.2%)	< 0.001
Post-extrication sensory	22 (8.1%)	17 (6.8%)	5 (21.7%)	0.027
Trauma deficit (any)	34 (12.5%)	27 (10.9%)	7 (29.2%)	0.018
Trauma motor	27 (9.7%)	21 (8.5%)	6 (24.0%)	0.025
Trauma sensory	18 (6.6%)	14 (5.6%)	4 (16.7%)	0.062

[1]Based on text information on EMS run sheets; considered to have deficit if sensory or motor deficits were mentioned. For some patients, injuries were described with no mention of neurological assessment.

Neurological assessments within individual patients were similar at post-extrication and in the trauma bay for overall deficits and sensory deficits ($p > 0.05$; Table 3). Documented motor deficits by EMS were concordant with those documented by the trauma team for the LSB group (29.2% vs. 25.0%; $p = 1.00$). However, for patients not placed on a spine board, a greater number of patients were recorded as having motor deficits in the trauma bay when compared to their EMS assessments (8.5% vs. 4.5%; $p = 0.01$). A review of the injury details for those with discordant motor assessments revealed poor documentation and only peripheral nerve injury due to fractures, but no central cord injury progression.

Table 3. Concordance of post-extraction neurological assessments and assessments done in the trauma bay.

Parameter	Patients with Deficit by Treatment Group					
	No Spine Board			Spine Board		
	Post Extraction N (%)	Trauma Bay N (%)	p Value[1]	Post Extraction N (%)	Trauma Bay N (%)	p Value[1]
Motor deficit	11 (4.5%)	21 (8.5%)	0.01	7 (29.2%)	6 (25.0%)	1.00
Sensory deficit	16 (6.5%)	14 (5.7%)	0.59	5 (21.7%)	3 (13.0%)	0.50
Any deficit	21 (8.5%)	27 (11%)	0.20	7 (30.4%)	6 (26.1%)	1.00

[1]Based on McNemar's test of proportions in dependent groups.

Those presenting on an LSB were subjected to more invasive, non-spinal procedures during their hospital stay compared to those who were not presenting on an LSB (84% vs. 63.5%, Table 4). These were primarily nasogastric and Dobhoff tube placements. No patient in either group suffered a delay in diagnosis of injuries. Complications between these two groups were comparable and not statistically significant.

Table 4. Procedures and complications for patients who arrived on a spine board or without spinal immobilization.

Parameter	Overall N (%)	Treatment Group		p Value
		No Spine Board N (%)	Spine Board N (%)	
Number of observations	277 (100%)	252 (91.0%)	25 (9.0%)	---
Surgical procedures (excluding spine)	181 (65.3%)	160 (63.5%)	21 (84.0%)	0.040
Nasogastric or Dobhoff tube	11 (4.0%)	8 (3.2%)	3 (12.0%)	0.066
PEG tube	7 (2.5%)	6 (2.4%)	1 (4.0%)	0.488
Tracheostomy	3 (1.1%)	3 (1.2%)	0 (0.0%)	1.000
Gastrostomy tube	3 (1.1%)	2 (0.8%)	1 (4.0%)	0.248
Delayed diagnosis	0 (0.0%)	0 (0.0%)	0 (0.0%)	---
Complication[1]	19 (6.9%)	16 (6.4%)	3 (12.0%)	0.395

PEG = Percutaneous endoscopic gastrostomy.
[1]For complications, n = 276 for overall and n = 251 for patients not on the spine board.

As would be expected due to higher ISS and lower GCS scores, patients placed on an LSB were admitted more often to the ICU (12.0% vs. 1.6%), spent more time in the ICU (2.0 vs. 1.2 days), more often required mechanical ventilation (28.0% vs. 7.1%), and required greater time on mechanical ventilation (1.2 vs. 0.4 days; Table 5). Mortality also was greater for patients arriving on an LSB (16.0% vs. 2.4%; p = 0.008) as was the proportion of patients placed on comfort care (12.0% vs. 1.6%; p = 0.18).

DISCUSSION

Of the one million blunt traumas each year in the U.S., only 0.5% results in a spinal cord injury.[4] The rarity of spinal cord injury has brought into question the need for placing most trauma patients on LSB. Subsequently, revised protocols for EMS spinal precautions limit LSB use to extrication purposes only, or for those with known

Table 5. Hospital utilization and discharge destination for patients who arrived on a spine board or without spinal immobilization.

Parameter	Overall N (%)	Treatment Group		p Value
		No Spine Board N (%)	Spine Board N (%)	
Number of observations	277 (100%)	252 (91.0%)	25 (9.0%)	---
Comfort care	7 (2.5%)	4 (1.6%)	3 (12.0%)	0.018
Intensive care unit admission	91 (32.9%)	77 (30.6%)	14 (56.0%)	0.010
Intensive care unit days	1.2 ± 3.5	1.2 ± 3.5	2.0 ± 2.9	0.003
Mechanical ventilation	25 (9.0%)	18 (7.1%)	7 (28.0%)	0.003
Ventilator days	0.5 ± 2.4	0.4 ± 2.4	1.2 ± 2.4	0.001
Hospital length of stay (days)	4.2 ± 7.2	4.1 ± 7.2	5.7 ± 6.8	0.083
Mortality	10 (3.6%)	6 (2.4%)	4 (16.0%)	0.008
Discharge destination[1]				1.000
Home or home with health care	181 (74.2%)	167 (74.2%)	14 (73.7%)	
Other facility or AMA[2]	63 (25.8%)	58 (25.8%)	5 (26.3%)	

[1]For discharge destination, only patients that survived hospitalization were included: N=244 for overall, N=225 for patients not on the spine board, and N=19 for patients on a spine board.
[2]AMA: against medical advice.

or suspected neurologic injury. Such protocols are followed easily and accurate for predicting need of SI.[4] Burton and colleagues[10] performed a study of 31,885 trauma patients using an EMS SI protocol for trauma patient spine assessment and selective patient immobilization. Of these patients, 154 were identified by hospital records as having acute spine fractures. They identified only one non-immobilized patient with an unstable spine fracture, but this patient suffered no long-term sequelae. In this single center, retrospective review, there were no patients found to meet criteria for SI that were not placed on LSB. This protocol application limited patients presenting on an LSB to only 9% of those studied, significantly lower than the reported 87% national average prior to the new SI guidelines.[10]

The current study's findings suggested an acceptance of the revised guidelines potentially could lower the cost of working up trauma patients. As previous studies have suggested, patients on an LSB for periods of time report increased pain, tissue breakdown, and respiratory compromise, which led to "false-positive exams for midline vertebral tenderness",[9] and therefore, increased imaging and cost of care.[4,8,12] Clemency et al.[12] in 2018 observed that patient charts before and after the implementation of the new SMR protocol demonstrated the decrease in backboard utilization was associated with a decrease in spine imaging in the ED.

Prehospital handling of trauma patients has been the primary focus of a possible cause of secondary cord injury.[3] In the presented study, for patients not placed on a spine board, a greater number of patients were

recorded as having motor deficits in the trauma bay when compared to their EMS assessments. Upon further review of charts, however, consistent documentation on-site by EMS pre- and post-extrication and trauma team assessment was lacking. The neurologic disparities were due to fractures or other peripheral injuries, not to spinal column injuries resulting in neurologic sequelae. No patients in this study had paralysis from a spinal cord injury. As 0.5% of all trauma patients have spinal injury, a much larger study involving multiple trauma centers is necessary to assess adequately how SI affects the number of spinal column or spinal cord injuries.

Several studies showed a low rate of prehospital personnel failing to provide SI where it was needed.[4,10,13,14] For example, Paterek et al.[13] examined 18 months of charts from an EMS service dispatched as "motor vehicle crash" or "fall". Their results revealed 0.3% (4/1,075) to have been under-immobilized. Furthermore, all four had altered mentation or intoxication, and presented no cervical spine injuries. Additionally, there was evidence suggesting EMS personnel were just as accurate and in agreeance with the spinal immobilization protocols as ER physicians. Browne et el.[15] showed EMS and ED providers were similar in their assessments of important predictive factors of cervical spine injuries in pediatric blunt trauma patients. The current study also demonstrated EMS and ED agreement, seeing that no patients were placed in SI after arriving as a trauma. Given the low rate of prehospital missed cervical spinal injury cases and the current study's findings, it was recommended that emergency services in the field were immobilizing patients properly as necessary per revised EMS protocol for SI.

The trauma services community can take much from this study. It suggested patients were arriving to trauma centers adequately treated in the field and appropriate patients were immobilized based on protocol. However, it has become apparent through the presented study that consistent documentation of patient injuries in the field pre- and post-extrication versus in-hospital trauma care providers needed to be improved. A more consistent, standard approach to documenting between the two groups may provide better patient care and guide future research efforts.

Limitations. This study had several limitations. As a retrospective review from one trauma center during a six month period, the findings were limited to the validity and reliability inherent in retrospective reviews. Of the approximately one million trauma patients in the U.S. seen annually, this study included only 277. Thus, the findings may not generalize to every trauma system and patient population. A larger, multicenter review spanning several years after these new EMS guidelines were implemented is needed to compare neurologic outcomes in spinal column injury patients who were placed on an LSB for immobilization versus those treated without LSB immobilization. Furthermore, 26.4% of patients arriving to the trauma bay without an LSB were positive for ETOH. This finding can be explained as EMS providers were unable to detect ETOH on patients due to either poor screening or more likely due to the patient having a small concentration of ETOH which was clinically undetectable. All trauma patients had blood ETOH screening upon arrival to the trauma bay, regardless of suspicion of ETOH presence. The ETOH positive category labels all patients who have a blood ETOH level > 0, many patients of which cannot be identified clinically as having previous ETOH intake.

CONCLUSIONS

The LSB was being used properly for more critically injured patients. Further research is needed to compare neurological outcomes for spinal restriction versus immobilization using a larger sample size and more consistent documentation of pre-extrication (EMS) examination.

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Keywords: spinal injuries, emergency medical services, immobilization, risk assessment, retrospective studies

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Treatment History as a Predictor for Change in Visual Acuity After Surgical Correction of Diabetic Retinal Traction Detachment

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ABSTRACT

Introduction. Tractional retinal detachment remains a leading cause of severe, persistent vision loss in those with diabetic retinopathy. The purpose of this study was to investigate factors in treatment history associated with outcomes of surgical repair for diabetic tractional retinal detachments.

Methods. A retrospective, cohort study design was used. Data on 64 eyes that underwent surgical correction for diabetic tractional retinal detachment were analyzed. For eyes that received any treatment within three months of surgery, the entire treatment history was recorded and analyzed. Eyes with no recorded treatment or only remote treatment outside of three months prior to surgery were considered treatment naïve.

Results. Of all eyes, 56% (n = 36) had received treatment for proliferative diabetic retinopathy in the three months prior to surgery. Among those treated, 50% (n = 18) of eyes had both laser and bevacizumab treatments and 44% (n = 16) had only bevacizumab injections. Average best corrected visual acuity (BCVA) for all eyes improved from 1.68 LogMAR (20/1,000) pre-operatively to 1.34 (20/400) post-operatively, p = 0.0017. Average BCVA in eyes with pre-operative treatment history improved from 1.73 (20/1,000) pre-operatively to 1.09 (20/250) post-operatively, p = 0.0006. Average BCVA in treatment-naïve eyes was 1.60 (20/800) pre-operatively and 1.66 (20/1,000) post-operatively, p = 0.638. Eyes treated only with intravitreal injections had an improvement in BCVA from 1.81 (20/1,200) pre-operatively to 0.91 (20/160) post-operatively, p = 0.006. There was no difference between tamponade agents when comparing mean change in BCVA, p = 0.944.

Conclusions. There was a relationship between intravitreal injection treatment history and a large improvement in BCVA, and a similar association between combined laser and injection treatment history and improvement in BCVA. These relationships, however, were not present when controlling for confounders in multivariate analysis. There were likely other factors in the patient's treatment history such as timing, quantity, and order of treatments that played a role in the bivariate association observed in this study. ***Kans J Med 2022;15:123-126***

INTRODUCTION

Diabetic retinopathy is a pervasive complication of diabetes mellitus, with an estimated prevalence of 28.5% to 40.3% among U.S. adults 40 years or older with diabetes mellitus.[1,2] Among this same population, the prevalence of vision-threatening retinopathy, defined as severe non-proliferative retinopathy, proliferative diabetic retinopathy (PDR), or macular edema, is estimated to be 4.4% to 8.2%.[1,2]

Although laser photocoagulation treatment for proliferative diabetic retinopathy is associated with favorable long-term visual acuity stability in most patients,[3] tractional retinal detachment (TRD) remains a leading cause of severe, persistent vision loss in those with diabetic retinopathy.[4] Despite better control of PDR with intravitreal injections as an adjunct to laser,[5] and effective control of non-proliferative diabetic retinopathy (NPDR) with intravitreal injections alone,[6] once a retinal detachment has developed, surgery is the only remaining intervention to prevent profound blindness. Pars plana vitrectomy (PPV) can be effective in improving anatomical and visual outcomes in patients with TRD.[7] Newer 23 and 25 gauge vitrectomy systems and even hybrid techniques have shown non-inferior outcomes to older 20 gauge instruments while offering advantages such as shorter operating times, reduced pain and inflammation,[7-11] minimal induced astigmatism, and improved patient comfort.[10]

Significant research has been done to identify outcome predictors among patients undergoing PPV for diabetic complications, with focus on surgical technique or pre-existing conditions.[7-9,12] For instance, the use of silicone oil as a tamponade agent has been associated with poorer outcomes when compared to C3F8 or SF6 gasses.[7-9] Regardless of poor outcomes in certain cohorts, the overall success rate defined as final anatomical reattachment approaches 80% for all studied eyes.[7] Although several studies and case reports have explored bevacizumab as a pre-surgical treatment,[12-17] little research focus has been given to pre-surgical treatment history of intravitreal injections and laser photocoagulation as outcome predictors for surgical repair of diabetic TRD. The purpose of this study was to identify factors in treatment history associated with outcome measures (i.e., change in visual acuity and retinal re-attachment rate) among patients who underwent surgical repair of diabetic tractional retinal detachments.

