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Pandemic Food Response in Primary Care to Minimize Exposure for Elderly Food Insecure Population

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ABSTRACT

Introduction. Stay-at-home orders during the first wave of the COVID-19 pandemic encouraged individuals, especially the elderly, to stock up on food and supplies and remain home to limit exposure to the SARS-CoV-2 virus. However, individuals with food insecurity may be able only to afford a few days of food at a time, causing frequent outings to obtain food. An emergency food delivery system decreases the need for frequent outings. This study investigated: (1) whether elderly family medicine patients with previously reported food insecurity were making frequent trips to obtain food during the lockdown, and (2) if social determinants of health screening data could be used successfully to identify patients in need of emergency food delivery during the pandemic.

Methods. Primary care patients 65 years and older with previously reported food insecurity were screened for referral to a community food delivery program. A cross-sectional secondary analysis of screening and referral data were conducted.

Results. Clinic staff called 52 patients and completed screening of 30. For 23/30 respondents (76.7%), reported monthly outings to obtain food exceeded the recommended stay-at-home guidelines. In our sample, 22/30 (73.3%) reported current food need, 14/30 (46.7%) reported two or fewer days of food, 28/30 (93.3%) reported receiving home food delivery would keep them from going out, 24/30 (80.0%) agreed to food delivery, and 17 patients received a food delivery.

Conclusions. Targeted screening and referral for food delivery may reduce the need for patients experiencing food insecurity to leave home during a pandemic or other disaster, potentially decreasing community exposure for a high-risk population. Primary care practices can utilize previously collected food insecurity and other social determinants of health data to identify and assist high-risk patients in a pandemic.

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INTRODUCTION

Food insecurity, the inability to afford sufficient food, is known to be linked to some of the same chronic conditions (e.g., diabetes, hypertension, coronary heart disease) listed by the U.S. Centers for Disease Control and Prevention (CDC) as risk factors for severe COVID-19 outcomes.[1,2] Recent reports described the impact of COVID-19 on food access and rates of food insecurity,[3-5] however, little has been written about the additional risk food insecurity poses on individuals who are already at risk for poor outcomes. Individuals with food insecurity often are able only to afford or store a few days' worth of food at a time.[6-8] This forces them into the community every few days for additional food. Therefore, a compounding risk may exist for these individuals who likely bear a high burden of chronic disease and increased community exposure to the virus.

A family medicine clinic participated in an emergency food response effort targeting individuals with a history of self-reported food insecurity who were at high risk of poor outcomes related to COVID-19 due to age (65 and older).[2] Clinic staff was concerned that this population would be unable to follow public health recommendations to stock up on one to two weeks of food and remain home, therefore experiencing elevated food access-related community exposure to the virus. Our research team conducted a secondary analysis of this emergency outreach to determine: (1) if previously collected social determinants of health screening data (i.e., food insecurity status) could be used to predict patients in need of emergency food delivery during the pandemic, and (2) whether elderly family medicine patients with previously reported food insecurity were making frequent trips out to obtain food during the lockdown.

The use of previously collected social determinants of health (SDOH) data to conduct targeted screening and referral for emergency food assistance to reduce community exposure during a pandemic are reported. Primary care clinics that regularly collect SDOH data may be in a good position to risk-stratify patients and support individuals at high risk of COVID-19 with food insecurity.

METHODS

Study Population. This project was completed in the family medicine department of an academic medical center in the Kansas City metropolitan area. Institutional Review Board approval was obtained to conduct cross-sectional secondary analysis of screening and referral data. Inclusion criteria consisted of patients that were at least 65 years old and who previously answered "yes" to the food insecurity question ("In the last 12 months, did you ever eat less than you should because there wasn't enough money for food?") on a social determinants of health (SDOH) screener during a patient care visit. All primary care patients are screened annually for a variety of SDOH needs using a modified version of the Health Leads screening tool[9] (see Appendix I). Patients were excluded if the last known address was outside the delivery zone (the Kansas City Metro area).

Procedures. In the Kansas City region, stay at home orders began at the end of March 2020. Project calls were made from April 1, 2020 through April 8, 2020. Clinical operations staff developed and reviewed a series of questions to assess current food insecurity, patient health, and knowledge of the pandemic and stay-at-home order. Staff called all eligible patients and asked the series of scripted questions (see Appendix II). If a patient could not be reached initially, a second attempt was made. Calls utilized the Doximity© dialer (Doximity, Inc.; San Francisco, CA.) and showed the department's clinic number. All data were recorded securely in the Research Electronic Data Capture software platform (REDCap®). The final question obtained verbal permission from the patient to pass their contact information to the community organization for a community health worker (CHW) to organize nonperishable food delivery, including the option for recurring deliveries.

CHWs recorded patient contact and food delivery data in a shared referral database. The survey was designed as an operational screening tool; therefore, response bias mitigation was not addressed.

Statistical Analysis. Descriptive calculations of patient survey responses were completed using Microsoft® Excel 2016. Statistical tests were completed comparing demographics between patients who met inclusion criteria but were unreachable or declined to participate (n = 22) and those who completed the survey (n = 30). Mean age was compared by Independent Samples t-test, and sex and race were compared by Pearson Chi-Square using IBS SPSS 27. Race was collapsed into dichotomous variables of Black/African American vs. not Black/African American. Partially completed surveys were included in the analysis and missing data were omitted from analysis of each variable. Estimated number of food outings in a 30-day period was calculated based on current self-reported food stores. When patients gave a range of days of food available, the lower limit of the range provided was used for calculations.

RESULTS

Fifty-two patients met the initial inclusion criteria. Forty-eight (92.3%) had a chronic medical condition elevating their risk of poor outcomes due to COVID-19. Characteristics of study participants are listed in Table 1. Fourteen individuals (26.9%) were unable to be reached, 29 individuals (55.7%) were reached with one phone call, and 9 (17.3%) required a second phone call. Three patients (5.8%) were not residing in the food delivery area or declined to participate. Thirty-five patients (67.3%) consented to a phone call, one patient was removed because they reported living in a care facility that provided daily meals, three patients declined to complete the survey, and 30 patients completed the entire screening survey.

Table 1. Patient characteristics.

Characteristic	Met Inclusion Criteria n = 52	Completed Screening n = 30*
Age, mean (range)	70 (65-84)	71 (65-84)
Sex, n (%)		
Male	23 (44.2%)	14 (46.6%)
Female	29 (55.8%)	16 (53.3%)
Race, n (%)		
Black	29 (55.8%)	17 (56.7%)
White	21 (40.4%)	12 (40.0%)
Other	2 (3.8%)	1 (3.3%)
Ethnicity		
Hispanic	3 (5.8%)	1 (3.3%)
Non- Hispanic	49 (94.2%)	29 (96.7%)

* No statistically significant differences were found for mean age (p = 0.199), sex (p = 0.68), and race (p = 0.879) between patients who met inclusion criteria but were unreachable or declined to participate (n = 22) and those who completed the survey (n = 30).

All respondents were aware of the pandemic in the Kansas City area and the stay-at-home orders. Two patients (6%) reported receiving negative test results for COVID-19. Of the contacted patients, 20 (64.7%) reported they needed food and 14 (46.7%) reported they had less than two days of food. The average number of days of food available for the household was five with the median of three (range 1 - 21). The estimated number of outings in a month to procure additional food ranged from 1 to 30 outings, with 10 as the median (Figure 1). Most patients (25/30; 83.3%) reported "I must go out" or "Different household member can go" to pick up additional food. Of the patients, 29 (96.7%) reported receiving home food delivery would keep them from going out (Table 2).

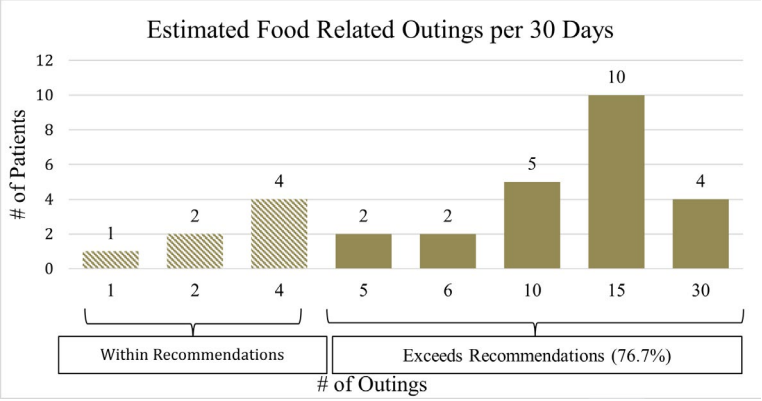

Figure 1. Estimated number of outings to access food in a 30-day period, based on patient-reported ability to stock food at home. Guideline groupings are based on public health recommendations (at the time of project calls) for at-risk individuals to stock 1-2 weeks' worth of food to limit trips to stores (n = 30 respondents).