METHODS

Participants. A retrospective chart review was performed at a single ophthalmology group practice for patients seen between January 1, 2011 and June 15, 2018 inclusive. Eligible patients were 18 years or older who underwent surgical repair of diabetic TRD. Patients who had fewer than 30 days of post-operative follow up were excluded.

Instrument. A list of eligible patients was compiled by filtering International Classification of Disease (ICD) and Current Procedural Terminology (CPT) codes for patients with diabetic retinopathy who underwent surgical repair of either vitreous hemorrhage or retinal lesion. A list of 445 patients was generated, from which patients who met the inclusion criteria were selected by co-investigators. Data were abstracted into REDCap®.[18] Data collected included patient demographics, pre-operative baseline measurements [e.g., treatment history, best corrected visual acuity (BCVA), intraocular pressure (IOP), and macula involvement], operating surgeon, surgical instruments and materials (e.g., instrument gauge, tamponade agent), post-operative

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measurements (e.g., peak BCVA, IOP, anatomical success), intra- and post-operative complications, hypertensive status, hemoglobin A1C, and renal status (i.e., dialysis).

If an eye received treatment in the three months prior to surgery, all treatment history for diabetic retinopathy was recorded regardless of date of administration. A remote history of treatment outside of the three months prior to surgery also was recorded, but these eyes were considered treatment-naïve for the purpose of this study, as three months has been used previously as a washout period when studying intravitreal bevacizumab.[19] All visual acuity measurements were converted to log of the minimum angle of resolution (logMAR) notation for analysis.[20]

Procedures. This study was approved by the University of Kansas School of Medicine-Wichita's Human Subjects Committee and the ophthalmology practice's privacy officer. All work was compliant with the Health Insurance Portability and Accountability Act of 1996, and the research adhered to the tenants of the declaration of Helsinki. A retrospective chart review was performed, data were abstracted, de-identified, and analyzed in SAS (Version 9.4) software (SAS® Int. Inc., Cary, NC).

Statistical Analysis. Descriptive statistics for nominal, categorical, and continuous variables were conducted using PROC FREQ and PROC UNIVARIATE in SAS. Shapiro-Wilk was used for the test of normality of continuous variables. Bivariate analysis was conducted using treatment type, surgeon, tamponade agent, and pre-operative characteristics [e.g., rhegmatogenous retinal detachment (RRD), macula involvement, and dialysis] by pre-operative to post-operative change in BCVA. Retinal re-attachment rate was not included as an outcome measure for statistical analysis due to all but one eye achieving anatomical re-attachment. In case of non-normal distribution with appropriate transformation operations, the rank transform approach to nonparametric methods was used as combination of PROC RANK and PROC GLM in SAS to enable use of covariates in the models tested for change in BCVA. Several longstanding nonparametric tests including Kruskal-Wallis are either exactly equivalent to rank transform tests or are nearly equivalent to them. Covariates-adjusted least-squares means (to estimate the marginal means over a balanced population) were used for pairwise comparisons of groups by Tukey test using Kramer adjustment. All statistical tests at $p \leq 0.05$ were significant.

RESULTS

A total of 64 eyes from 53 patients were included in the study (Table 1). Eyes that had pre-or post-operative acuities of light perception (LP) or no light perception (NLP) could not be converted to LogMAR.[20] Two eyes improved from LP to count fingers (CF), three eyes improved from LP to hand motion (HM), and one eye improved from NLP to HM. One eye developed neovascular glaucoma and worsened from 20/400 to NLP.

Table 1. Patient characteristics.

Variable	
Number of eyes	64
Number of patients	53
Number (percent) of eyes in males	26 (41%)
Number (percent) of eyes in females	38 (59%)
Mean age at surgery (years)	49
Mean pre-operative IOP (mm Hg)	15
Mean post-operative day 1 IOP (mm Hg)	17
Number (percent) hypertensive patients	46 (72%)
Number (percent) dialysis patients	13 (20%)
Number (percent) type I DM	14 (22%)
Number (percent) type II DM	50 (78%)

Of all eyes, 56% (n = 36) had received treatment for proliferative diabetic retinopathy in the three months prior to surgery. Among those treated, 50% (n = 18) of eyes had both laser and bevacizumab treatments, 44% (n = 16) had only bevacizumab injections, one eye had only laser photocoagulation, and one eye had only ranibizumab injections. Seventeen percent (n = 11) of all studied eyes had received remote treatment longer than three months prior to surgery, and 27% (n = 17) of all studied eyes had no recorded treatment.

Three surgeons operated and used 25G instruments on all procedures except one, which used 20G instruments. Thirty-five percent (n = 25) of eyes were tamponaded with silicone oil, 13% (n = 8) with C3F8, 14% (n = 9) with SF6, and 14% (n = 9) with air. Sixteen percent (n = 10) of eyes had a combined tractional and rhegmatogenous retinal detachment, and 31% (n = 20) had macula involvement.

The most common complications were post-operative vitreous hemorrhage (38%, n = 24) and re-detachment (9%, n = 6). No intra-operative complications were reported. Of note, one eye did not achieve final anatomical success but BCVA did not change from CF pre-operatively. Among all eyes, mean post-operative IOP was 17 mm Hg (range: 5 - 38 mm Hg), and 22% (n = 14) of eyes had an IOP greater than 21 mmHg at the one-day post-operative visit.

Average BCVA for all eyes improved from 1.68 (20/1000, SD 1.07) pre-operatively to 1.34 (20/400, SD 1.05) post-operatively, p = 0.0017 (Figure 1).

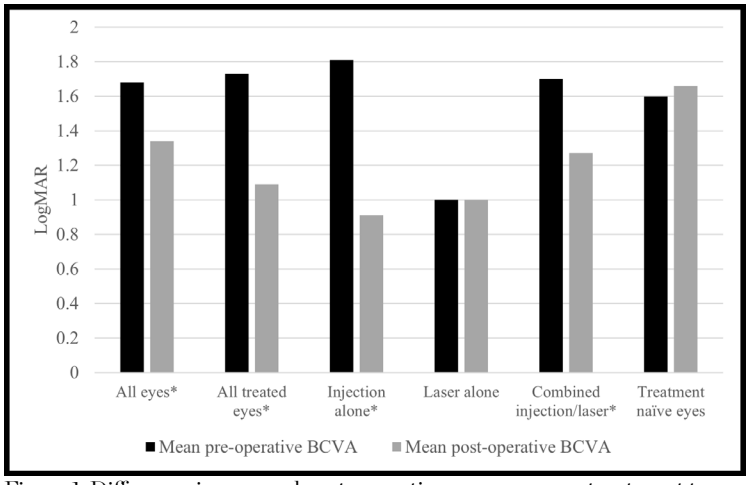

Figure 1. Difference in pre- and post-operative means among treatment types. *p < 0.05 when comparing pre-operative to post-operative BCVA

When comparing average change of pre-operative to post-operative BCVA between treatment types, eyes with treatment history of only injections changed 1.031 LogMAR, which was better than 0.091 LogMAR for treatment-naïve eyes, p = 0.031. Mean change of pre-operative to post-operative BCVA for eyes with treatment history of combined laser and injections was 0.529 LogMAR and was not different from any other treatment types, including no treatment. There was no difference between tamponade agents when comparing mean change in BCVA, p = 0.944. When comparing post-operative BCVA between tamponade agents, silicone oil (1.77 LogMAR, 20/1,200 snellen) and no tamponade (1.73 LogMAR, 20/1,000) were worse than air (0.66 LogMAR, 20/90) and SF6 (0.43 LogMAR, 20/50), p = 0.001. C3F8 (1.163 LogMAR, 20/300) was not different from any other agent.

One surgeon's (A) cases had an average BCVA improvement from pre-operative to post-operative of 1.125, p = 0.002, and the other two surgeons' (B, C) mean changes in BCVA pre-operatively to post-operatively were not different than zero (0.217, p = 0.286 and 0.282, p = 0.086). The improvement by 1.125 for surgeon A was greater than the improvements by 0.217 and 0.282 for surgeons B and C respectively, p = 0.021. Of note, surgeons A and C had fewer treatment-naïve eyes, and surgeon B had the largest number of cases (Table 2).

Table 2. Number of cases by surgeon.

Surgeon	A	B	C
Total number of cases	18	35	11
Treatment-naïve	2	24	1
Any treatment	16	11	9
Laser photocoagulation only	0	0	1
Laser plus injection	8	4	6
Injection only	8	7	2
One injection	7	4	1
Two injections	0	1	0
Three or more injections	1	2	1

Presence of a rhegmatogenous component (p = 0.166) or macular involvement (p = 0.273) did not have an association with change in visual acuity. Final reattachment was achieved on 98% (n = 63) of eyes. Six eyes re-detached, and five were reattached successfully with seven more surgeries total. Treatment type (p = 0.158), tamponade agent (p = 0.620), or surgeon (p = 0.059) were not associated with a change in the pre-operative to post-operative BCVA when analyzed in ANOVA (p = 0.092).

DISCUSSION

This study suggested that all eyes with any treatment history, treatment history of injection only, and treatment history of both injection and laser had pre-operative to post-operative improvements in visual acuity. Nearly half of all eyes (44%, n = 28) in this study had not received any form of treatment for their retinopathy in the three months prior to the date of surgery. This differed from a prior study that reported only 15% had untreated eyes.[7] By excluding remote treatments beyond three months, the current study may have elevated this proportion artificially. Instrumentation gauge in this study reflected trends of surgeons' increased use of 25G instruments,[8-11] and a re-detachment rate of nine percent and no reported intra-operative complications in this study were consistent with similar literature reports.[21]

There appeared to be no consensus for method of reporting visual acuity as an outcome of interest, with some studies using categorical data to report outcomes,[3,7,21] whereas others reported means of pre- and/or post-operative acuities.[8,9,12,22] The current study averaged the delta of the pre- and post-operative BCVA for bivariate and multivariate analysis. While there was no Snellen conversion for a change in LogMAR, this method has the advantage of utilizing continuous data for the eye's pre-operative acuity and may better account for the severity of the disease prior to surgical intervention. While this method may overestimate the surgical results of eyes with pre-surgical poor acuity due to dense vitreous hemorrhage or other media opacities but an intact neurosensory macula, the potential value of controlling a confounding factor was worth considering. For example, when analyzing tamponade agent by post-operative BCVA, the current study found similar results to prior research,[7,8] suggesting silicone oil was associated with poorer visual outcomes. When using change in pre- to post-operative BCVA, however, the current study suggested no difference in results between tamponade agents.

In bivariate analysis, treatment type and operating surgeon were associated with a change in BCVA. A prior study that retrospectively evaluated intravitreal bevacizumab within one month of surgery found BCVA improvements in all analysis groups, even those not receiving a pre-operative injection.[16] The current study expanded on that finding in that eyes with a three month or more history of intravitreal injection treatment were associated with a large improvement in pre-operative to post-operative BCVA. Where this study differed was the suggestion that vision in treatment-naïve eyes did not improve pre- to post-operative. The visual improvement in injected eyes may be a result of the better proliferative diabetic retinopathy control physicians are achieving with injections,[23] or an improvement in vitrectomy technique, as others have suggested.[13,16]

The surgeon (A) with a significant difference between pre- and post-operative acuities had a low proportion of treatment-naïve eyes and a high proportion of eyes with a history of single bevacizumab injections. This suggested the surgeon may be using bevacizumab as a pre-treatment for a higher proportion of their surgical cases, and this usage pattern certainly fit previous studies' definition of bevacizumab pre-treatment.[16,17] However, caution must be exercised with bevacizumab pre-treatment as there have been reports of rapid progression of TRD following intravitreal bevacizumab.[14,15]

Regardless, when the variables of operating surgeon, treatment type, and tamponade agent were all controlled for in multivariate analysis, none of these variables were associated with a change in BCVA from pre- to post-operation. This lack of association may be due to other factors in the treatment history, such as timing, quantity, or order of treatments. While the number of eyes analyzed in the current study was like other studies evaluating diabetic TRD outcomes,[8,17,22] the relative

infrequency of this diabetic complication made it challenging to power a study with so many potential confounding factors.

Limitations. Although the study was to include the collection of information regarding patients' control of diabetes and hypertension, these data were not readily available in all patients' charts. Of the 46 patients who were reportedly hypertensive, blood pressure measurements were not available, although all were documented to be on an oral antihypertensive. The length of diabetes prior to surgery and hemoglobin A1C also was missing from most charts. These missing data prevented this study from controlling for possible systemic confounders of hypertension and diabetes control, which have not been established to be associated with poor visual outcome, but have been theorized to be significant with a larger sample size.[22] Another limitation of this study was the lack of control for media opacities, specifically dense vitreous hemorrhage and timing of cataract extraction, if performed. This limitation potentially overestimated an association with acuity change, but if included, these extra variables likely would diminish the statistical power of the analysis further.