Table 2. Screening survey results.

Screening Questions	Yes/Total Responses (%)
Homebound prior to pandemic	3/33 (9%)
Able to stock up on food?	15/33 (45%)
Currently in need of food?	22/33 (67%)
How do you get food?*	
Family or friends will drop off	6/30 (20%)
Different household member can go	11/30 (36.7%)
I must go out	14/30 (46.7%)
Food delivery would keep them home*	29/30 (96.7%)
Would like referral to food delivery*	24/30 (80%)
Received food delivery	17/24 (70.8%)

*Three participants declined to answer these questions.

A total of 24/30 patients (80%) requested a referral to a community-based organization for food delivery. Seven patients were either unable to be contacted or declined services after referral. Seventeen patients received a food delivery, which was 70.8% of those who requested a referral and 32.7% of all patients who met inclusion criteria.

DISCUSSION

Health experts recommend patients at high risk for poor outcomes from COVID-19 limit interactions with other people.[2,10] Public health recommendations during our screening period (April 2020) included stocking up on one to two weeks of food and supplies to limit trips to stores.[11,12] Food insecure patients may be unable to stock up on food due to financial limitations, lack of transportation, or an inability to safely

store food items. Patients then must go to the store to purchase additional food every couple of days, potentially exposing themselves to the virus each time. In our sample, 80.6% of patients had food access-related community exposure either directly or through someone else in the home. For most patients (76.7%), estimated outings per month to procure additional food exceeded the recommended guidelines. Therefore, this population not only has increased risk of poor outcomes (due to age and comorbid conditions)[2], they also may have increased exposure to the virus. This means food insecurity may act as an additional risk factor for this already high-risk population.

The local county health department and other community-based organizations developed an emergency food delivery system during the initial phases of COVID-19. This project leveraged existing partnerships with these organizations to address patient needs rapidly. The primary care clinics regularly collect information on food insecurity in this patient population, allowing quick identification of the target population. Using clinic-to-community linkage to food resources is proving efficient and effective in primary care clinics.[13,14] In addition, food delivery programs may alleviate barriers to transportation which are known to be associated with food insecurity.[15]

This study had several limitations. It had a small sample size and was conducted in a single primary care department at a single academic center. Food insecurity was identified by patient response to a routine SDOH questionnaire collected at primary care appointments (see Appendix). It was possible that a patient may have developed food insecurity since the most recent screening, meaning they would not be identified for the initial cohort. In addition, most of the data was self-reported during the screening process, which may result in response bias. Some patients reported a previous food need had been met since the last appointment and no longer needed assistance. External validity was limited, since the sample size was small and represented patients presenting to one primary care clinic in an urban academic medical center.

Future direction will include a chart review of these at-risk individuals to investigate subsequent COVID-19 positivity rate, hospitalizations, ventilator need, and death compared to a matched population who did not receive food delivery. Evidence is building that racial and ethnic minorities are at higher risk for poor outcomes due to COVID-19.[16] Food insecurity was also higher in these populations than in the white population.[17] In this dataset, the majority of patients (59.4%) were of a racial/ethnic minority. Additional investigations are needed to evaluate the interactions between race/ethnicity, social needs, and COVID-19 clinical outcomes.

The main goal of this emergency referral response was to keep patients safe by reducing the need for community exposure for a high risk-population during a pandemic. Additionally, the ability to reduce exposure and potentially prevent complications in a high-risk population may assist with conserving resources, such as personal protective equipment, patient beds, and ventilators. Primary care practices can utilize previously collected SDOH data to identify and assist high-risk patients. The continued development of community relationships is integral to the ability of a health care organization to provide emergency services rapidly. The authors recommended the following priority areas for primary care practices to be prepared to engage in rapid response to social needs in an emergency: collect SDOH screening results for all patients, invest in relationships with community organizations able to respond to social needs, and assign staff (CHWs, social workers, trainees) to reach out to and triage high-need patients during emergencies. Understanding the effect food delivery has on reducing community exposure for individuals who are at risk of poor COVID-19 outcomes can help guide future pandemic and disaster planning.

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Keywords: food insecurity, food assistance, pandemic, COVID 19, poverty

APPENDIX I

SDOH Screening Questions

	In the last 12 months, did you ever eat less than you should because there wasn't enough money for food?	YES	NO
	In the last 12 months, has your utility company shut off your service for not paying your bills?	YES	NO
	Are you worried that in the next 2 months you may not have stable housing?	YES	NO
	Are you afraid you might be hurt in your home by someone you know?	YES	NO
	Are you afraid you might be hurt in your apartment building or neighborhood?	YES	NO
	Do problems getting child care make it difficult for you to work or study?	YES	NO
	In the last 12 months, have you needed to see a doctor, but could not because of cost?	YES	NO
	In the last 12 months, did you skip medications to save money?	YES	NO
	In the last 12 months, have you ever gone without health care because you didn't have a way to get there?	YES	NO
	Do you have problems understanding what is told to you about your medical conditions?	YES	NO
	Do you often feel that you lack companionship?	YES	NO

COVID Emergency Food Response Screening Questions

Are you aware of the COVID-19 disease in Kansas City?	yesno 1 Yes 0 No
Special population	checkbox 1 Healthcare worker 2 KUMC faculty, staff, student 3 Public safety occupation (EMS, police, fire) 4 Involved in illness cluster from faculty or institution (healthcare, school, corrections, homeless/shelters) 5 Severe lower respiratory illness 6 Lives in group setting 7 Homeless/shelter 8 Other
Specify other population	text
Have you been tested for COVID-19?	radio 0 No 1 Yes at KU Med 2 Yes somewhere else
Specify where pt got tested	text
Date of testing	text (date_mdy)
Was COVID-19 test positive?	yesno 1 Yes 0 No
Have you been advised that your symptoms might be consistent with COVID and asked you to stay home?	yesno 1 Yes 0 No
If provider feels that patient meets testing criteria, refer patient to RN coordinator.	dropdown 0 Patient referred 1 Patient not referred
Are you aware of the stay-at-home order?	yesno 1 Yes 0 No
Are you staying home?	checkbox 0 Yes, I was home bound prior to the pandemic 1 Yes, I am quarantined due to either having symptoms or possible exposure 2 Yes, I am following the self-isolation recommendations 3 No, I am going to the groce 4 No, I am visiting family or friends 5 No, I still have to work 6 No, I don't want to stay home and am not worried

Who is patient isolating with?	checkbox 0 Significant other 1 Children 2 Parents 3 Other family 4 Friends 5 No one
Section header: Food Questions Did you stock up on food due to COVID-19?	yesno 1 Yes 0 No
Comments for stock-up	notes
How many days' worth of food do you think you currently have?	text
How many people are in the home?	text
If you get low on food, is someone in the home able to go get more, would family or friends drop off food, or would you have to go get more?	radio 1 Someone in the home able to go get more 2 Family or friends drop off food 3 You have to go get more
Would receiving food keep you from going out in the community or minimizing your exposure to others?	yesno 1 Yes 0 No
Are you currently in need of food?	yesno 1 Yes 0 No
Great, we hope you stay healthy. Please reach out if anything changes. (Hang up)	descriptive
Would patient be interested in someone bringing them food?	yesno 1 Yes 0 No
We are partnering with the Community Health Council of Wyandotte County and Cross-Lines Community Outreach. They are setting up deliveries of food to patient's front doors. Boxes may consist of shelf stable items like oats, beans, pasta, and/or canned vegetables. Would you like us to pass along your name, phone number for them to connect with you?	yesno 1 Yes 0 No
Okay, call your primary care office if anything changes. (Hang up)	descriptive
Wonderful, someone will be in contact with you soon.	descriptive

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Supraspinatus Fatty Infiltration Correlation with Handgrip Strength, Shoulder Strength, and Validated Patient-Reported Outcome Measures in Patients with Rotator Cuff Tears

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ABSTRACT

Introduction. The purpose of this study was to investigate the relationships between supraspinatus atrophy on magnetic resonance imaging (MRI) and other objective parameters in patients with rotator cuff tears. It was hypothesized that high-grade supraspinatus fatty infiltration would be correlated negatively with handgrip strength, shoulder strength, and patient-reported outcome measures (PROMs).

Methods. Patients with MRI-proven rotator cuff tears treated by a single sports medicine fellowship-trained orthopaedist at a single institution underwent comprehensive preoperative evaluation including bilateral handgrip and shoulder strength measurements with dynamometers and multiple online questionnaires from the Surgical Outcomes SystemTM (Arthrex, Naples, FL). Available shoulder MRIs were reviewed to grade supraspinatus fatty infiltration severity according to the 5-tier Goutallier system and an alternate 3-tier classification scheme. Difference analysis and Spearman (rho) rank order correlation were applied to the collected data to define the relationships between supraspinatus fatty infiltration and key variables including handgrip strength, shoulder strength, and scores derived from the shoulder PROMs.

Results. Ninety of the 121 patients enrolled in the study had shoulder MRIs available for review. There was no correlation found between supraspinatus fatty infiltration and handgrip strength, shoulder abduction strength, or any of the seven common shoulder PROM scores evaluated. There was statistically significant, albeit weak, correlation between MRI-derived fatty infiltration and shoulder external rotation strength.

Conclusions. Contrary to the hypothesis, high-grade supraspinatus fatty infiltration is largely unrelated to and should not be considered predictive of handgrip strength, shoulder strength, or common shoulder PROM scores. ***Kans J Med 2022;15:155-159***

INTRODUCTION

Shoulder pain is one of the most frequent musculoskeletal complaints seen by general practitioners and specialists.[1-6] Subacromial impingement is the most common shoulder disorder[6,7] and has been associated significantly with rotator cuff tendinopathy.[2,6-10] About 20 years ago, rotator cuff tears accounted for 4.5 million annual physician visits and 40,000 inpatient surgeries.[11] Now, over 300,000 rotator cuff repair procedures are performed annually and there has been a dramatic shift from open surgeries on inpatients to arthroscopic procedures in the outpatient setting.[9,12] Being able to diagnose patients with shoulder pain correctly through inquiry, physical exam findings, and imaging is crucial for orthopaedists to recommend proper treatment.

In a previous study, we examined the correlation of handgrip and shoulder strength with patient-reported outcomes measures (PROMs) in patients with rotator cuff tears.[13] Herein, the earlier study was extended to include fatty infiltration in the rotator cuff musculature. Historically, Goutallier et al.[14] showed on computed tomography (CT) scans that patients undergoing rotator cuff repair had greater fatty tissue infiltration within the rotator cuff compared to their normal asymptomatic counterparts. The Goutallier classification system, though originally derived from CT imaging, was found to be highly and easily reproducible on magnetic resonance imaging (MRI).[15]

The purpose of this study was to investigate the relationships between fatty infiltration of the rotator cuff found on shoulder MRI and other preoperative objective parameters of patients diagnosed with rotator cuff tears. These objective measures included absolute and percentage loss of handgrip strength, shoulder abduction strength, and shoulder external rotation strength as well as validated PROMs. It was hypothesized that increased fatty infiltration within the rotator cuff musculature would be correlated negatively with handgrip strength, shoulder strength, and shoulder PROM scores.

METHODS

Patient Enrollment. The study was approved by the local Institutional Review Board. All patients signed a consent form prior to participation in the study. One orthopaedic sports medicine fellowship-trained surgeon (DJP) enrolled patients undergoing rotator cuff repair surgery in the study from October 2018 to June 2021. Patients between the ages of 25 and 75 years who presented with shoulder pain, shoulder weakness on exam, and an MRI confirming a rotator cuff tear were included in the study. Patients were excluded if they had any history of cervical spine pathology, previous upper extremity surgery, significant upper extremity trauma, or any acute fracture of the upper extremities.

At their initial appointment, all patients underwent a complete physical exam, including bilateral handgrip and shoulder strength testing. Since there was no control group in the study, percentage loss of strength of the affected extremity was calculated as the net difference in strength of the affected extremity and the unaffected extremity divided by the strength of the unaffected extremity. These calculated values for percentage loss of handgrip strength, shoulder abduction strength, and shoulder external strength were analyzed separately from the values for absolute handgrip strength and absolute shoulder strength.

Patient-Reported Outcome Measures. All enrollees were asked to complete a set of questions which were emailed to them upon completion of their initial clinical encounter. These questionnaires were completed online as part of the Surgical Outcomes System (SOS™; Arthrex, Naples, FL, USA). The following PROMs were included within the SOS™: Simple Shoulder Test (SST), visual analog scale

(VAS), American Shoulder and Elbow Surgeons Standardized Shoulder Assessment Form (ASES) function score, Single Assessment Numerical Evaluation (SANE), and Veteran RAND 12-Item Health Survey (VR-12) mental and physical health scores.

Developed to assess the functional limitations of the affected shoulder in the context of the patient's activities of daily living (ADLs), the SST has been found to be a reliable and valid test to evaluate functional gains and losses over time.[16] It consists of 12 "yes-or-no" questions inquiring about whether the injury affects his or her ability to perform a physical function.[17]

The VAS allows for communication of the patient's subjective assessment of pain through a numerical rating scale between zero and ten.[18] It has been regarded as a valid and reliable tool for measuring both acute and chronic levels of pain.[19]

As a standardized form adopted by the American Shoulder and Elbow Surgeons, the ASES index score is an equally-weighted combination of the VAS and a 10-question inquiry on ADLs (function score), which is heavily dependent on shoulder range of motion that is free from pain.[20] Specifically regarding outcome assessments for rotator cuff disease, the ASES function score demonstrated acceptable reliability and internal consistency.[21]

The SANE rating, introduced as an easier method to obtain outcomes data, is historically a written response to the following question: "How would you rate your shoulder today as a percentage of normal (0% to 100% scale with 100% being normal)?"[22] It was found to have good correlation with two well established, more prohibitive shoulder rating scores. More importantly, in regards to patients' functional changes following rotator cuff repair surgery, it showed reliability and acceptable precision.[23]

Lastly, the VR-12 is a 12-item health questionnaire developed from a more extensive survey, the VR-36.[24] The goal of the VR-12 and VR-36 is to measure the functional role of a patient and the physical or emotional problems that limit the patient's ability to fulfill that role in the social or cultural environment.[25] Modification of these surveys, from an originally dichotomized "yes-or-no" answer to a 5-point ordinal answer in selected question items, has increased the precision and validity of the physical and mental role limitation components.[26]

Grip Strength Testing Protocol. In addition to a standard physical exam, all patients underwent bilateral strength testing for handgrip, shoulder abduction, and shoulder external rotation. Difference between the affected and unaffected sides was noted. All strength measurements were obtained first on the unaffected extremity, then on the affected extremity. The handgrip strength measurements were obtained with a Dynatron hydraulic hand dynamometer (Dynatronics Corporations, Salt Lake City, UT, USA). Handgrip strength with this type of instrument has been found to be valid and reliable for healthy and ailing patients.[27-29] Procedural posture had the patient seated with the shoulder at 0° flexion, abduction, and rotation; elbow flexed at 90° and forearm and wrist in neutral rotation.[29] Of the five customizable sizing positions on the dynamometer, position two or three was used based on patient preference. Each patient underwent three measurements, requiring contraction of a full grasp for five seconds with a one-minute rest period in between each attempt. Peak force was recorded for analysis.

Shoulder Strength Testing Protocol. Shoulder abduction and external rotation strength testing with a handheld dynamometer has been found to be reliable and valid.[30-32] All strength measurements were performed with the patient in the seated position and were obtained by a digital handheld dynamometer (Lafayette Instrument Company, Lafayette, IN, USA). Method of evaluation was noted to be a "make test" with the examiner stabilizing the dynamometer on the extremity in a fixed position against which the patient would push.[33] For abduction testing, an attempt would be made to have the shoulder of interest in 90° abduction and the elbow in 90° flexion. The dynamometer was placed on the lateral aspect of the distal humerus, just proximal to the elbow. If 90° abduction could not be reached, maximum shoulder abduction was used. The patient was instructed to apply a force perpendicular to the dynamometer.

For external rotation testing, the shoulder was in a neutral position with 90° elbow flexion and 0° forearm pronation. The dynamometer was positioned on the distal portion of the dorsal forearm, just proximal to the wrist. The patient was instructed to exert a laterally directed force perpendicular to the dynamometer, while maintaining position of the elbow at the side of the body. As with handgrip strength measurements, three trials were performed bilaterally with the unaffected extremity first, followed by the affected side. Interval rest periods between shoulder trials were 30 seconds. The examiner monitored the patient for any excessive shoulder elevation, trunk bending, or pelvic weight shifting which were considered compensatory movements prompting repeat measurement. The mean value for each set of trials was used in data analysis.

MRI Fatty Infiltration Classification. The classic Goutallier classification, originally described with CT imaging, proposed five grades of muscular fatty degeneration. In Grade 0, there was no fat deposition; in Grade 1, the muscle contained some fatty streaks; in Grade 2, fatty infiltration was important, but still more muscle than fat; in Grade 3, muscle and fat were equal; and in Grade 4, more fat than muscle was present.[14] Fuchs et al.[15] found that the Goutallier classification system was as reproducible with MRI as it was with CT scans. Slabaugh et al.[34] modified the Goutallier categories and created a simplified 3-tier classification scheme, combining Grades 0-1 (normal to mild fatty infiltration) and Grades 2-3 (moderate fatty infiltration), while maintaining Grade 4 (severe fatty infiltration) in its own category.