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Keywords: diabetic retinopathy, bevacizumab, retinal diseases, visual acuity, retrospective studies

KANSAS JOURNAL of MEDICINE

An Overview of Tobacco Policies in Kansas Unified School Districts

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ABSTRACT

Introduction. In 2019, 25.8% of Kansas high school youth reported using any form of tobacco product. Schools can prevent and reduce youth tobacco use by adopting comprehensive tobacco policies, which include all tobacco products, on school grounds and at school-sponsored, off-campus events, for all individuals at all times, and integrate cessation services for students who violate the tobacco policy. The purpose of this study was to determine the prevalence of comprehensive tobacco policies in unified school districts (USD) across Kansas to determine how many schools have adopted such policies.

Methods. All 286 USDs in Kansas were eligible to participate in this study including elementary, middle, and high schools. Participating schools were asked to upload their policies to a website developed by the Kansas Department of Health and Environment (KDHE). Frequencies and percentages were computed to identify the type of tobacco products prohibited, the locations where tobacco use is prohibited, who is prohibited from using tobacco, when tobacco is prohibited, and consequences of students' violation of the tobacco policy.

Results. Several USD policies met some of these comprehensive recommendations; however, 97.9% (n = 280) did not. In other words, 2.1% of USD policies (n = 6) were comprehensive in Kansas. Most districts (98.3%, n = 281) presented policies prohibiting use of all forms of tobacco for students, but policies often offered more leniency for faculty/staff and visitors. Fewer districts presented policies prohibiting use of all tobacco products for staff/faculty (73.1%, n = 209) and visitors (45.8%, n = 131) of policies.

Conclusions. Nearly all USDs in Kansas have an opportunity to strengthen their tobacco policies. Relatively simple edits can be made to prohibit all tobacco products, prohibit use on school grounds and at school-sponsored, off-campus events, ensure these policies apply to everyone, at all times, and integrate cessation resources for students who violate the tobacco policy. ***Kans J Med 2022;15:127-130***

INTRODUCTION

Smoking is the leading cause of preventable death in the United States.[1] This leads to a national expense of $170 billion in direct medical costs annually, which could be saved if the initiation of tobacco products among youth were prevented.[2] In 2019, 16.2% of Kansas adults smoked combustible cigarettes. This exceeded the national median of 14.0%.[3,4] In 2019, 25.8% of Kansas high school youth reported currently using any form of tobacco product, including combustible cigarettes, cigars, smokeless tobacco, and electronic cigarettes (e-cigarettes).[5] In the U.S., 89.7% of smokers started using tobacco products before they were 18 years old.[3]

From 2011 through 2018, the use of combustible cigarettes decreased among youth in the U.S.[3] However, youth usage of e-cigarettes has surged. The number of middle and high school students using e-cigarettes rose from 3.6 million in 2018 to 5.3 million in 2019, a difference of about 1.7 million.[3] In 2019, 22.0% of high school students in Kansas reported using e-cigarettes within the last 30 days.[5]

An important strategy to prevent and reduce youth tobacco use is the adoption of comprehensive policies that prohibit any use of tobacco in schools.[6-10] Comprehensive tobacco policies must prohibit all people (e.g., students, faculty/staff, and visitors) at all locations (e.g., inside, on school grounds, in vehicles, and at school-sponsored, off-campus events) from using all tobacco products (including e-cigarettes) at all times (e.g., during school hours and non-school hours) and include some form of tobacco intervention (e.g., cessation resources) for students violating the tobacco policy as the school's disciplinary action.

School tobacco policies are most effective when they prohibit use of all tobacco products, for all people, at all locations, and at all times.[4,6,11] Additionally, tobacco policies are most effective when schools uphold consistent consequences for students who violate tobacco policy.[6,12,13] The Kansas Department of Health and Environment (KDHE) recommended that consequences for students' violation of a tobacco policy have supportive disciplines, such as tobacco training or cessation program.[4] Such an intervention can be more effective than suspension or detention in promoting more positive student outcomes, such as improved likelihood of tobacco cessation.[12,14]

It is unknown how many school districts in Kansas have adopted comprehensive tobacco policies. This information is needed to reduce youth tobacco use. Therefore, the purpose of this study was to determine the prevalence of comprehensive tobacco policies in USDs across Kansas.

METHODS

Participants. All USDs in Kansas were eligible to participate in this study. Each USD had a policy which encompasses policies for all public schools located in the USD, including elementary, middle, and high schools. Private schools in Kansas were not included in this study, this was the only exclusion. Participation was voluntary and schools were not provided an incentive to participate.

Instrument. A Microsoft® Excel document was created by KDHE that established the variables that were to be abstracted from the policies. Variables assessed included "Do the districts have a policy prohibiting tobacco use?", "Are e-cigarettes included in the policy?", "Types of tobacco prohibited for students, faculty/staff, and visitors?", "Where is tobacco prohibited?", "When is tobacco use prohibited?", and "What is the student enforcement for the policy?".

Procedures. This study was deemed to be "not human subjects" by the University of Kansas Medical Center's Institutional Review Board. The Kansas Department of Education (KDE) requires every USD to have a structured policy book. This book includes topics such as student, faculty, and visitor policies. Although the structure of the policy books is standardized, the policies are not; each policy varies for

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each USD. KDE does not require USDs to have a tobacco policy for all three subgroups, and if a USD does not have one, the section title is included but the content is left blank. If a school district has a tobacco policy, these sections can include which tobacco products are disallowed, the locations that products are disallowed, and punitive measures for breaking policies.

To conduct this study, staff in the Kansas Department of Education (KSDE) e-mailed all 286 eligible schools on October 17, 2019, requesting that the superintendent of each USD submit their current tobacco policies for students, faculty/staff, and visitors. The e-mail included a link to a secure KDHE website. Participating schools were asked to submit their policies to the 2019 Kansas Comprehensive Tobacco-Free Schools Database. The website was designed for school personnel to upload their current tobacco policies. If the policy was not submitted by November 1, 2019, the school district was called by a Master of Public Health (MPH) student from the University of Kansas School of Medicine-Wichita. A maximum of three attempts were made to obtain school district participation.

Once all policies were submitted, the MPH student accessed the database to review the policies, then abstracted information and entered it into the Microsoft® Excel document developed by KDHE staff. Any tobacco policy that did not specify which products were prohibited were coded as "tobacco products not specified".

The data abstracted from the submitted policies were assessed by the research team to determine: 1) if school districts have a tobacco policy; 2) the type of tobacco products (including e-cigarettes) included in the policy; 3) the individuals the policy applies to (e.g., students, faculty/staff, and visitors); 4) the locations where tobacco is prohibited (e.g., in school buildings, on school grounds, in school vehicles, and school-sponsored, off-campus events); 5) when tobacco use is not permitted (e.g., during school hours, after school hours, at all times); and 6) what enforcement is included in the policy (e.g., cessation resources, tobacco education, suspension, detention, report to local law enforcement).

Analysis. Each policy was reviewed to identify which level (e.g., student, faculty/staff, and visitors) was most appropriate for each variable (e.g., prohibited tobacco products, locations, times the policy is enforced such as during school hours). Categories were pre-defined and associated with evidence-based tobacco policies. The primary outcomes for this study were the frequencies and percentages of the policies' inclusion of which tobacco products were prohibited, where tobacco products were prohibited, and when tobacco products were prohibited for each separate level and consequences of students' violation of tobacco policy.

RESULTS

All 286 USDs in Kansas were asked to participate, and all 286 participated in this study. Of the 105 counties represented, 34.3% (n = 36) were frontier [fewer than 6.0 persons per square mile (ppsm)], 32.4% (n = 34) were rural (6.0-19.9 ppsm), 18.1% (n = 19) were densely-settled rural (20.0-39.9 ppsm), 9.5% (n = 10) counties were semi-urban (40.0-149.9 ppsm), and the remaining 5.7% (n = 6) counties were urban (150.0 ppsm or more).[15]

Tobacco Products. The specific prohibited tobacco products were noted in 98.3% (n = 281) of student policies, 73.1% (n = 209) of faculty/staff policies, and 45.8% (n = 131) of visitor policies (Table 1). One (0.3%) student policy specified that only combustible cigarettes were prohibited.

Table 1. Tobacco products prohibited in school district policies.

Products Prohibited	Student Policy % (n)	Faculty Policy % (n)	Visitor Policy % (n)
Tobacco-free (all "tobacco" products are prohibited, including e-cigarettes)	98.3% (281)	73.1% (209)	45.8% (131)
Smoke-free (only combustible products are prohibited)	0.3% (1)	0.0% (0)	0.0% (0)
Tobacco products not specified (does not specify which tobacco products are prohibited)	1.4% (4)	26.9% (77)	54.2% (155)

Tobacco Prohibition by Location. Nearly all policies (98.3%, n = 281) prohibited some form of tobacco product (smoke free or tobacco free) in at least one of the following locations: school buildings, school grounds, school owned vehicles, or school sponsored events (Table 2). Nearly all (98.3%, n = 281) student policies prohibited some type of tobacco use in school buildings, on school grounds (e.g., parking lots), and in school vehicles. In 95.1% (n = 272) of student tobacco policies, some type of tobacco use was prohibited at school-sponsored, off-campus events (as a location).

Table 2. Policy locations prohibiting some type of tobacco use.

Location	Student Policy % (n)	Faculty Policy % (n)	Visitor Policy % (n)
In school buildings	98.3% (281)	71.3% (204)	45.1% (129)
On school grounds (parking lots and playing fields)	98.3% (281)	66.8% (191)	40.2% (115)
In school-owned vehicles	98.3% (281)	70.6% (202)	40.6% (116)
School-sponsored, off-campus events	95.1% (272)	36.0% (103)	9.8% (28)

In 71.3% (n = 204) of the policies, faculty/staff were prohibited from using some type of tobacco product in school buildings. In 66.8% (n = 191) and 70.6% (n = 202) of the policies, faculty/staff were prohibited from using some type of tobacco product on school grounds and in school-owned vehicles, respectively. In 36.0% (n = 103) of the policies, faculty/staff were prohibited from using some type of tobacco product at school-sponsored, off-campus events.

In 45.1% (n = 129) of the policies, visitors were prohibited from using some type of tobacco product in school buildings. In 40.2% (n = 115) and 40.6% (n = 116) of policies, visitors were prohibited from using some type of tobacco product on school grounds and in school-owned vehicles, respectively. In 9.8% (n = 28) of the policies, visitors were

prohibited from some type of tobacco product at school-sponsored, off-campus events.

Individuals Prohibited from Some Type of Tobacco Use. In 25.2% (n = 72) of the policies, only students (not faculty/staff or visitors) were prohibited from using some type of tobacco product (Table 3). In 14.7% (n = 42) of the policies, students and faculty/staff were prohibited from using some type of tobacco product; visitors were not addressed in these policies. In 9.8% (n = 28) of the policies, all possible individuals, including students, faculty/staff, and visitors, were prohibited from using some type of tobacco product.

Table 3. Location and individuals prohibited from some type of tobacco use.

Policy	Percent (n)
Tobacco-free for students only	25.2% (72)
Tobacco-free for all (faculty/staff and visitors excluded from policy at school-sponsored, off-campus events)	17.5% (50)
Tobacco-free for students and faculty/staff only	14.7% (42)
Tobacco-free for all (no exceptions)	9.8% (28)
Tobacco-free for all (visitors excluded from policy at school-sponsored, off-campus events)	8.0% (23)
Other (e.g., varying locations and individuals included in policy)	24.8% (71)

Location and Individuals Prohibited from Some Type of Tobacco Use. In 24.8% (n = 71) of all policies, the locations where tobacco usage was disallowed varied for students, faculty/staff, and visitors. In 17.5% (n = 50) of the policies, tobacco prohibitions were applicable to everyone, although this excluded faculty/staff and visitors from school-sponsored, off-campus events. The remaining 8.0% (n = 23) of the policies were applicable to everyone; visitors were excluded from school-sponsored, off-campus events.

Consequences for Students' Violation of a Tobacco Policy. The most common consequence for students' violation of a tobacco policy was law enforcement notification (Table 4). More than one-third of policies (36.7%, n = 105) presented this as the only consequence of student violation. Suspension was the second most common consequence, with 32.2% (n = 92) of policies. An additional 23.8% (n = 68) of policies stated law enforcement notification, notification of parents, and participation in a tobacco intervention, such as cessation services. Only 3.5% (n = 10) of policies did not state consequences for students' violation for the tobacco policy.

Table 4. Consequences for students' violation of a tobacco policy.

Consequences	Percent (n)
Law enforcement notification	36.7% (105)
Suspension	32.2% (92)
Parent notification, participation in tobacco intervention, and law enforcement notification	23.8% (68)
Not stated	3.5% (10)
Parent notification	1.0% (3)
Suspension and law enforcement notification	1.0% (3)
Parent and law enforcement notification	0.7% (2)
Report to principal	0.7% (2)
Detention	0.3% (1)

DISCUSSION

Tobacco policies in schools can be an effective strategy to reduce tobacco use among youth in the U.S. and in Kansas. Considering the increase of youth tobacco use, especially the use of electronic cigarettes,[4] and because youth who use electronic cigarettes are four times more likely to use combustible cigarettes later in life,[16] it is necessary to identify whether school districts offer the maximum protection for students.