In this study, fatty infiltration of the supraspinatus muscle belly was assessed by a senior orthopaedic resident (GMM) who reviewed the shoulder MRI of the enrolled patients. The supraspinatus muscle-tendon unit was selected for evaluation, since it is involved most commonly in patients with rotator cuff injury.[35] A T1-weighted oblique-sagittal image cut closest to the lateral border of the scapular spine and medial border of the coracoid process was selected for the grading of fatty infiltration.[36] Fatty infiltration of the supraspinatus on the available MRIs was graded according to the Goutallier classification[14] and the modified system described by Slabaugh.[34] Both data sets were used for

analysis. The evaluation was blinded to the clinical and patient-reported outcome findings.

Statistical Analysis. Descriptive statistics, difference analysis, and Spearman (rho) rank order correlation were applied to the data from the two fatty infiltration classification schemes. The key variables analyzed included handgrip strength, absolute shoulder strengths, percentage loss of both handgrip, and shoulder strengths, and all scores derived from the PROMs. Relationships were reported as either positive (direct) or negative (indirect) correlations. Statistical Package for Social Sciences (SPSS, version 23; IBM®, Armonk, NY, USA) was used for all data analysis. The alpha value was set at 0.05.

RESULTS

This study of a cross-sectional cohort enrolled 121 patients, 71 males and 50 females. The average age of all patients was 59.3 years, ranging from 33 to 75. The right shoulder more often was affected. Eighty-six patients (71%) and 35 (29%) patients noted right-sided and left-sided shoulder complaints, respectively. Regarding hand dominance, 106 patients (88%) were right-handed. Dominant shoulder complaints were found in 87 patients (72%).

Handgrip, shoulder abduction, and external rotation strength data are shown in Table 1. Mean strength on the affected side was less than strength on the unaffected side for all three measures. While the differences in shoulder abduction and external rotation strengths achieved statistical significance, the side-to-side difference in handgrip strength was not statistically significant.

Table 1. Handgrip and shoulder strength of the affected and unaffected sides.

	Affected Side*	Unaffected Side*	p Value
Handgrip strength, kg	33.4 (12.7)	36.1 (12.4)	0.095
Shoulder abduction strength, kg	5.0 (4.9)	8.0 (4.1)	< 0.001[a]
Shoulder external rotation strength, kg	6.1 (3.9)	8.4 (4.4)	< 0.001[a]

*Tabulated strength values are mean (standard deviation)
[a]Statistically significant, p < 0.05.

Ninety of the 121 enrolled patients had shoulder MRI evaluations available for review at the time of the study. Data derived from assessment of supraspinatus fatty infiltration severity using the 5-tier Goutallier and modified 3-tier classifications schemes were analyzed in search of correlations with other preoperative measured parameters (Table 2). The negative correlations of shoulder external rotation strength and percentage loss of handgrip strength with supraspinatus fatty infiltration achieved statistical significance for both fatty infiltration classification schemes. However, the relatively low Spearman rho coefficients (≤ 0.35 in each case) indicated relatively weak, albeit statistically significant, correlations. All other correlations investigated did not achieve statistical significance.

Table 2. Supraspinatus fatty infiltration correlated with other preoperative measures.

Preoperative Measures	Goutallier Classification (0 - 4)		3-tier Classification (1 - 3)	
	Spearman's rho	p Value	Spearman's rho	p Value
Handgrip strength	-0.069	0.519	0.138	0.193
SH abduction strength	-0.143	0.117	0.024	0.823
SH ER strength	-0.348	0.001[a]	-0.214	0.042[a]
% Handgrip strength loss	-0.210	0.047[a]	-0.350	0.001[a]
% SH Abd strength loss	0.034	0.754	-0.020	0.855
% SH ER strength loss	0.183	0.084	0.145	0.174
SANE score	-0.129	0.342	-0.045	0.744
ASES function score	-0.186	0.169	-0.119	0.383
ASES index score	-0.113	0.406	-0.115	0.399
VAS score	0.050	0.713	0.110	0.419
VR-12 physical health score	-0.108	0.486	-0.092	0.552
VR-12 mental health score	0.116	0.395	0.068	0.616
SST score	-0.083	0.442	-0.030	0.780

Abbreviations: SH, shoulder; ER, external rotation; Abd, abduction; SANE, Single Assessment Numerical Evaluation; ASES, American Shoulder and Elbow Surgeons; VAS, visual analog scale; VR, Veteran RAND; SST, Simple Shoulder Test
[a]Statistically significant, p < 0.05.

DISCUSSION

The purpose of the study was to correlate supraspinatus fatty infiltration on MRI with measurable preoperative parameters including handgrip strength, shoulder strength, and PROMs. First, the study demonstrated a negative correlation between supraspinatus fatty infiltration and absolute shoulder external rotation strength. This finding, though statistically significant, was relatively weak regardless of which fatty infiltration classification system was used in the data analysis. Thus, as the rotator cuff musculature progressively was replaced by fat, it was found that the absolute strength of shoulder external rotation decreased as expected.

Previous studies have shown that fatty infiltration in rotator cuff musculature correlates with decreasing shoulder strength.[37-39] Gerber et al.[39] showed that supraspinatus atrophy and fatty infiltration correlated negatively with absolute contractile strength via intraoperative electric nerve stimulation, but cautioned that correlations with clinical strength measurements may be difficult secondary to rotator cuff tear pain. This may explain why supraspinatus fatty infiltration was not correlated with absolute shoulder abduction strength and only weakly

correlated with absolute external rotation strength in our study.

Second, the results showed a negative correlation between supraspinatus fatty infiltration and percentage loss of handgrip strength, irrespective of whether the Goutallier or 3-tier classification data were analyzed. Thus, as the fatty infiltration increased in the affected shoulder, the relative difference between the affected and unaffected handgrip strengths decreased. This finding was contrary to the expectation. This finding may be related to overcompensation during handgrip strength testing on the affected side, but there were no data to support this hypothesis. Although ipsilateral handgrip strength and shoulder strength have been correlated in other previous studies,[40,41] including our own,[13] there was no correlation between fatty infiltration and absolute handgrip strength in the present study.

Third, no correlation between supraspinatus fatty infiltration and any standard shoulder PROM was found. In this regard, the results are contrary to other authors who investigated smaller patient cohorts. For example, Lapner et al.[42] showed a higher preoperative supraspinatus Goutallier grade was associated with a lower ASES score in a 62-patient cohort. Davis et al.[43] did not evaluate Spearman correlations between fatty muscle and PROMs, but found a significant inverse association between Goutallier grade and ASES score in a 15-patient cohort during both univariate and multivariate linear regressions. The larger sample size in our study may help to explain the difference in results of the presented study compared to these previous studies.

The presented study had several limitations. Since the sample size was derived from the practice of a single surgeon at a single location, the ability to draw conclusions for a more heterogenous demographic population was limited. High responder burden associated with completing multiple preoperative PROMs may have caused inaccurate or incomplete patient responses. Incomplete data, such as having only 75% of the shoulder MRIs available for direct review, may have reduced the power of the study to find other statistically significant correlations. Intrarater reliability was not determined for fatty infiltration grading or strength measurements, which were both done by single investigators. Lastly, no control group was available, though an attempt was made to use the unaffected extremity as a control. While the data were characterized by extremity dominance, the 0-10% difference in handgrip strength based on hand dominance published in the literature[44] was not accounted for in the data analysis.

CONCLUSIONS

In this study, no statistically significant relationships between supraspinatus fatty infiltration and specific preoperative parameters, including handgrip strength, shoulder abduction strength, and pertinent shoulder PROMs were found. For both the Goutallier and the 3-tier classification systems, statistically significant but weak negative correlations between supraspinatus fatty infiltration and absolute shoulder external rotation strength were found. Taken together, these findings indicated that, contrary to the hypothesis, high-grade supraspinatus fatty infiltration was largely unrelated to and should not be considered predictive of handgrip strength, shoulder strength, or common shoulder PROM scores.

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Keywords: patient reported outcome measures, rotator cuff, shoulder pain, orthopedic procedures, treatment outcome

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2020 Annual Report of the Kansas Poison Control Center at The University of Kansas Health System

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ABSTRACT

Introduction. This is the 2020 Annual Report of the Kansas Poison Control Center (KSPCC) at The University of Kansas Health System. The KSPCC receives calls from the public, law enforcement, healthcare professionals, and public health agencies.

Methods. Encounters reported to the KSPCC from January 1, 2020 through December 31, 2020 were analyzed for caller location, demographics, exposure substance, nature of exposure, route of exposure, interventions, medical outcome, and location of care. Encounters were classified as human or animal exposure, confirmed non-exposure, or information call (no exposure).

Results. There were 19,780 total encounters, including 18,492 human exposure cases. These cases were primarily female (53.6%, n = 9,911) and pediatric (19 years of age or less; 59.5%, n = 10,995). Acute cases (82.7%, n = 15,294), unintentional exposures (73.8%, n = 13,643), and ingestions (85.9%, n = 15,901) were most common. The most common reported substance was household cleaning products (n = 937) in pediatric (children ≤ 5) and analgesics (n = 1,335) in adults. An increase in exposures to disinfectants and household cleaning products was seen. Moderate (n = 1,812) or major (n = 482) clinical outcomes were seen in 12.4% of cases. There were 18 deaths in 2020 reported to the KSPCC.

Conclusions. Over 18,400 exposures were managed by the KSPCC in 2020. Pediatric exposures remained the most common encounter. An increase in exposures to disinfectants and other household cleaning products was seen. This report supported the continued value of the KSPCC to both public and acute healthcare in the state of Kansas.
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INTRODUCTION

This is the 2020 Annual Report of Kansas Poison Control Center (KSPCC) at The University of Kansas Health System. The KSPCC is a 24-hour, 365 day/year, healthcare information resource serving the state of Kansas. It was founded in 1982 and is one of the 55 poison control centers certified by the American Association of Poison Control Centers (AAPCC) in the United States. The KSPCC is staffed by 11 certified specialists in poison information who are either critical care trained nurses or Doctors of Pharmacy. There is 24-hour back-up provided by five board-certified clinical and medical toxicologists.

The KSPCC receives calls from the public, law enforcement, healthcare professionals, and public health agencies. Encounters may involve an exposed animal or human (Exposure Call) or a request for information with no known exposure (Information Call). The KSPCC follows all cases to make management recommendations, monitor case progress, and document medical outcome. This information is recorded electronically in the Toxicall® data management system and uploaded in near real-time to the National Poison Data System (NPDS).

NPDS is the data warehouse for all the nation's poison control centers.[1] The average time to upload data for all poison centers is 6.51 ([6.12, 8.68]; median [25%, 75%]) minutes, creating a near real-time national exposure database and surveillance system. The KSPCC has the ability to share NPDS real time surveillance with state and local health departments and other regulatory agencies. The analysis and summary of all encounters reported to the KSPCC from January 1, 2020 through December 31, 2020 are reported below.

METHODS

All KSPCC encounters recorded electronically in the Toxicall® data management system from January 1, 2020 to December 31, 2020 were analyzed. Cases were first classified as either an exposure or suspected exposure (Human Exposure, Animal Exposure, Non-Exposure Confirmed Cases) or a request for information with no reported exposure (Information Call). Extracted data included caller location, age, weight, gender, exposure substance, number of follow-up calls, nature of exposure (i.e., unintentional, recreational, or intentional), exposure scenario, route of exposure (oral, dermal, parenteral), interventions, medical outcome (no effect, minor, moderate, severe, or death), disposition (admitted to noncritical care unit, admitted to critical care unit, admitted to psychiatry unit, lost to follow-up, or treated and released) and location of care (non-healthcare facility or healthcare facility). For this analysis, a pediatric case was defined as any patient 19 years of age or less. This was consistent with NPDS methodology. Similarly, NPDS descriptions of the medical outcomes of cases were used: minor - minimally bothersome symptoms, moderate - more pronounced symptoms, usually requiring treatment, and major - life threatening signs and symptoms. Data were analyzed using Microsoft® Excel (Microsoft Corp, Redmond, WA).

RESULTS

The KSPCC logged 19,780 total cases in 2020. This was a decrease of 809 cases (3.9%) compared to 2019. In 2020, there were 18,492 human exposure cases, 55 non-exposure confirmed cases, 104 animal exposure cases, and 1,129 information calls. For information calls, drug information (n = 324) was most common reason for calling. Table 1 describes the encounter types.

The KSPCC made 32,650 follow-up calls in 2020. Follow-up calls were done in 59.7% of human exposure cases. One follow-up call was made in 24.7% of human exposure cases and multiple follow-up calls (range 2-65) were made in 35.0% of cases. For human exposure cases which required a follow-up call, an average of three follow-up calls were performed per case.

The KSPCC received calls from all 105 counties and every hospital in Kansas. The county with the largest number of calls was Sedgwick County with 3,101. In addition, calls were received from 47 other states, the District of Columbia, and Puerto Rico.

Overall, a majority of human exposure cases (53.6%, n = 9,911) were female. In children younger than 13 years of age, a majority were male, but this gender distribution was reversed in teenagers and adults. In fact, in the age group involving children 13-19 years of age, 66.1% of cases were female. Approximately 59.5% (n = 10,995) of human exposures involved a child (defined as age 19 years or less).

Table 2 illustrates distribution of human exposures by age and gender. Patients two years of age were the most common age group involved in encounters reported to the KSPCC. For adults, the age group of 20-29 years old was most encountered. Seventy-one exposures occurred in pregnant women (0.4% of all human exposures). Of these exposures, 31.0% (n = 22) occurred in the first trimester, 43.7% (n = 31) occurred in the second trimester, and 19.7% (n = 14) occurred in the third trimester. Most exposures in pregnant women (73.2%, n = 52) were unintentional exposures, with 25.3% (n = 18) resulting from intentional exposures. There were no reported deaths to KSPCC in a pregnant woman in 2020.

Table 1. Encounter type.

	N	%
Exposure		
Human exposure	18,492	99.04
Animal exposure	104	0.56
Subtotal	**18,596**	**94.01**
Non-exposure confirmed cases		
Human non-exposure	55	100.00
Subtotal	**55**	**0.28**
Information call		
Drug information	324	28.70
Drug identification	55	4.87
Environmental information	74	6.55
Medical information	69	6.11
Occupational information	5	0.44
Poison information	124	10.98
Prevention/safety/education	10	0.89
Teratogenicity information		
Other information	32	2.83
Substance abuse	10	0.89
Administrative	44	3.90
Caller referred	382	33.84
Subtotal	**1,129**	**5.71**
Total	**19,780**	**100.00**

For human exposures, 67.3% (n = 12,448) of calls originated from a residence (own or other), while 92.8% (n = 17,177) of these exposures occurred at a residence (own or other). Calls from a healthcare facility accounted for 25.8% (n = 4,771) of human exposure encounters. Table 3 further details the origin of human exposure cases and the site of the exposure. Most human exposures, 82.7 % (n = 15,294), were acute cases defined as exposures occurring over eight hours or less. Chronic exposures, defined as exposures occurring over eight hours, accounted for 2.0% (373) of all human exposures. Acute on chronic exposures, defined as single exposure that was preceded by a chronic exposure over eight hours, totaled 2,675 (14.5%). Ingestion was the most common route of exposure (80.9%, n = 15.901) documented (Table 4).

The most common reported substance in those less than six years of age was household cleaning products (n = 937), followed closely by cosmetics/personal care products (n = 882). Table 5 lists the substances most frequently involved in exposures for those ≤ 5 years old and compares their rank to last year. For adult cases (> 19 years of age), analgesics (n = 1,335) and sedative/hypnotics/antipsychotics (n = 1,110) were the most frequently involved substances, as seen in Table 6. There was no change in the rank order of substances in adults. Among all encounters, analgesics (11.8%, n = 2,812) were the most frequently encountered substance category. Table 7 is a summary log for all exposures categorized by category and sub-category of substance (available online only at journals.ku.edu/kjm).

In 2020, there was a total of 369 plant exposures reported to the KSPCC. The single most common plant exposure encountered was to pokeweed (Phytolacca Americana; n = 39). Table 8 lists the top five most encountered plants.

Unintentional exposures were the most common reason for exposures (73.8%, n = 13,643), while intentional exposures accounted for 22.4% (n = 4,133) of exposures. Table 9 lists reasons for human exposures. Most unintentional exposures, 58.1% (n = 7,873) occurred in the ≤ 5-year-old age group. In patients less than 13 years of age, 97.7% (n = 8,814) of ingestions were unintentional. However, in the 13 to 19-year-old group, intentional exposure was most common (71.4%, n = 1,403). In total, suspected suicide attempts accounted for 17.3% (n = 3,207) of human encounters. When a therapeutic error was the reason for exposure, a double dose was the most common scenario (35.7%; n = 826).

Most encounters (65.8%, n = 12,174) were managed in a non-healthcare facility (i.e., a residence). Of the 5,998 encounters managed at a healthcare facility, 43.2% (n = 2,594) were admitted. Table 10 lists the management site of all human encounters.