Comprehensive tobacco policies must prohibit all people, at all locations, from using all tobacco products at all times and include some form of tobacco intervention as a consequence for students violating the tobacco policy as a form of discipline. It is essential to identify the number of Kansas USDs with comprehensive school tobacco policies to know how schools are helping to address the current issue with tobacco usage in youth. Although several policies met some of these recommendations, only 2.1% (n = 6) of the USD policies met comprehensive tobacco policy criteria.

The six USD policies that were comprehensive were in counties with varying population densities. Fifty percent (n = 3) of the policies were in a county classified as frontier; 33.3% (n = 2) were in a county classified as rural; and 16.7% (n = 1) of the policies were in a county classified as urban. None of the six counties shared borders with each another.

The results of this study suggested that school tobacco policies in Kansas vary largely from one USD to another. It is a positive first step that nearly all policies (98.3%) prohibit students' use of all tobacco-related products. Nearly all policies prohibited some type of tobacco product in at least one location on campus. Nearly all student policies prohibited some type of tobacco use in school buildings, on school grounds, and in school vehicles. In 95.1% (n = 272) of student tobacco policies, school-sponsored, off-campus events prohibited some type of tobacco use.

The results show that many schools were not consistent in what locations were included in their tobacco policies. Only 9.8% (n = 28) of policies had all areas for all individuals on campus. Although 25.2% (n = 72) of policies covered all areas, these policies only applied to students. Visitors often were left out of locations altogether in policies. In 72.7%

(n = 208) of policies, visitors were left out of some or all locations in the tobacco policies, with 45.2% (n = 94) of these policies specifically excluding visitors from school-sponsored, off-campus events.

A weakness in most Kansas USD policies is that not all faculty/staff are required to adhere to the tobacco policies. In Kansas, 25.2% of the policies (n = 72) prohibited only students from using some form of tobacco; faculty/staff and visitors were not prohibited from using tobacco in these policies. Prohibiting faculty/staff and visitors from tobacco use can improve attitudes toward comprehensive school tobacco policy implementation.[17] Faculty/staff and visitors play a key part in being positive role models for youth, and inclusion of them in the policy is needed for effective implementation. Additionally, inclusion of all faculty/staff can make policies easier to enforce when everyone is prohibited from using tobacco products on school grounds or events. As no other studies similar to the current study have been published, it is unclear how the prevalence of comprehensive tobacco policies in unified school districts across Kansas compares to other states. The field of tobacco prevention and treatment would benefit from extending this research to other states.

Kansas school districts can strengthen their tobacco policies by incorporating interventions or training for students who violate school tobacco policies about the risks of tobacco usage into their disciplinary actions. Only 23.8% of policies included an interventional opportunity as a consequence for students who violate the tobacco policy. This type of disciplinary action can produce positive outcomes (i.e., decreased use in the future), as it seeks to support youth using tobacco products to help them quit rather than solely punishing them. This allows students to learn more about the dangers of tobacco use and helps them in the long-term by teaching the risks and providing tools to quit.[17]

In Kansas, there was a lack of comprehensive tobacco policies adopted in the school districts throughout the state. School districts should be doing more to address tobacco use in youth. To protect Kansas youth adequately, school districts have an important opportunity to update their policies to prohibit tobacco products more comprehensively.

Limitations. This study includes all Kansas USDs, and generalizability beyond Kansas is limited. A limitation of this study was that it is unknown how well schools uphold their policies. Although policies may be comprehensive, if they are not followed or enforced properly, they are not as effective. Also, even though policies may include positive student intervention, the specific intervention being used was not included in the policies. It is important that an evidence-based curriculum be used as the educational component for the best results.

CONCLUSIONS

This study suggested that nearly all school districts in Kansas have an opportunity to revise and strengthen their policies to reduce youth tobacco use, including e-cigarettes. Necessary edits to these policies include prohibiting everyone from using any tobacco product on school property and at all school-sponsored, off-campus events, and more supportive violation consequences, such as a cessation intervention for students. By updating these policies, schools may have a substantial impact on preventing early tobacco usage among Kansas students.

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Keywords: tobacco, smoke-free policy, schools, Kansas

KANSAS JOURNAL of MEDICINE

Implementation of Effective Smoking Cessation Strategies for People Living with HIV: A Pilot Implementation Study

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ABSTRACT

Introduction. Use of tobacco products carries significant long-term health risks, and rates of smoking in persons living with HIV are as high as two to three times that of the general population. This study aimed to increase assessment of readiness to quit smoking and provide cessation counseling to patients receiving HIV care through an infectious disease clinic.

Methods. This study was a pilot implementation in a single-center teaching hospital. In total, 603 active patients with HIV were followed in clinic at the time of the study start; of these, 79 were active tobacco smokers (13%) and eligible for the intervention. Providers were educated on recommendations for tobacco smoking cessation counseling, intervention strategies, and options for treatment. Patients who smoked tobacco were assessed for readiness to quit. Cessation counseling and tobacco cessation mediations or nicotine replacement were provided at the discretion of the patient and physician based on visit discussions. Primary outcome measures were increase in assessment of readiness to quit and in providing cessation counseling. Secondary measures included tabulation of the number of patients provided with a tobacco smoking cessation treatment and those with a successful quit episode.

Results. There was a moderate increase in patients assessed for readiness to quit and who received tobacco smoking cessation counseling and treatment medications during the pilot. In total, 11 patients (8.7%) reported quitting smoking for at least two weeks.

Conclusions. Additional work on streamlined mechanisms to identify tobacco use and provide efficient and effective tobacco smoking cessation counseling are needed in this high-risk population.

Kans J Med 2022;15:131-134

INTRODUCTION

Use of tobacco products significantly increases the risk of chronic debilitating health disorders, ranging from cardiovascular disease to birth defects or malignancy.[1] With one in seven people worldwide using tobacco, it is imperative to raise awareness of this epidemic and implement effective smoking cessation strategies. Smoking rates in persons living with HIV (PLHIV) are of concern, as rates are discordant with total smoking prevalence in the United States over the past several decades.[2] Conservative estimates reported 47% of PLHIV smoke while this has trended down to 19.8% of the general population.[3-5]

Active efforts to address tobacco use are essential to mitigate health impacts of smoking and to educate those unaware of long-term ill-effects. Among patients cognizant of the harms and who are contemplating quitting, cessation counseling, along with nicotine-replacement has been shown to double the success rate of quitting.[1] Although these evidenced-based cessation strategies exist, they are not tailored to any specific patient population and feasibility of addressing these in a routine outpatient visit must be explored.

This study was performed in a university-based infectious disease (ID) clinic and although the percentage of tobacco smokers in PLHIV was found to be lower than the reported estimates, given ill effects of tobacco use and a lack of a best practice to approach the problem, this pilot implementation project was developed. The first aim of this study was to increase the compliance of assessment of readiness to quit and tobacco smoking cessation counseling to 90% within the clinic. The second aim was to reduce the number of HIV-positive tobacco smokers currently following in the ID clinic by 5% during the study period of six months. Aims were measured by (1) marking of the "Ready to quit" tab in the electronic medical record (EMR) Epic 02 Substance and Sexual History tab, and marking whether cessation counseling was provided, as well as (2) tabulating smoking cessation prescriptions ordered during the pilot and evaluating for attempts at tobacco smoking cessation at the conclusion of the study period.

METHODS

This project was exempted from formal informed consent by the Human Subjects Committee of the University Medical Center.

Considering the five domains of the Consolidated Framework for Implementation Research (CFIR),[6] an intervention was constructed. During the routine clinic visit for HIV-positive patients who were considered active tobacco smokers at the start of the project, tobacco smoking cessation counseling and/or intervention strategies such as phone and text counseling and tobacco cessation mediations or nicotine replacement were offered by the physician. Current smokers were defined as an adult who has smoked 100 cigarettes in his or her lifetime and who currently smokes cigarettes.

The inner setting for the intervention was one university-based ID clinic. The outer settings affecting implementation efforts included the background patterns of tobacco smoking in PLHIV. The individuals involved included the patient, three clinic nurses, two HIV pharmacists, and the ID physicians. Prior to the project start, all clinic staff were educated on the pilot process, EMR tabs, and project intervention. Physician providers in the clinic were provided three-minute smoking cessation counseling scripts to engage patients in a discussion of benefits of and options for smoking cessation counseling and treatment (see Appendix). This included specific contacts for telephone/text message smoking cessation counseling which were provided to patients via a brochure created by the study team. At the project start, patients were notified of the project verbally.

Tobacco smoking status was addressed for all clinic patients. The "Ready to quit" tab in the Epic EMR Substance and Sexual History section, which can be selected after asking the patient "Are you ready to quit smoking tobacco?", was used when applicable. Proceeding with

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cessation counseling and/or intervention strategies such as phone and text counseling and tobacco cessation mediations/nicotine replacement remained at the discretion of the patient and physician based on their readiness to quit. Prescriptions for smoking cessation medications or nicotine replacement were offered to those interested. Medications were individualized based on patient preference, prior cessation medication trials, past medical history, as well as review of primary insurance coverage and Missouri and Kansas Ryan White Aids Drugs Assistance Program formularies to avoid cost barriers. Patients were provided medication counseling at their visit by an HIV clinic pharmacist.

In the month following the six-month pilot project, assessment of patients who quit tobacco smoking was attempted through review of the EMR. To fill gaps or inaccuracies in documentation, follow-up phone calls were made to active tobacco smokers to attempt to confirm which patients had stopped tobacco smoking for two weeks or longer with the intent of remaining abstinent. Those who were documented in the chart or reported by phone call to have quit tobacco smoking for two weeks or longer were considered to have a "quit" episode.

Measures included the difference in PLHIV who identified as tobacco smokers at the beginning of the study and were assessed for readiness to quit both pre- versus post-intervention as well as those provided smoking cessation counseling pre- versus post-intervention. Numbers of patients were quantified by tally. The number of patients who were prescribed tobacco smoking cessation medications during the intervention period also was tallied. Quantification of these patient numbers was verified for accuracy through the review of the EMR. Finally, the total number of patients who had a quit episode during the study period was calculated. This pilot implementation project was not powered to detect statistically significant differences in reported quitters.

RESULTS

There were 603 patients with HIV followed actively in clinic at the time of the study. The clinic population included patients 18 years of age or older identifying as men, women, or non-binary. Additional demographics were not collected during this pilot project. Of the total active clinic patients, 79 were active tobacco smokers (13%). In the visit preceding the project start, 22/79 (28%) of these patients had been assessed for readiness to quit and 14/79 (18%) were provided counseling on tobacco smoking cessation. Post-intervention, this increased to 56/79 (71%) of patients who smoked being assessed for readiness to quit with 35/79 (44%) of patients being provided smoking cessation counseling (Figure 1). In total, 24 patients were provided with a smoking cessation medication or nicotine replacement and 11 patients reported quitting tobacco smoking, thus reducing the number of HIV-positive tobacco smokers following in the ID clinic by more than 5% during the pilot period of six months.

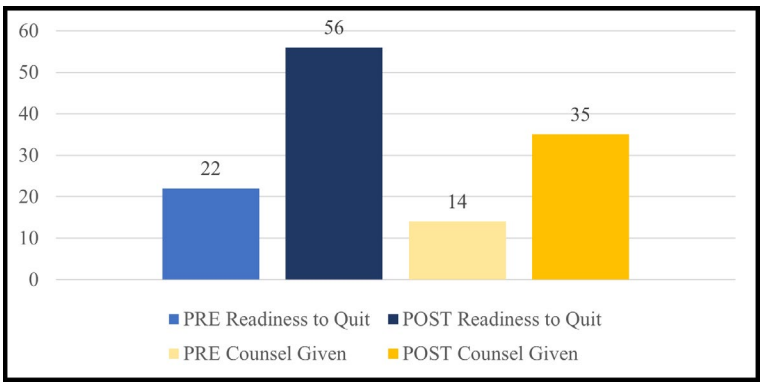

Figure 1. Number of patients who were assessed for readiness to quit smoking and for whom cessation counseling was given pre- and post-intervention.

DISCUSSION

Increased rates of depression, attempting to improve sense of well-being by smoking, and lack of social support in PLHIV may account for increased tobacco smoking prevalence in this group.[7] Simply assessing a patient's interest in quitting could be beneficial as data suggested HIV-positive patients have increased interest in quitting despite a higher prevalence of smoking.[5] Screening, along with brief interventions, and referrals for treatment programs for tobacco smoking cessation in an HIV clinic in non-treatment seeking smokers, found that those who participated in the intervention smoked fewer cigarettes per day, were less nicotine dependent, had fewer urges to smoke, and decreased withdrawal symptoms compared to non-participants.[7]

Using this framework, the pilot study had several strengths. First, tobacco smoking counseling practices of an entire ID clinic of PLHIV in a teaching hospital were evaluated. EMR visit functions were utilized as a point-in-time assessment for tobacco use status, readiness to quit, and whether counseling was provided during a visit. However, given the relatively low tobacco smoking percentage within this ID clinic population of PLHIV, it was unclear how generalizable cessation counseling practices, or the intervention, would be in larger HIV practices with a higher volume of active tobacco smokers.

As with many interventions including counseling, time can be a limiting factor in the intervention's success with potential for a cost-associated lost opportunity to address other patient or provider concerns. Provider comfort in addressing tobacco smoking and in prescribing tobacco smoking cessation medications may have created selection bias; however, efforts were made to adjust for limitations by having clinic nurses begin the workflow of assessment for smoking and by having medication discussions introduced by the same two HIV pharmacists independent of the provider. Furthermore, if patients did not report readiness to quit to the rooming nurse, additional selection bias may have been introduced as physicians may not have offered further counseling and treatment to these patients. Furthermore, assessing a quit episode of two weeks may not translate to a prolonged or permanent smoking cessation status leading to a falsely high success rate of the intervention, though the National Health Interview Survey defined a quit attempt at having stopped smoking for one day or longer with the intention of quitting.[8]

In summary, providers in the clinic were asked to provide smoking cessation counseling to HIV-positive smokers by engaging them in a three-minute provided script to discuss benefits of and options for

smoking cessation. Physicians also were asked to provide patients contacts for telephone and text message smoking cessation counseling and prescriptions for smoking cessation medications or nicotine replacement to reduce nicotine dependence[7] and improve the success rate of quitting.[1] While moderate increases were noted in the number of patients assessed for readiness to quit and in those provided counseling in this study, large gaps remain in those whose tobacco smoking was not addressed at the visit.

An implication of the pilot project was that the workflow for smoking cessation counseling is feasible and could be successful in increasing rates of tobacco use counseling and subsequent successful quit episodes in PLHIV. Further optimization of workflow within the EMR clinic visit encounter may be considered for improved capture of tobacco smoking discussions at each appointment.

As tobacco smoking tabs are not hard-stops in the EMR to proceed with the visit, a modification such as a best-practice alert presumably would increase compliance with addressing the issue. Given the multitude of goals of the physician during each routine encounter, an additional team member whose sole purpose was addressing tobacco smoking may increase time available for discussion of tobacco smoking cessation, especially if this could be conducted outside the timeframe allotted to the provider.

In considering the framework for implementation research, the implications of this pilot project were that in a larger scope and over a longer period this intervention could be successful, and this was supported by the SQUIRE framework for quality.[6,9] Developing a more efficient, yet effective tobacco smoking cessation workflow in a clinic practice could increase compliance with this quality measure and should be a priority in clinics treating PLHIV.

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Keywords: HIV infections, smoking, smoking cessation, counseling, pilot projects

APPENDIX

Example smoking assessment script for providers:
"Do you currently smoke cigarettes? (If yes) Are you ready to quit? CLICK YES OR NO BUTTON UNDER EPIC EMR SUBSTANCE & SEXUAL HISTORY.

As you know smoking has many negative health impacts. For most people, the best way to stop smoking is with a combination of medication and support. Have you tried Wellbutrin or Chantix before? (If so, how did these work for you? Did you have any side effects?) Have you tried nicotine replacement products? Which of these options do you think would work best for you?

Now let's talk about support. [Hands U-KanQuit brochure from clinic room] One way to get support for quitting is by getting set up with the U-KanQuit line. Another way is to get text message support from Smokefree TXT. Which sounds better for you? What plan can I help you make today to stop smoking?" CLICK COUNSELING GIVEN BUTTON UNDER EPIC EMR SUBSTANCE & SEXUAL HISTORY.

KANSAS JOURNAL of MEDICINE

Improving Stewardship of *Clostridioides difficile* Testing with EMR and Provider Phone Calls

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ABSTRACT

Introduction. Modern laboratory techniques cannot differentiate between *Clostridium difficile* colonization and infection; therefore, testing must be indicated clinically. To reduce hospital-onset of *C. difficile* infections (HO-CDI), Ascension Via Christi Hospitals (AVCH) in Wichita intervened in three stages by introducing: 1) a *C. difficile* testing algorithm; 2) an electronic medical record (EMR)-based decision support system to enforce said algorithm; and 3) phone calls from the infection prevention department to providers to discontinue tests not collected within 24 hours of the order. The goal of this study was to determine if these interventions improved the HO-CDI rate.

Methods. At AVCH, the three study periods were compared: baseline with algorithm training only, the EMR intervention, and the EMR intervention with additional phone calls (EMR with phone calls). Data were abstracted from the hospital EMR.

Results. A total of 311 charts were reviewed. Adherence to the algorithm increased from 34% at baseline to 52% after the EMR intervention ($p = 0.010$). During the EMR with phone calls period, more tests were discontinued (87%; $n = 39$) compared to baseline (54%; $n = 15$) and EMR (54%; $n = 15$; $p = 0.003$). The HO-CDI rate ranged from 8.5 cases per 10,000 patient-days at baseline, to 7.9 during EMR, to 4.0 during EMR with phone calls ($p = 0.007$).

Conclusions. The EMR and EMR with phone call interventions were associated with a significant decrease in the HO-CDI rate and an increase in provider adherence to the algorithm.

Kans J Med 2022;15:135-138

INTRODUCTION

Clostridioides difficile colonization is common among intestinal flora.[1] Infection is precipitated when prescribed antimicrobials disrupt the intestinal flora and lead to *C. difficile* overgrowth. *C. difficile* infections (CDI) continue to be one of the most prevalent hospital-acquired infections in the United States, comprising 12.1% of all healthcare-associated infections in 2011.[2] In 2015, CDI inpatient management was estimated to be 6.3 billion US dollars, requiring 2.4 million days of hospital stay.[3] Inpatient management of hospital-onset *C. difficile* infection (HO-CDI) is estimated to cost $34,157 per case.

In general, HO-CDI is defined as a positive *C. difficile* test collected 72 hours post-admission under the Medicare Hospital-Acquired Condition (HAC) Reduction program.[4] Hospitals with HAC scores greater than the 75th percentile among total HAC scores receive a 1% payment reduction which applies to all Medicare charges for the hospital within the applicable fiscal year.[5]

Current testing techniques may suggest the presence of the *C. difficile* toxin or organism but are unable to differentiate between asymptomatic carriers of *C. difficile* and those with true infection.[6] Therefore, laboratory testing for *C. difficile* needs to be supported by clinical indications of infection, as over-testing may lead to unneeded treatment and an increased rate of HO-CDIs, thus an inaccurate HAC score percentile.[6,7] Treatment of patients for CDI includes contact precautions and antibiotics. If the patient does not have true CDI, these put the patient at risk for anxiety, less interaction with health care workers, as well as antibiotic related adverse events such as drug-drug interactions and multidrug resistant organisms.[6,8] Unnecessary vancomycin paradoxically also has been shown to increase rates of *C. difficile*.[8]

To reduce clinically unnecessary *C. difficile* testing, Ascension Via Christi Hospitals (AVCH) introduced a *C. difficile* testing algorithm (Figure 1) along with training on its usage. To encourage usage of the testing algorithm, AVCH later introduced an electronic medical record (EMR)-based decision support system which notifies providers when ordering a *C. difficile* test that does not adhere to the testing algorithm. Similar interventions have been shown to reduce clinically unnecessary *C. difficile* testing up to 16%.[7,9,10] However, few studies have identified additional strategies that can be used in conjunction with EMR-based decision support systems to further reduce unnecessary *C. difficile* testing.[11] Therefore, AVCH supplemented their EMR-based decision support system with the assignment of a dedicated registered nurse from the infection prevention department to call ordering providers, asking them to cancel the test if it was no longer needed, based on AVCH's *C. difficile* testing algorithm.

The purpose of this study was three-fold. First, this study aimed to determine whether there was an increase in provider adherence to the AVCH *C. difficile* testing algorithm when supplemented with an EMR-based decision support system compared to algorithm training only (baseline). Second, this study examined the utility of the supplemented phone calls to prompt the cancelation of unnecessary tests. Finally, this study sought to determine if the EMR-based decision support system (with algorithm training) or the EMR system with algorithm training and phone calls intervention were associated with reductions in the HO-CDI rate.

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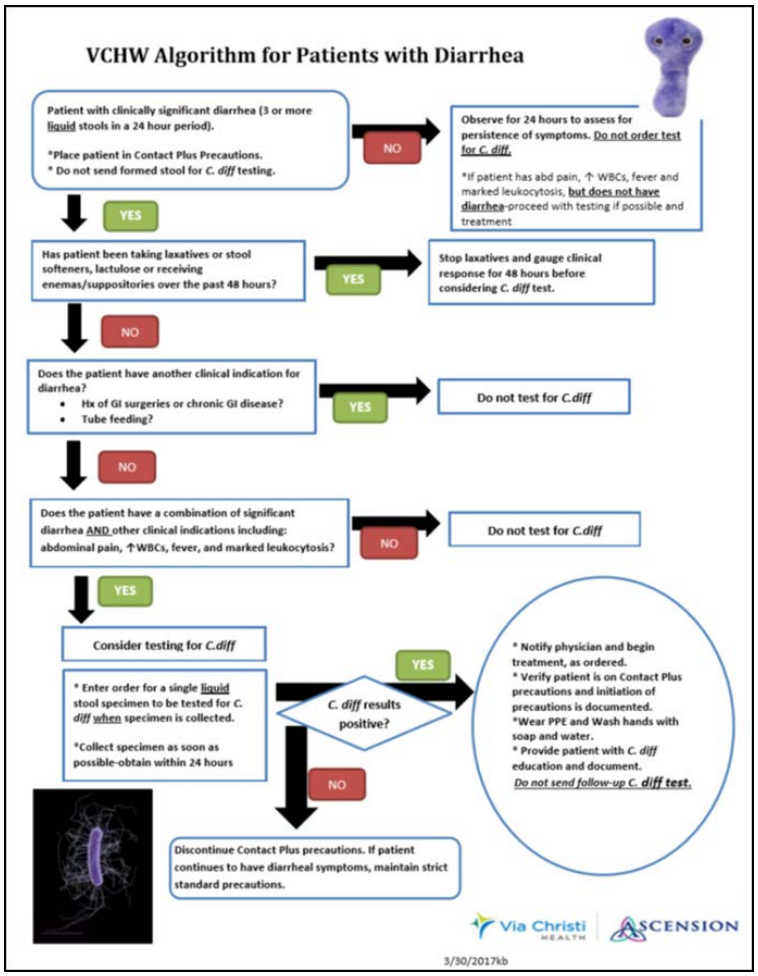

Figure 1. *C. difficile* testing algorithm.

METHODS

Participants. Patients included in this study were 18 years or older with a *C. difficile* test ordered at Ascension Via Christi Hospital (AVCH; at St. Francis or St. Joseph) in Wichita, Kansas. Study periods included: baseline (algorithm provider training only) from May 1, 2017 through September 30, 2018; EMR-based decision support system from November 1, 2018 through October 31, 2019; and EMR with a registered nurse calling ordering providers (EMR with phone calls) from November 19, 2019 through February 29, 2020. There were no exclusion criteria.

As this was a retrospective study, the microbiology lab at AVCH queried all *C. difficile* tests ordered during the study periods to identify eligible patients for this study. Among the 2,928 patients eligible for the baseline period, 131 patients were randomly sampled. Likewise, 121 patients of the 1,970 eligible patients were randomly sampled from the EMR period. All patients (n = 45) for whom a phone call was made were eligible and selected for the EMR with phone calls study period.

Instrument. All data were abstracted from AVCH's EMR via manual chart review. Demographic variables (e.g., insurance status, age) were abstracted to characterize the patient population. Abstracted information included variables related to the *C. difficile* testing algorithm, such as signs and symptoms of CDI (e.g., fever, liquid stools), pharmacologic causes of diarrhea (e.g., laxative, stool softener usage), alternate causes of diarrhea (e.g., chronic gastrointestinal disease), and previous positive *C. difficile* tests. Whether a stool sample collection was delayed (not collected within 24 hours of the test order) or within 72 hours of hospital admission also were abstracted. Data abstracted for discontinued and rejected tests included whether stool sample collection was delayed and within 72 hours of hospital admission. Indicators of severity (e.g., toxic megacolon, vasopressor usage, in hospital mortality) were abstracted to document patient outcomes.

The primary outcome of this study was the percentage of tests that were ordered according to the algorithm during the baseline and EMR periods to determine if there was a difference in algorithm adherence. The secondary outcome was the percentage of discontinued tests with delayed sample collection to determine if there was a difference between baseline, EMR, and EMR with phone calls. Finally, the overall HO-CDI rate was measured to determine if there were differences amongst the number at baseline, during the EMR intervention, and during the EMR with phone call intervention.

Procedures. This project was approved by the Institutional Review Boards at the University of Kansas School of Medicine and Ascension Via Christi Hospital. On March 30 and 31, 2017, the *C. difficile* testing algorithm was introduced to providers at AVCH internal medicine staff meetings. This algorithm required three or more liquid stools within a 24-hour period, no diarrhea causing drugs (e.g., laxatives, suppositories) within 48 hours, no other known causes of diarrhea (e.g., Crohn's disease, Roux-en-Y), and an indication of an infection (e.g., abdominal pain, fever, leukocytosis). Alternatively, if a provider suspected toxic megacolon in a patient not producing stool but has other signs of *C. difficile* infection, testing was recommended. Although not stated in the algorithm, this exception was understood by providers.