Among human exposures, 14,756 involved exposures to pharmaceutical agents, while 8,926 involved exposure to non-pharmaceuticals. Because an encounter could include numerous pharmaceutical agents and non-pharmaceutical agents, this total was greater than the total number of encounters. However, 83.9% (n = 15,508) of all human exposures were exposed to only a single substance. Among these single substance exposures, the reason for exposure was intentional in 26.2% (n = 2,113) of pharmaceutical-only cases, compared to 4.0% (n = 300) of non-pharmaceutical single substance exposures.

When medical outcomes were analyzed, 25.2% (n = 4,659) of human exposures had no effect, 20.0% (n = 3,696) had minor effect, 9.8% (n = 1,812) had moderate effect, and 2.6% (n = 482) major effects. Moderate effects were more common in the 13 to 19-year-old group, while major effects were more common in those over 20 years of age. Moderate and major effects were most common in those with intentional encounters. More serious outcomes were related to single-substance pharmaceutical exposures, accounting for 11.1% (n = 2) of the fatalities. Table 11 lists all medical outcomes by age and Table 12 lists outcomes by reason for exposure.

Table 2. Distribution of human exposures by age and gender.

	Male		Female		Unknown Gender		Total		Cumulative Total	
Age	N	% of age group total	N	% of age group total	N	% of age group total	N	% of total exposure	N	%
< 1 year	448	50.79	432	48.98	2	0.23	882	4.77	882	4.77
1 year	1,289	52.74	1,151	47.09	4	0.16	2,444	13.22	3,326	17.99
2 years	1,334	52.83	1,186	46.97	5	0.20	2,525	13.65	5,851	31.64
3 years	622	54..85	511	45.06	1	0.09	1,134	6.13	6,985	37.77
4 years	330	56.99	248	42.83	1	0.17	579	3.13	7,564	40.90
5 years	199	54.97	161	44.48	2	0.55	362	1.96	7,926	42.86
Unknown ≤ 5 years	0	0.00	1	50.00	1	50.00	2	0.01	7,928	42.87
Child 6-12 years	609	55.72	477	43.64	7	0.64	1,093	5.91	9,021	48.78
Teen 13-19 years	662	33.72	1,297	66.07	4	0.20	1,963	10.62	10,984	59.40
Unknown child	4	36.36	3	27.27	4	36.36	11	0.06	10,995	59.46
Subtotal	**5,497**	**50.00**	**5,467**	**49.72**	**31**	**0.28**	**10,995**	**59.46**	**10,995**	**59.46**
20-29 years	842	44.43	1,052	55.51	1	0.05	1,895	10.25	12,890	69.71
30-39 years	678	42.14	927	57.61	4	0.25	1,609	8.70	14,449	78.41
40-49 years	411	36.60	712	63.40	0	0.00	1,123	6.07	15,622	84.48
50-59 years	399	39.39	612	60.41	2	0.20	1,013	5.48	16,635	89.96
60-69 years	309	37.41	517	62.59	0	0.00	826	4.47	17,461	94.42
70-79 years	199	38.42	319	61.58	0	0.00	518	2.80	17.979	97.23
80-89 years	113	38.44	181	61.56	0	0.00	294	1.59	18,273	98.82
≥ 90 years	26	34.67	49	65.33	0	0.00	75	0.41	18,348	99.22
Unknown adult	49	41.88	67	57.26	1	0.85	117	0.63	18,465	99.85
Subtotal	**3,026**	**40.51**	**4,436**	**59.38**	**8**	**0.11**	**7,470**	**40.40**	**18,465**	**99.85**
Unknown age	12	44.44	8	29.63	7	25.93	27	0.15	18,492	100.00
Total	**8,535**	**46.16**	**9,911**	**53.60**	**46**	**0.25**	**18,492**	**100.00**	**18,492**	**100.00**

Table 3. Origin of call and site of exposure for human exposure cases.

Site	Site of Caller		Site of Exposure	
	N	%	N	%
Residence				
Own	12,145	65.68	16,671	90.15
Other	303	1.64	506	2.74
Workplace	212	1.15	380	2.05
Healthcare facility	4,771	25.80	96	0.52
School	17	0.09	106	0.57
Restaurant/food service	0	0.00	28	0.15
Public area	80	0.43	156	0.84
Other	923	4.99	231	1.25
Unknown	41	0.22	318	1.72

Table 4. Route of human exposures.*

	Human Exposures		
Route	**N**	**% of all routes**	**% of all cases**
Ingestion	15,901	80.86	85.99
Dermal	1,413	7.19	7.64
Inhalation/nasal	1,170	5.95	6.33
Ocular	671	3.41	3.63
Bite/sting	162	0.82	0.88
Parenteral	168	0.85	0.91
Unknown	123	0.63	0.67
Aspiration (with ingestion)	13	0.07	1.00
Otic	22	0.11	0.12
Other	10	0.05	0.05
Vaginal	5	0.03	0.03
Rectal	6	0.03	0.03
Total number of routes	**19,664**	**100.00**	**106.34**

*Some cases may have multiple routes of exposure documented.

Table 5. Substance categories most frequently involved in exposures for age ≤ 5 years old.

Substance Category	Previous Year Rank	All Substance	%	Single Substance Exposures	%
Cleaning substances (household)	2	937	11.20	902	11.85
Cosmetics/personal care products	1	882	10.54	857	11.26
Analgesics	3	712	8.51	625	8.21
Dietary supplements/herbals/homeopathic	6	547	6.54	523	6.87
Foreign bodies/toys/miscellaneous	4	486	5.81	466	6.12
Antihistamines	5	441	5.27	394	5.18
Vitamins	8	409	4.89	355	4.66
Topical preparations	7	365	4.36	352	4.63
Pesticides	9	301	3.60	281	3.69
Plants	12	210	2.51	206	2.71
Gastrointestinal preparations	10	210	2.51	178	2.34
Cardiovascular drugs	11	194	2.32	113	1.48
Electrolytes and minerals	14	175	2.09	162	2.13
Hormones and hormone antagonists	13	159	1.90	122	1.60
Arts/crafts/office supplies*	16	146	1.75	136	1.79

*Essential oils 15 previous year

Table 6. Substance categories most frequently involved in exposures of adults (> 19 years).

Substance Category	All Substance	%	Single Substance Exposures	%
Analgesics	1,335	11.78	555	10.17
Sedative/hypnotics/antipsychotics	1,110	9.80	304	5.57
Antidepressants	931	8.22	294	5.39
Cardiovascular drugs	808	7.13	235	4.31
Alcohols	627	5.53	71	1.30
Antihistamines	503	4.44	194	3.56
Cleaning substances (household)	529	4.67	408	7.48
Pesticides	392	3.46	314	5.76
Anticonvulsants	430	3.79	108	1.98
Hormones and hormone antagonists	366	3.23	188	3.45
Stimulants and street drugs	285	2.52	114	2.09
Fumes/gases/vapors	267	2.36	230	4.22

Table 6. Substance categories most frequently involved in exposures of adults (> 19 years). *cont.*

Substance Category	All Substance	%	Single Substance Exposures	%
Chemicals	229	2.02	193	3.54
Muscle relaxants	207	1.83	61	1.12
Cold and cough preparations	199	1.76	93	1.70

Table 8. Top 5 most frequent plant exposures.

Botanical Name or Category	N
Phytolacca americana (L.) (Botanic name)	39
Plants: non-toxic	33
Oxalates (Species unspecified)	31
Cherry (Species unspecified, wild & domesticated)	28
Plants-general-unknown	17
Total of all plant calls	369

Table 9. Reason for human exposure cases.

Unintentional	N	%
Unintentional - general	8,540	46.02
Unintentional - therapeutic error	2,309	12.05
Unintentional - misuse	1,713	9.03
Unintentional - environmental	474	2.06
Unintentional - occupational	284	1.05
Unintentional - bite/sting	163	0.09
Unintentional - food poisoning	136	0.07
Unintentional - unknown	24	0.01
Subtotal	**13,643**	**73.08%**
Intentional		
Intentional - suspected suicide	3,207	17.03
Intentional - misuse	469	2.05
Intentional - abuse	358	1.09
Intentional - unknown	99	0.05
Subtotal	**4,133**	**22.04%**
Adverse reaction		
Adverse reaction - drug	346	1.09
Adverse reaction - food	76	0.04
Adverse reaction - other	63	0.03
Subtotal	**485**	**2.06%**
Unknown		
Unknown reason	132	0.07
Subtotal	**132**	**0.07%**
Other		
Other - malicious	57	0.03
Other - withdrawal	22	0.01
Other - contamination/tampering	20	0.01
Subtotal	**99**	**0.05%**
Total	**18,492**	**100.00**

Table 10. Management site of human exposures.