Regarding the algorithm's requirement of three liquid stools within 24 hours, tests ordered for patients who could produce a stool sample upon admission were considered to have fulfilled this requirement as this waiting to observe three liquid stools could delay diagnosis and endanger participants.

On October 1, 2018, the EMR-based decision support system was added to supplement the testing algorithm and was designed to notify providers if they were attempting to order a *C. difficile* test that did not adhere to the testing algorithm. Data abstraction did not include charts in April 2017 or October 2018 to allow providers a month to learn the testing algorithm and to ensure there were no glitches in the EMR-based decision support system.

Beginning November 19, 2019, a dedicated registered nurse called the providers caring for patients with an ordered *C. difficile* test with delayed collection, as the preferred population for *C. difficile* testing was patients with at least three unformed stools in a 24-hour period.[12] If the test did not adhere to the protocol or the patient was no longer symptomatic, the provider was advised to discontinue the test. If the provider deemed that the test was needed, regardless of algorithm adherence, prompt specimen collection was recommended, as a further delay of collection could lead to misclassification of community onset CDI as HO-CDI.

Statistical Analysis. Data were abstracted from the EMR into REDCap® for management.[13] SAS 9.4 (SAS/STAT Inst., Cary NC)

was used for all data analyses. The socio-demographic characteristics were summarized using descriptive statistics. Means and standard deviations (or medians and interquartile ranges) were reported for continuous variables; counts and percentages were reported for categorical variables. Likelihood ratio chi-square and Fisher's exact tests were used to test the association and agreement for the categorical and nominal variables. Further, the Cochran-Mantel-Haenszel test was used to reveal associations between categorical and nominal variables after controlling for the strata variables in the multiway tables. The nonparametric one-way Kruskal-Wallis test was performed to test the difference between groups for age and length of stay. The Dwass, Steel, Critchlow-Fligner (DSCF) test was used for multiple comparisons. All statistical tests at $p \leq 0.05$ were considered significant.

RESULTS

A total of 311 patient charts with *C. difficile* tests were reviewed. For all time periods, nearly one-third (31%; n = 96) of these tests were discontinued, and 5% (n = 14) were rejected by the lab due to the stool sample being solid. This resulted in data from 201 patients, the final sample size.

On average, patients were 64 years of age (SD 16.3). Most (61%; n = 123) were female, and 87% (n = 174) had healthcare coverage. The average length of stay was 10 days.

Algorithm Criteria. The proportion of tests that met algorithm criteria for diarrhea ranged from 81% (n = 81) at baseline to 84% (n = 80; p = 0.345) with the EMR. The proportion of tests that did not meet algorithm criteria for stool softeners, laxatives, lactulose, or enemas decreased from 19% (n = 19) at baseline to 9% (n = 9; p = 0.045) with the EMR. In addition, the proportion of tests that did not meet algorithm criteria for alternate causes of diarrhea decreased from 28% (n = 28) at baseline to 14% (n = 13; p = 0.011) with the EMR. Finally, the proportion of tests that met all algorithm criteria increased from 34% (n = 34) at baseline to 52% (n = 49; p = 0.010) with the EMR.

Tests with Delayed Sample Collection. Of all the charts reviewed during all study time periods, 100 had delayed sample collection. In general, there was no difference between tests with delayed sample collection (48%; n = 16) and those that did not have delayed sample collection (44%; n = 78; p = 0.63) when meeting algorithm requirements. During the EMR with phone calls period, of the 107 tests with delayed sample collection, phone calls were made for 44% (n = 47). More tests were discontinued (87%; n = 39) compared to baseline (54%; n = 15) and EMR (54%; n = 15, p = 0.003).

HO-CDI Rate. The EMR and EMR with phone call interventions were associated with a decrease in the HO-CDI rate. The HO-CDI rate ranged from 8.5 cases per 10,000 patient-days at baseline, to 7.9 during EMR, to 4.0 during EMR with phone calls (p = 0.007).

30-Day Readmissions. Among all hospitalized patients diagnosed with CDI, there was no significant change associated with the EMR or the EMR with phone call interventions with regards to 30-day readmissions. CDI readmissions ranged from 20% (n = 42) at baseline, to 18% (n = 35) during EMR, to 13% (n = 6) during EMR with phone calls (p = 0.547).

Table 1. Algorithm adherence criteria and outcomes at baseline and with the EMR.*

Adherence Criteria and Outcomes	Baseline % (n)	EMR % (n)	p Value (one-sided)
3 stools in 24 hours	81% (81)	84% (80)	0.345
Acute kidney injury	37% (37)	27% (26)	0.099
Algorithm fidelity	34% (34)	52% (49)	0.010
Antibiotics within 30 days	65% (65)	44% (42)	0.003
Chemo within 30 days	19% (19)	15% (14)	0.274
Drugs that cause diarrhea (e.g., laxatives)	19% (19)	9% (9)	0.045
Hemodialysis	9% (9)	4% (4)	0.146
Other causes of diarrhea	28% (28)	14% (13)	0.011
Positive test outside 30 days	11% (11)	7% (7)	0.266
Positive test within 30 days	4% (4)	1% (1)	0.200
Proton pump inhibitor usage	35% (35)	35% (33)	0.545
Signs of infection	66% (66)	67% (67)	0.480
Test collected after 72 hours	33% (33)	29% (28)	0.354
Toxic megacolon	3% (3)	2% (2)	0.693
Vasopressor usage (per event)	15% (15)	8% (8)	0.114

*Shaded rows are statistically significant.

DISCUSSION

This study examined the utility of interventions to reduce unnecessary *C. difficile* testing at AVCH in Wichita, KS. The EMR-based decision support system was associated with improved provider adherence to the testing algorithm than at baseline as well as a decrease in the HO-CDI rate. This aligned with similar studies which have decreased HO-CDI rates and increased adherence to hospital *C. difficile* testing algorithms.[7,9,10,14] Neither EMR or the EMR with phone call interventions were associated with an increase in 30-day hospital readmissions, vasopressor usage, or toxic megacolon, suggesting that diagnosis or treatment of CDI was not delayed. However, the current study suggested that there were still patients receiving treatment for a positive *C. difficile* test that was ordered, but not in compliance with the algorithm, indicating the need for further intervention. Additional interventions should include options in the EMR for providers to report why they were non-adherent to testing so these reasons can be targeted better or included in testing algorithms.

The EMR with phone calls intervention resulted in an increased percentage of discontinued *C. difficile* tests compared to baseline and EMR as well as a decrease in the overall HO-CDI rate. The further decrease in HO-CDI was expected as provider phone calls were a stronger intervention than an EMR prompt. Although the phone call intervention targeted a relatively small group of tests, the total effect of the phone calls was greater due to the prospective benefits of educating providers. In other words, providers who received phone calls likely followed the algorithm more closely with future patients. It was expected that the need for the phone calls will decrease as providers are more

educated about *C. difficile* testing. However, this study was limited by the relatively short study period of EMR with phone calls as compared to the other time periods. Further studies should explore this intervention for longer periods of time to accumulate more data on the effects of such phone calls. Similarly, more than one designated person making phone calls to providers could improve fidelity to the interventions. An improved intervention might require the provider to reorder the test after 24 hours had passed without sample collection. This may decrease testing further by causing providers to reevaluate the patient's clinical condition.

Limitations. An important study limitation was that the EMR with phone calls intervention was not evaluated during all seasons, as *C. difficile* infections tended to have the highest incidence in the spring and lowest in the fall.[15] To account for the limitations, future studies must examine these and other interventions for longer periods of time to reduce C. difficile testing that is not indicated clinically.

CONCLUSIONS

This study suggested that an EMR-based decision support system, combined with phone calls to providers, can reduce *C. difficile* testing that is not indicated clinically. This intervention was associated in a decrease in the HO-CDI rate.

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Perceived Barriers to Clinical Trials Participation: A Survey of Pediatric Caregivers

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ABSTRACT

Introduction. Pediatric clinical trials are difficult to conduct, leading to off-label use of medication in children based on results of trials with adults. As a unique population, children deserve to have appropriately tested therapies. The purpose of this study was to evaluate pediatric caregivers' beliefs and perceived barriers to participation in clinical trials.

Methods. The study was completed within the Sunflower Pediatric Clinical Trials Research Extension (SPeCTRE), an affiliate of the IDeA States Pediatric Clinical Trials Network (ISPCTN). This was a cross-sectional survey, adapted from the Pediatric Research Participation Questionnaire. A convenience sample of pediatric caregivers was recruited in three areas of a highly rural Midwestern state between 2017 and 2018.

Results. A total of 159 caregivers completed surveys; the majority (72.3%) were previously familiar with clinical trials, but less than 20% had ever been invited to participate. Caregivers were willing to consider enrolling their child if a physician in whom they had high trust recommended the trials ($H = 10.1$, $p = 0.04$) and if there were perceived benefits, such as access to tests and medications not covered by insurance (correlation coefficient [CC] = 0.4, $p < 0.01$) and compensation for time and travel (CC = 0.3, $p = 0.04$).

Conclusions. Trust in their physician highly influences likelihood of a caregiver consenting to have their child participate in a clinical trial. Therefore, to facilitate opportunities for children to participate in clinical trials, physicians need to be trained so they can offer trials locally. In addition, trials need to offer benefits, such as increased access to tests and medications as well as appropriate compensation.

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INTRODUCTION

Clinical trial data are the gold standard for evaluating the safety, effectiveness, and feasibility of therapies and treatments.[1,2] However, such data rarely exist for pediatric populations.[3] As a result, treatments for pediatric patients often are prescribed "off label", meaning the use of these treatments is based on extrapolation from trials with adults.[4-6] Such practices are assumed to be safe and effective but are not optimal due to a variety of physiological, ethical, and practical concerns related specifically to children.[5,7-10] With little evidence supporting these treatments and in light of the potential risks, it is important that treatments be tested specifically in pediatric populations.

In the early 2000s, legislation requiring pediatric clinical trials for new pharmaceuticals was passed.[11] This legislation resulted in a considerable improvement in access to such trials for children.[12] Even with these mandates, however, pediatric clinical trials remain relatively uncommon. First, pediatric trials are difficult to conduct, posing a variety of logistical, ethical, and economic challenges.[12,13] Second, because children are defined as a vulnerable population, special procedures are required of the researchers, and disagreements can arise about a child's autonomy in choosing to participate.[14] Finally, participant engagement may be a challenge due to previously identified barriers among adults, including distrust of researchers, limited access to trials, and socioeconomic barriers such as need for travel and time off work.[15-17]

To address the limited access to pediatric clinical trials, the IDeA States Pediatric Clinical Trials Network (ISPCTN) was formed.[18] As part of this national collaborative, the Sunflower Pediatric Clinical Trials Research Extension (SPeCTRE) network was developed in Kansas. One of the initial goals of the ISPCTN network was to establish a means of assessing and creating opportunities for clinical trial research in children in the United States. Therefore, the purpose of the current study was to evaluate caregivers' (i.e., parents, foster parents, adoptive parents) perceived barriers to participation in clinical trials, and to assess whether barriers differed regarding self-participation versus child participation. Secondary aims were to assess whether perceived barriers of caregivers aligned with those identified in previous studies of caregivers, and whether specific barriers amenable to intervention could be identified. A second study was designed to evaluate perceived barriers of providers and healthcare staff to participation in clinical trials (Smith, under review); those data are reported elsewhere.

METHODS

The 48-item survey was adapted from the Pediatric Research Participation Questionnaire (PRPQ) by an expert panel of SPeCTRE network members. In addition to basic demographics and children's free/reduced lunch status, the survey consisted of closed-ended questions that measured perceptions and barriers of participants to clinical trials on a 5-point Likert-type scale (1 = Strongly Disagree, 2 = Disagree, 3 = Neutral, 4 = Agree, 5 = Strongly Agree). Specifically, questions addressed beliefs about clinical trials in general (general beliefs), beliefs about the benefits of clinical trials to self (self-benefit beliefs), and trust in primary care providers (PCP). General belief questions addressed respondents' beliefs about the overall purpose and safety of clinical trials. Self-benefit questions were related to respondents' beliefs of personal value and benefits gained from participation in clinical trials. Questions related to trust in their PCP addressed respondents' trust that their PCP would make recommendations in the best interest of their patients. Reported child's free/reduced lunch status was used as a proxy for household income level.

A convenience sample of adult pediatric caregivers (at least 18 years of age) was recruited from outpatient clinics and back-to-school fairs

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in two urban areas and a county fair in a rural area of Kansas. At time of invitation, caregivers were told about the study, informed the survey would take approximately 10 minutes to complete, and given the option to complete the survey on paper or electronically via a provided tablet.

Data were managed using REDCap® (Research Electronic Data Capture) hosted at the University of Kansas Medical Center. REDCap® is a secure, web-based application designed to support data capture for research studies, providing 1) an intuitive interface for validated data entry, 2) audit trails for tracking data manipulation and export procedures, 3) automated export procedures for seamless data downloads to common statistical packages, and 4) procedures for importing data from external sources.[19] The University of Kansas Medical Center Institutional Review Board (KUMC IRB) approved and monitored the study. Survey participation was voluntary and provided without incentive. Descriptive and statistical analyses were performed in IBM SPSS Statistics 23 using frequency, measures of central tendency, variance, t-test, and nonparametric statistical methods, including Spearman's Correlation Coefficient and Kruskal-Wallis H-Test.

RESULTS

A total of 161 individuals responded to the survey and 159 met criteria for inclusion. The majority of respondents (77.0%) were surveyed in urban regions; 5.7% were surveyed in rural regions, and 17.6% had missing location information.

Respondent Characteristics. The largest proportion of respondents were female (67.9%), non-Hispanic White (43.4%), college-educated (31.4%), and had private or employer-provided insurance (42.8%; Table 1). Respondents' age ranged from 19 to 65 years, with a median age of 34 years. The average household size was four individuals, with an average of two children. Approximately 11.9% of respondents were living in households with income at or below $45,510 (the household income level to meet federal qualification for reduced lunch).

History with Clinical Trials. The majority of survey respondents (72.3%) were familiar with clinical trials, but only 19.5% had been invited to participate. Of those invited, 48.4% of respondents (11.2% of the total), and 29.0% of their children (6.8% of the total), had participated in a clinical trial. Of those caregivers who had participated in a clinical trial, 77.8% had at least some college education. No significant correlations were found between respondents ever participating in a clinical trial and their insurance status (r_s = 0.111, p = 0.224) or type of health coverage (r_s = -0.110, p = 0.225).

Factors Influencing Likeliness to Participate and Allow Child to Participate in Clinical Trials. No significant correlations were observed between age or sex and participant general beliefs, self-benefit beliefs, or trust in their PCP (Table 2). A significant positive correlation was observed between respondents' education levels and self-benefit beliefs (H = 7.355, p = 0.025), but not with general beliefs (H = 1.496, p = 0.473) or trust in their PCP (H = 4.328, p = 0.115). A significant positive correlation was observed between respondents' employment status and trust in their PCP (H = 1154.0, p = 0.011), but not with general beliefs (H = 1647.0, p = 0.860) or self-benefit beliefs (H = 1472.0, p = 0.264).

Table 1. Respondent characteristics.

	N	%
Total Respondents	**159**	
Gender		
Female	105	67.9
Male	23	14.5
Missing	28	17.6
Race & Ethnicity		
Non-Hispanic White	69	43.4
Non-Hispanic Black	23	14.5
Hispanic white	14	8.8
Other	16	10.1
Missing	37	23.3
Education		
HS or less	44	27.7
Some college	34	21.4
College grad or higher	50	31.4
Missing	31	19.5
Employment status		
Employed	85	53.5
Unemployed/other	41	25.8
Missing	33	20.8
Health Coverage		
Private/employer	68	42.8
State	29	18.2
None	29	18.2
Missing	33	20.8

Table 2. Demographics and the degree of positive beliefs related to clinical trials.

Respondent Characteristics	General Beliefs	Self-Benefit Beliefs	Trust in PCP
Age t (p value)	-0.776 (0.440)	-0.463 (0.645)	-1.115 (0.267)
Sex H (p value)	1210.5 (0.834)	1232.0 (0.730)	1131.0 (0.932)
Level of education H (p value)	1.496 (0.473)	7.355 (0.025)*	4.328 (0.115)
Employment status H (p value)	1647.0 (0.860)	1472.0 (0.264)	1154.0 (0.011)*

*Indicates statistical significance.

No significant correlations were observed between respondents' demographics (age, gender, education level, employment status, and type of health coverage) or self-benefit beliefs and their likeliness to participate or allow their child to participate in a clinical trial (Table 3). Participants with more positive general beliefs about clinical trials were more likely to consider enrolling themselves (H = 13.284, p = 0.010) or their child (H = 13.623, p = 0.009) in fitness-related trials, but not clinical trials in general (H = 6.364, p = 0.174; H = 9.172, p = 0.057). Participants also were willing to consider enrolling their child in broader clinical trial opportunities if the trial was recommended by a trusted physician (p = 0.04).

Significant positive correlations were observed between respondents' likeliness to participate in clinical trials and certain benefits offered (Table 4), including gaining access to tests and medications not covered by insurance (r_s = 0.357, p = 0.010), free transportation (r_s = 0.300, p = 0.032), compensation for time and travel (r_s = 0.513, p < 0.01), and having alternative participation options, such as telehealth (r_s = 0.325, p = 0.020). Similarly, the likelihood of respondents' allowing their child to participate in clinical trials was correlated significantly with the benefits of having access to tests and medications not covered by insurance (r_s = 0.407, p = 0.003) and receiving compensation for time and travel (r_s = 0.296, p = 0.035).

Respondents' likelihood of participating in clinical trials increased with an increase in the number of benefits provided from the study (H = 10.596, p = 0.031). However, no statistically significant relationship was observed between respondents' likelihood of allowing their child to participate in clinical trials and an increased number of benefits provided from the study (H = 1.867, p = 0.760).

Offering trials through telehealth (r_s = 0.354, p = 0.011), on-site (r_s = 0.410, p = 0.003), or at a local practice or clinic (r_s = 0.374, p = 0.007) were correlated significantly with respondents' increased likelihood of participating (Table 5). However, these alternative modes of participation were not correlated significantly with respondents' likelihood of allowing their child to participate in clinical trial studies, unless the trial was on-site and recommended by their doctor (r_s = 0.318, p = 0.023) or was at a local practice or clinic and related to fitness (r_s = 0.279, p = 0.047).

Respondent Preferences for Learning about Clinical Trials. The majority of respondents reported they would prefer receiving information about clinical trial research studies from their health care provider (73.0%). Moreover, 69.8% of those selected only their health care provider and no other sources (e.g., webinar, telemedicine, educational brochure). Less than a quarter of respondents (23.9%) would prefer this information from more than one source.

DISCUSSION

The purpose of this study was to evaluate caregivers' perceived barriers regarding their child's participation in clinical trials and to determine if these barriers were consistent with those identified in previous studies. A major barrier appears to be that most respondents (80.5%) had never been invited to participate in a clinical trial. Less than one-fifth of survey respondents in this study had ever been invited, a finding consistent with a previous study of adolescent and young adult cancer patients in which only 13% of respondents were offered the opportunity to participate in a trial.[20] Of those in our study who had ever been invited to participate in a clinical trial, nearly half of adults and a third of children ended up participating.

Respondents to our survey who had participated in a clinical trial were likely to have at least some college education. This finding could reflect that trials were more likely to be offered to those with higher education or could reflect higher perceived self-benefit from clinical trials by those with more years of education, as our respondents reported. Patients with higher socioeconomic status were shown to be more likely to enroll in clinical trials.[21] In addition, having positive general beliefs about clinical trials significantly increased respondents' willingness to have their child participate in physical fitness research, and willingness to participate in physical fitness research themselves. Respondents also were more inclined to allow their child to participate if a trial was recommended by a physician and if they reported high physician trust. Our results suggested physical fitness trials may be an optimal entrée to engage caregivers and children in clinical trials. Future studies should evaluate whether engagement in low-risk fitness trials can increase perceived benefits and enhance willingness to engage in broader clinical trials, such as those for medications.

Further, our results suggested participants preferred hearing about clinical trials from their personal physician. These results are similar to findings from previous studies.[16,22] The preferred location for participation was at a local office. This finding emphasized the importance of having clinical trial sites in various geographic areas. Training local physicians and focusing on capacity-building related to their participation in clinical trials should be a focus of future interventions to enhance clinical trials access/conduct in underserved areas.

Finally, specific benefits of the trial to provide access to tests or medications not covered by insurance, free transportation, compensation for time and travel, and some options for alternative participation such as telehealth also increased willingness to participate in clinical trials as reported by caregivers for both themselves and their children. These findings contrasted with the findings of a previous study of asthma patients in which compensation was not a factor in parents' discussion of risks and benefits and was mentioned in only 10% of adolescents' responses.[23] However, results of a sister survey of physicians and healthcare staff by our team found providers also identified the importance of incentives for participants as a key factor in participation (Smith, under review).

This study had several limitations. First, due to the convenience sampling methodology of survey distribution, responses were not generalizable to non-urban regions. We were unable to demonstrate differences between rural and urban, as the majority of participants were recruited from two urban areas of the state. Second, complete demographic data were missing for about 20% of participants, so drawing conclusions about any demographic variables was difficult. The data that were reported indicated income levels that were generally higher than those reported in state level data. Third, the PRPQ

Table 3. Respondent characteristics correlated with likeliness to participate and allow their child to participate in clinical trials.

Respondent Characteristics	Any Clinical Trials		If Recommended by Doctor		If Related to Improving Fitness	
	Self	Child	Self	Child	Self	Child
Age t (p value)	-1.716 (0.094)	1.226 (0.228)	1.161 (0.253)	-1.415 (0.165)	-0.712 (0.481)	1.141 (0.261)
Gender CC (p value)	0.054 (0.712)	0.039 (0.788)	0.084 (0.568)	0.125 (0.393)	0.007 (0.963)	0.195 (0.180)
Level of education CC (p value)	-0.160 (0.274)	0.017 (0.907)	0.210 (0.148)	0.160 (0.273)	0.135 (0.357)	-0.053 (0.716)
Employment status CC (p value)	-0.233 (0.110)	0.016 (0.913)	-0.282 (0.052)	-0.200 (0.173)	-0.074 (0.618)	-0.165 (0.264)
Health insurance carrier CC (p value)	0.048 (0.751)	-0.21 (0.890)	-0.128 (0.395)	-0.058 (0.703)	-0.191 (0.204)	-0.141 (0.352)
General beliefs H (p value)	6.364 (0.174)	13.623 (0.009)*	4.708 (0.319)	8.596 (0.072)	13.284 (0.010)*	13.623 (0.009)*
Self-benefit beliefs H (p value)	3.325 (0.505)	2.853 (0.583)	6.008 (0.199)	3.8886 (0.422)	5.980 (0.201)	2.853 (0.583)
Trust in PCP H (p value)	9.202 (0.056)	7.358 (0.118)	7.259 (0.123)	10.082 (0.039)*	9.315 (0.054)	7.358 (0.118)

*Indicates statistical significance

Table 4. Likeliness of participating in a clinical trial given certain benefits.

Benefits Offered	Any Clinical Trials		If Recommended by Doctor		If Related to Improving Fitness	
	Self	Child	Self	Child	Self	Child
Tests/medications not covered by insurance CC (p value)	0.357 (0.010)*	0.407 (0.003)*	0.430 (0.002)*	0.329 (0.018)*	0.277 (0.049)*	0.177 (0.214)
Free transportation CC (p value)	0.300 (0.032)*	0.253 (0.073)	0.430 (0.002)*	0.360 (0.009)*	0.375 (0.007)*	0.361 (0.009)*
Compensation for time and travel CC (p value)	0.513 (0.000)*	0.296 (0.035)*	0.541 (0.000)*	0.294 (0.036)*	0.472 (0.000)*	0.306 (0.029)*
Alternative participation options CC (p value)	0.325 (0.020)*	0.204 (0.151)	0.342 (0.014)*	0.230 (0.104)	0.391 (0.005)*	0.335 (0.016)*

*Indicates statistical significance

Table 5. Comparison of likeliness of participating in a clinical trial given alternative options for participation.

Options for Participation	Any Clinical Trials		If Recommended by Doctor		If Related to Improving Fitness	
	Self	Child	Self	Child	Self	Child
Telephone participation CC (p value)	0.193 (0.175)	0.150 (0.294)	0.207 (0.145)	0.165 (0.247)	0.129 (0.365)	0.129 (0.367)
Internet participation CC (p value)	0.177 (0.213)	0.193 (0.175)	0.151 (0.290)	0.169 (0.235)	0.177 (0.215)	0.183 (0.198)
Telehealth CC (p value)	0.354 (0.011)*	0.222 (0.118)	0.339 (0.015)*	0.239 (0.091)	0.203 (0.154)	0.155 (0.279)
Local practice/clinic CC (p value)	0.374 (0.007)*	0.177 (0.214)	0.202 (0.156)	0.089 (0.533)	0.284 (0.044)*	0.279 (0.047)*
On-site CC (p value)	0.410 (0.003)*	0.271 (0.055)	0.460 (0.001)*	0.318 (0.023)*	0.347 (0.013)*	0.235 (0.097)

*Indicates statistical significance

was developed originally for use with caregivers of children with sickle cell disease or asthma and has been used among caregivers of children with cancer.[23] This study differed from those in that it did not focus on a particular disease state or on patients or families with documented health conditions. The modified tool has not been validated yet. Finally, the nature of this self-report data allowed us to assess only reported likelihood of participation in clinical trials, not actual participation. In spite of these limitations, this study provided insight into areas that may increase clinical trial participation of caregivers and their children.

CONCLUSIONS

In conclusion, the findings of this study suggested that caregivers were more likely to allow their child to participate in clinical trials when invited by a trusted physician. Less than a fifth of study respondents had ever been invited. To facilitate increased clinical trial participation for pediatric patients, local primary care physicians should be recruited to offer opportunities for trials to their patients. Physical fitness trials should be considered as an initial strategy for enhancing pediatric participation as willingness to participate in these trials was higher than willingness to participate in general clinical trials. Additional research is needed to investigate perceived barriers that physicians may have in offering clinical trials as a treatment option to their patients, more specifically, pediatric patients. In addition, the trials should offer benefits, such as access to tests and medications, transportation, or compensation that make participation attractive to caregivers.