Site of Management	N	%
Managed in healthcare facility		
Treated/evaluated and released	3,153	17.01
Admitted to critical care unit	1,230	6.07
Admitted to noncritical care unit	722	3.09
Admitted to psychiatric facility	642	3.05
Patient lost to follow-up/left AMA	251	1.04
Subtotal (managed in healthcare facility)	**5,998**	**32.04**
Managed on site, non-healthcare facility	12,174	65.08
Other	40	0.02
Refused referral	260	1.04
Unknown	20	0.01
Total	**18,492**	**100.00**

Table 11. Medical outcome of human exposure cases by patient age.

	≤ 5 Years		6-12 Years		13-19 Years		≥ 20 Years		Unknown Child		Unknown Adult		Unknown Age		Total	
Outcome	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
No effect	2,692	33.96	276	25.25	457	23.28	1,225	16.66	1	9.09	7	5.98	1	3.07	4,659	25.19
Minor effect	946	11.93	226	20.68	649	33.06	1,854	25.21	4	36.36	16	13.68	1	3.07	3,696	19.99
Moderate effect	107	1.35	59	5.40	427	21.75	1,217	16.55	0	0.00	2	1.71	0	0.00	1,812	9.80
Major effect	13	0.16	1	0.09	87	4.43	381	5.18	0	0.00	0	0.00	0	0.00	482	2.61
Death	0	0.00	0	0.00	1	0.05	16	0.22	0	0.00	0	0.00	0	0.00	17	0.09
No follow-up, nontoxic	259	3.27	30	2.74	5	0.25	48	0.65	0	0.00	3	2.56	1	3.07	346	1.87
No follow-up, minimal toxicity	3,639	45.90	462	42.27	224	11.41	1,836	24.97	4	36.36	43	36.75	7	25.09	6,215	33.61
No follow-up, potentially toxic	204	2.57	21	1.92	83	4.23	377	5.13	2	18.18	34	29.06	15	55.06	736	3.98
Unrelated effect	68	0.86	18	1.65	30	1.53	399	5.43	0	0.00	12	10.26	1	3.07	528	2.86
Death, indirect report	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	1	3.07	1	0.01
Total	**7,928**	**100.00**	**1,093**	**100.00**	**1,963**	**100.00**	**7,353**	**100.00**	**11**	**100.00**	**117**	**100.00**	**27**	**100.00**	**18,492**	**100.00**

Table 12. Medical outcome by reason for exposure in human exposures.

	Unintentional		Intentional		Other		Adverse Reaction		Unknown		Total	
Outcome	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
No effect	3,801	27.86	807	19.53	8	8.08	31	6.39	12	9.09	4,659	25.19
Minor effect	2,295	16.82	1,255	30.37	15	15.15	108	22.27	23	17.42	3,696	19.99
Moderate effect	470	3.44	1,240	30.00	10	10.10	67	13.81	25	18.94	1,812	9.80
Major effect	47	0.34	401	9.70	5	5.05	7	1.44	22	16.67	482	2.61
Death	5	0.04	10	0.24	0	0.00	0	0.00	2	1.52	17	0.09
No follow-up, nontoxic	328	2.40	12	0.29	1	1.01	4	0.82	1	0.76	346	1.87
No follow-up, minimal toxicity	5,941	43.55	136	3.29	22	22.22	109	22.47	7	5.30	6,215	33.61
No follow-up, potentially toxic	452	3.31	219	5.30	17	17.17	25	5.15	23	17.42	736	3.98
Unrelated effect	303	2.22	53	1.28	21	21.21	134	27.63	17	12.88	528	2.86
Death, indirect report	1	0.01	0	0.00	0	0.00	0	0.00	0	0.00	1	0.01
Total	**13,643**	**100.00**	**4,133**	**100.00**	**99**	**100.00**	**485**	**100.00**	**132**	**100.00**	**18,492**	**100.00**

Use of decontamination and specific therapies, including antidotal therapy, is detailed in Tables 13a and 13b. There were 18 deaths in 2020 reported to the KSPCC. All but one death involved patients 20 years of age or older, and ten of the deaths involved intentional exposures. There was one death in a 13-year-old. Table 14 details the 18 reported deaths (available online only at journals.ku.edu/kjm).

Table 15 compares key statistics from 2015 to 2020. Overall case volumes have declined since 2016. There was also a slight decline in calls from healthcare facilities in 2020. The number of deaths increased from 2019 to 2020.

Table 13a. Decontamination provided in human exposures.[1]

Decontamination	N	%	N	%
Activated charcoal administered[2]	270	1.46	29	0.37
Cathartic	17	0.09	5	0.06
Ipecac administered	2	0.01	1	0.01
Lavage	1	0.01	0	0.00
Other emetic	143	0.77	60	0.76
Whole bowel irrigation	10	0.05	0	0.00
Total	**443**	**2.40**	**95**	**1.20**

[1]Total human exposures = 18,492; Total exposures in children ≤ 5 years = 7,928.
[2]Activated charcoal counts = single and multiple doses.

Table 13b. Therapy provided in human exposures by age.

Therapy	≤ 5 Years	6-12 Years	13-19 Years	≥ 20 Years	Unknown Child	Unknown Adult	Unknown Age	Total
Decontamination								
Cathartic	5	4	2	6	0	0	0	17
Charcoal, multiple doses	0	0	6	5	0	0	0	11
Charcoal, single dose	29	5	99	126	0	0	0	259
Dilute/irrigate/wash	5,956	594	363	2,400	5	38	3	9,359
Food/snack	1,741	157	84	438	0	3	0	2,423
Fresh air	74	41	64	530	5	16	2	732
Ipecac	1	0	0	1	0	0	0	2
Lavage	0	0	0	1	0	0	0	1
Other emetic	60	3	15	65	0	0	0	143
Whole bowel irrigation	0	1	0	9	0	0	0	10
Other therapies						0	0	0
Alkalinization - systemic	0	0	35	94	0	0	0	129
Alkalinization - urinary	1	0	6	11	0	0	0	18
Amyl nitrite	0	0	0	1	0	0	0	1
Antiarrhythmic	1	0	3	13	0	0	0	17
Antibiotics	18	7	23	181	0	0	0	229
Anticonvulsants	0	0	2	15	0	0	0	17
Antiemetics	18	16	207	243	0	0	0	484
Antifungals	0	0	0	1	0	0	0	1
Antihistamines	14	11	29	82	0	0	0	136
Antihypertensives	0	0	4	22	0	0	0	26
Antipsychotics	0	1	8	52	0	0	0	61
Antivenom (immune fab fragment) – not specified	1	3	1	18	0	0	0	23
Antivenom - elapidae	0	0	0	2	0	0	0	2

Table 13b. Therapy provided in human exposures by age. *cont.*

Therapy	≤ 5 Years	6-12 Years	13-19 Years	≥ 20 Years	Unknown Child	Unknown Adult	Unknown Age	Total
Other therapies						0	0	0
Antivenom/antitoxin (non-fab) – not specified	0	0	0	1	0	0	0	1
Atropine	2	2	4	12	0	0	0	20
Benzodiazepines	18	7	126	388	0	0	0	539
Blood products	0	0	1	4	0	0	0	5
Calcium	71	6	1	48	0	0	0	126
Cardioversion	0	0	0	1	0	0	0	1
Continuous Renal Replacement Therapy (CRRT)	0	0	0	6	0	0	0	6
CPR	0	0	3	12	0	0	0	15
Deferoxamine	0	0	2	0	0	0	0	2
ECMO	0	0	0	2	0	0	0	2
EDTA	1	0	0	0	0	0	0	1
Fluids, IV	62	44	629	1,509	0	0	0	2,244
Flumazenil	0	0	5	29	0	0	0	34
Folate	0	0	1	50	0	0	0	51
Fomepizole	0	0	0	9	0	0	0	9
Glucagon	2	0	2	25	0	0	0	29
Glucose, > 5%	3	0	4	38	0	0	0	45
Hemodialysis	0	0	2	14	0	0	0	16
Hemoperfusion	0	0	1	0	0	0	0	1
High dose insulin/glucose	0	0	0	8	0	0	0	8
Hydroxocobalamin	0	0	0	3	0	0	0	3
Hyperbaric oxygen	0	0	0	9	0	0	0	9
Hypothermia protocol	0	0	0	2	0	0	0	2
Insulin	1	0	0	32	0	0	0	33
Intubation	3	1	27	160	0	0	0	191
L-Carnitine	1	0	1	4	0	0	0	6
Leucovorin	0	0	0	1	0	0	0	1
Lipid emulsion therapy	0	0	2	2	0	0	0	4
Magnesium	0	0	40	141	0	0	0	181
Methylene blue	0	0	1	3	0	0	0	4
NAC, IV	1	13	96	174	0	0	0	284
NAC, PO	0	4	20	22	0	0	0	46
Naloxone	17	2	38	175	0	0	0	232
Neuromuscular blocker	0	0	2	21	0	0	0	23
Octreotide	2	0	1	5	0	0	0	8
Opioid analgesia	2	0	6	27	0	0	0	35
Other	36	32	75	323	0	4	0	470
Oxygen	6	5	50	402	0	0	0	463
Pacemaker	0	0	0	4	0	0	0	4
Physostigmine	1	0	2	3	0	0	0	6
Phytonadione	0	0	0	12	0	0	0	12