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Keywords: pediatrics, clinical trial as topic, clinical trial protocols as topic, caregiver

KANSAS JOURNAL of MEDICINE

Cardiovascular Implantable Electronic Device Removal in a Patient with Negative Blood Cultures

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INTRODUCTION

Rates of cardiovascular implantable electronic device (CIED) infection over past decades have been on the rise. CIED infections are associated with twice the risk for in-hospital death.[1] Diabetes mellitus and renal dysfunction are identified risk factors for developing CIED infections,[2] and blood cultures are not always positive in patients with CIED vegetations.[3] With more patients receiving CIEDs, recognition and appropriate management of CIED infections are essential. This case report discusses a patient with pacemaker lead vegetations without bacteremia in the presence of suspected infectious source who underwent removal of the CIED system.

CASE REPORT

A 65-year-old male presented with a two-day history of worsening pain in his left lower extremity (LLE) with associated increased swelling and presence of skin ulcerations. He recently had completed a 10-day antibiotic course of sulfamethoxazole-trimethoprim for the skin lesions. On physical examination, the patient had bilateral pitting edema and skin ulcerations with minimal clear drainage on the anterior surface of the LLE with associated tenderness. The right leg had a small ulcer along a prior incision scar at a previous amputation site. The patient denied any fever, chills, or chest pains.

His pertinent past medical history included ischemic cardiomyopathy requiring coronary bypass surgery (CABG) about five years prior to presentation and a biventricular pacemaker-cardiac resynchronization therapy device about three years ago. He had atherosclerotic peripheral vascular disease, hypertension, and type-2 diabetes mellitus with right below knee amputation, bladder cancer in remission, and tobacco use for about 45 years.

A Doppler ultrasound of the LLE on presentation showed occlusion of the left posterior tibial and peroneal arteries. While an MRI of the leg was not possible due to a non-MRI compatible implantable cardioverter device (ICD), an x-ray did not reveal features of osteomyelitis. His work-up revealed leukocytosis (white blood count of 12.6 x 10^9/L) with an elevated sedimentation rate (47 mm/h) and C-reactive protein (CRP; 5.2 mg/dL), making the diagnosis of osteomyelitis still plausible. An echocardiogram revealed an estimated ejection fraction of 20 to 25% with diffuse hypokinesis. A 1.1 cm by 2.6 cm flat apical (mural) thrombus and a mobile density measuring 1.4 cm by 0.9 cm on the patient's pacemaker wire were noted. These findings were confirmed with a transesophageal echocardiogram, which revealed a mid- to large-sized, 1.5 cm by 0.7 cm vegetation on the right atrial pacing wire, and another vegetation of mid-size on the ventricular lead (Figure 1).

On admission, the patient was started on broad-spectrum antibiotics and anticoagulation for the mural thrombus. After a multi-disciplinary team discussion, the patient underwent removal of the ICD and the 3-lead defibrillator system, and surgical debridement of the defibrillator pocket. The patient's wound culture from lesions on his LLE grew *Pseudomonas putida* and *Enterococcus faecalis*, and the final report for his blood cultures and lead-tip cultures post-device explantation were negative. The patient's post-procedural clinical status deteriorated, progressing to cardiogenic shock and renal failure requiring hemodialysis and ionotropic support. The patient died 18 days post-hospitalization due to a massive gastrointestinal bleed suspected secondary to acute bowel ischemia.

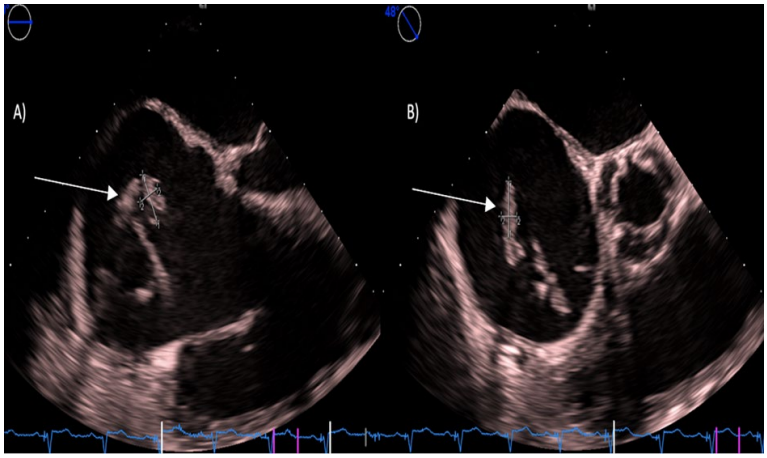

Figure 1. Images from transesophageal echocardiogram. A) Mid-esophageal, 4-chamber view, showing the mobile right atrial thrombus (arrow); B) Mid-esophageal, aortic valve short axis view, demonstrating vegetations (arrow) along the right ventricular lead.

DISCUSSION

Staphylococcus species have shown to be responsible for about 60-80% of most reported cases of infected CIED systems, although it is important to identify and treat other potential infectious causes.[3] Gram negative bacteria only account for a minority of CIED infections. Therefore, initiation of broad-spectrum antibiotics with Staphylococcus coverage is central to the initial management. Recommendations for duration of antimicrobial therapy ranges between 10-14 days from the time of CIED removal.[4] Per the American Heart Association guidelines,[3] removal of the CIED is a Class I recommendation for all patients with a definite CIED infection, evidenced by valvular/lead endocarditis or sepsis or in occult staphylococcal bacteremia. In cases of occult persistent gram-negative bacteremia, it is considered to be a reasonable option. About 5% of lead-adherent masses, in fact, may represent a thrombus instead or a fibrin tissue growth on the lead, for which reason CIED removal is not usually an immediate consideration in patients without bacteremia.[5]

Despite the absence of bacteremia, device explantation was determined to be the next best step in the patient's case after undertaking a heart-team approach involving specialists from cardiology, cardiothoracic surgery, and infectious disease. There were several risk factors

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that put the patient at high risk for a CIED infection. First, the presence of lead vegetations in the setting of recent completion of an antibiotic course prior to presentation may have contributed to the negative blood cultures. Infected skin ulcerations subsequently were suspected on wound culture results. Additionally, the patient's underlying risk factors including poor glycemic control and vasculopathy, with some suspicion for osteomyelitis, put him at an increasingly high risk for bacteremia.

Diagnosis of CIED infection requires a high index of suspicion in the setting of lead vegetations or endocarditis despite negative blood cultures. Such patients may have underlying risk factors, markers suggestive of an inflammatory process, and a suspected source of infection. A decision to proceed with device removal must be taken by a heart-team approach.

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Keywords: artificial pacemaker, endocarditis, device removal, cardiology, case reports

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Unusual Cause of Stroke in a Middle-Aged Woman

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INTRODUCTION

Many ischemic strokes are considered cryptogenic as they occur without a well-defined etiology. However, uncovering the pathophysiology affects prognosis, outcome, and management. The Trial of Org 10172 in Acute Stroke Treatment (TOAST) began classifying ischemic strokes as large-artery atherosclerosis, cardioembolic, small-vessel occlusion, stroke of other determined etiology, and stroke of undetermined etiology.[1] Twenty-five to forty percent of ischemic strokes are considered cryptogenic strokes, which are diagnosed through exclusion. The Northern Manhattan Study showed that the prevalence of cryptogenic strokes was higher in African Americans and Hispanics than in Caucasians.[2] No clear risk association has been found for age and gender.[3,4]

Multiple mechanisms have been proposed for cryptogenic strokes such as cardiac embolism secondary to atrial fibrillation, paradoxical embolism through a cardiac septal defect, undefined thrombophilia, and sub-stenotic cerebrovascular disease.[5] However, there are other important and unidentified mechanisms to uncover.

This case study describes a middle-aged woman who presented for an ischemic stroke and was found to have a stenosis of the brachiocephalic vein, likely secondary to chronic pleurisy or congenital malformation.

CASE REPORT

A 44-year-old white female with no significant past medical history except for recurrent left-sided pneumonia presented to the emergency department with left leg numbness and dysarthria. Social history was noncontributory. She was found to have a right middle cerebral artery territories ischemic stroke on magnetic resonance imaging (MRI). Computerized tomography (CT) of the head and CT angiography of the neck were normal. Tissue plasminogen activator was not administered as she was outside the time window. A 2D echocardiogram with bubble study was performed with an injection of the saline contrast through the left antecubital vein. The bubbles appeared initially in the left-sided cardiac chambers before the right-side chambers, which is extremely unusual (Figure 1).

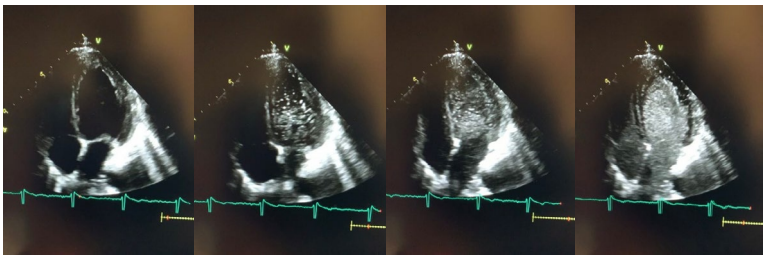

Figure 1. Bubble study showing bubbles in the left-sided chambers before the right.

A CT angiogram of the chest showed a persistent left superior vena cava (SVC) with anomalous venous vasculature consistent with severe stenosis of the brachiocephalic vein with significant collateralization (Figure 2). A transesophageal echocardiography showed a small patent foramen ovale with small densities on the mitral valve (Figure 3).

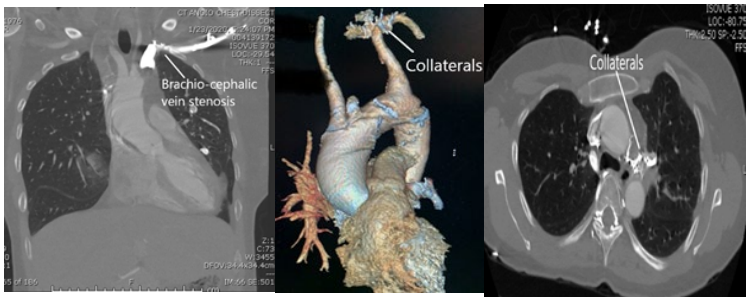

Figure 2. 2D and 3D CT angiogram of the chest showing the brachiocephalic vein stenosis with extensive collateralization.

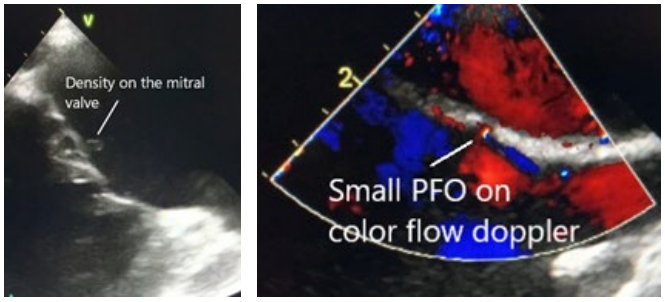

Figure 3. On the left: Small density suggestive of a vegetation on the mitral valve. On the right: Small PFO seen on color flow doppler.

Upper and lower extremities venous Doppler ultrasounds were negative for thrombus. The patient was started on warfarin for anticoagulation and antibiotics for possible endocarditis. She was referred to a congenital heart disease program in a larger community.

DISCUSSION

The patient was found likely to have an embolic stroke on MRI. The carotid arteries were normal, and she had no cardiovascular risk factors. No significant arrhythmias were found on electrocardiogram or telemetry. A suspicion for a cardiac source of embolization was raised. A 2D echocardiogram with bubble study was ordered to rule out a cardiac mass or a patent foramen ovale or atrial septal defect. The bubbles were injected in the left anti-cubital vein and unexpectedly appeared in the left-side chambers initially, instead of the right. This raised the suspicion for anomalous venous return from the left upper extremity to lead the bubbles straight to the left atrium. A persistent left SVC typically would drain the bubbles into the coronary sinus then the right atrium (90% of the cases); 10% of patients with persistent left SVC have a direct connection to the left atrium.[2] A CT angiogram of

the chest was ordered to evaluate for the left SVC, uncovering severe stenosis of the brachiocephalic vein leading to large collaterals, which in turn anastomosed with the pulmonary veins. Congenital anomalies of the brachiocephalic vein also were a possibility.

On further interrogation, the patient admitted to a history of recurrent pneumonia on the left side which may have caused pleurisy and contributed to the stenosis of the brachiocephalic vein. The densities on the mitral valve may have been new or healed vegetations and could be due to bacterial showering of the left-sided valves from the left upper extremity venous drainage. The patient was treated for possible infectious endocarditis as well as thromboembolic event from the venous malformations. The medical team was fortunate that the IV was placed on the left side, otherwise her venous malformation may have never been discovered. The patent foramen ovale was small and unlikely to have contributed to the patient's presentation.

CONCLUSIONS

The pathophysiology of cryptogenic stroke likely is heterogeneous. This case report proposed a new and unusual mechanism of an ischemic stroke in a young, middle-aged woman. The acute management was similar to other ischemic stroke subtypes and the prognosis tended to be better with a lower long-term risk of recurrence.[6,7] However, in this case, a cardiothoracic surgeon was consulted to evaluate for possible lobectomy and the interventional radiology service was consulted for stenting of the brachiocephalic vein. After review of the case, it was recommended to transfer the patient to a congenital heart disease team for further evaluation and treatment of this complex vascular patient. Thus, addressing the vascular pathology likely will resolve the cause of her strokes and reduce the risk of recurrence.

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