Table 13b. Therapy provided in human exposures by age. *cont.*

Therapy	≤ 5 Years	6-12 Years	13-19 Years	≥ 20 Years	Unknown Child	Unknown Adult	Unknown Age	Total
Potassium	3	2	119	295	0	0	0	419
Potassium iodide	0	0	1	3	0	0	0	4
Propofol	2	0	12	102	0	0	0	116
Rabies immune globulin	0	0	0	5	0	0	0	5
Rabies vaccine	0	1	0	6	0	0	0	7
Sedation (other)	6	2	35	143	0	0	0	186
Sodium Bicarbonate - metabolic acidosis	1	0	4	15	0	0	0	20
Sodium Bicarbonate - nebulized	0	0	0	2	0	0	0	2
Steroids	9	2	9	65	0	0	0	85
Succimer	7	1	0	2	0	0	0	10
Surgical intervention	1	0	1	2	0	0	0	4
Thiamine	0	0	2	75	0	0	0	77
Vasopressors	2	0	13	72	0	0	0	87
Ventilation, non-invasive (CPAP, BiPAP)	0	0	1	14	0	0	0	15
Ventilator	3	1	26	171	0	0	0	201

Table 15. 2015 to 2020 comparison of select statistics.

	2015	2016	2017	2018	2019	2020
Total cases	20,109	21,965	21,431	21,072	20,589	19,780
Calls from healthcare facilities	4,267	4,514	4,892	5,224	5,195	4,771
Moderate or major outcomes	1,688	1,971	2,170	2,340	2,416	2,294
Deaths	13	15	16	7	14	18

DISCUSSION

The ongoing importance of the KSPCC is reflected in trends that have seen rates of poisonings and overdoses increase at an alarming rate over the last decade. According to the Annual Surveillance Report of Drug-Related Risks and Outcomes, drug poisoning-related hospitalizations in the United States have increased 26% over the last two years that data were available.[2,3] The National Center for Health Statistics noted over 70,000 overdose related deaths in 2019.[4] Similarly, the KSPCC consistently has seen an increase in the number of cases from healthcare facilities and cases with moderate or major medical outcomes. Since 2015, calls from healthcare facilities have increased by 11.8%, with a slight decrease in calls from healthcare facilities in 2020 compared to 2019.

Cases from healthcare facilities still account for approximately 25% of the cases reported to the KSPCC.[5-8] Moderate/major outcomes have increased steadily by 36% since 2015. The percent of cases with a moderate/major outcome was 10.1% of overall cases in 2015 compared to 2020 where these cases account for 11.6% of overall case volume. The decrease in calls from healthcare facilities in 2020 partially may be explained by the impact of COVID-19 on hospital's patient volumes. The most apparent decreases in call volumes were in the months of August to December of 2020. However, the KSPCC also noticed an increase in calls regarding cleaning substances and disinfectants in 2020 compared to prior years. This was substantial enough that cleaning substances and disinfectants became the number one substance category involved in exposures in children ≤ 5 years and increased by 19% in adults compared to 2019.[7] In total, the KSPCC saw a 30% increase in calls regarding bleaches, 46% increase in household disinfectants, and 35% increase in calls regarding hand sanitizers compared to 2019. The number of deaths reported to the KSPCC increased by 28.6%, from 14 in 2019 to 18 in 2020. With the exception of 2018, there has been a steady increase in the number of deaths reported since 2015.[5-8]

The 2020 KSPCC statistics continued to mirror those seen nationally by the other 54 accredited poison control centers nationwide. In 2019, 2,573,180 encounters were logged by poison control, including 2,148,141 human exposures.[1] Overall, encounters showed a 1.70% (n = 42,942) increase from 2018 to 2019, while healthcare facility human exposure cases remained nearly steady with a slight decrease of 0.495%. More serious outcomes (moderate, major, or death) continued to increase. Nationwide, the five substance classes most frequently involved in all human exposures were analgesics, household cleaning substances, cosmetics/personal care products, antidepressants, and sedatives/hypnotics/antipsychotics, while the top five most common

exposures in children age 5 years or less were cosmetics/personal care products, household cleaning substances, analgesics, foreign bodies/toys/miscellaneous, and dietary supplements/herbals/homeopathic.

National poison center data demonstrated that calls regarding household cleaners and disinfectants increased by 20.4% and 16.4%, respectively, just from January to March 2020 (the onset of the COVID-19 pandemic).[9] In May of 2020, an internet survey on knowledge and cleaning practices surrounding COVID-19 showed that 60% of participants had increased the frequency of home cleaning, and 39% indicated they had engaged in high-risk practices not recommended by either the U.S. Centers for Disease Control and Prevention or manufacturer (e.g., gargling or drinking diluted bleach solutions, misting body with a disinfectant product or spray).[10] Finally, there were 2,619 exposure-related fatalities reported nationwide in 2019.

Several important limitations must be noted when interpreting poison center data. Reporting exposures to the KSPCC is voluntary and the KSPCC is not contacted regarding all poisonings in the state of Kansas. In particular, exposures with no or minimal effects may not be reported. Furthermore, in most cases, there is no objective confirmation of exposure.

CONCLUSIONS

The 2020 KSPCC annual report demonstrated that the center received over 19,700 total calls, including more than 18,400 human exposures. While pediatric exposures remain the most common, there continues to be a significant number of calls from healthcare facilities and for cases with serious outcomes. COVID-19 appears to have impacted the type of calls received in 2020, with an increase in exposures to disinfectants and other household cleaning products. The experience of the KSPCC remains similar to national data. This report supported the continued value of the KSPCC to both public and acute healthcare in the state of Kansas.

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Keywords: drug overdose, poisoning, ingestion, toxicology, antidotes

KANSAS JOURNAL of MEDICINE

Causes of Anemia in Patients Seen in a Rural Community Hematology Clinic

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ABSTRACT

Introduction. Anemia is a common medical disorder seen in consultation by hematologists. This study was performed to determine the incidence of the etiologies causing anemia in patients referred to the hematologists at Tammy Walker Cancer Center (TWCC) in the rural Kansas community of Salina. An additional goal of the study was to compare the frequencies of different etiologies for anemia in this cohort of patients with those previously reported by four academic medical centers.

Methods. A retrospective review of the medical records of 152 patients seen at TWCC between August 2015 and May 2019 was performed. The patient's history and physical exam, complete blood count, and various additional hematologic studies ordered at the discretion of the TWCC hematologist were used to determine the etiology of each patient's anemia.

Results. The most common causes of anemia found in the chart review were iron deficiency (48.7%), hematologic malignancy (14.5%), chronic inflammation (13.8%), renal insufficiency (11.2%), and unexplained anemia (9.9%). While the incidences of anemia due to hematologic malignancy, chronic inflammation, and renal insufficiency were like that reported previously by four academic medical centers, significantly more iron deficiency and less unexplained anemia were found in the patients referred to TWCC.

Conclusions. The causes of anemia in patients seen at TWCC were similar to those reported by academic medical centers; however, the incidences were different. The differences in findings may reflect dissimilarities in the demographics of referral populations, the duration, and extent of the evaluation at TWCC, or referral patterns.

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INTRODUCTION

In 2012, the prevalence of anemia in the United States was estimated to be 7.1%, representing an increase of 3.1% since 2003.[1] The rising prevalence of anemia is concerning due to the adverse events associated with the impairment of oxygen delivery to tissues leading to organ dysfunction and the compensatory cardiovascular mechanisms such as increased stroke volume and heart rate.[2] Anemia is particularly problematic for the older population. A systematic review of studies of the effects of anemia in older patients found that anemia was associated with a greater risk for cardiovascular disease and cognitive impairment, as well as more frequent hospitalizations, longer hospitalizations, and increased mortality.[3] In older patients, anemia increased the risk for death, first all-cause hospitalization, and first cardiovascular hospitalization.[4] Recognition and correction of the underlying cause for the anemia, resulting in an increase in the hemoglobin level, was associated with improved quality of life in patients with cancer, chronic kidney disease, HIV/AIDS, rheumatoid arthritis, inflammatory bowel disease, heart failure, and diabetes, and in surgical patients.[2]

Multiple studies have described the etiology, effects, and treatment of anemia and found a significant proportion of patients without a readily identifiable cause for anemia.[5-8] The NHANES III study of the approximately three million anemic patients older than 66 reported that 33.6% of the cases had no readily identifiable cause.[5] A prospective study of outpatients older than 65 with anemia referred to the hematology clinics at either Stanford Hospital and Clinics or Veteran Affairs Palo Alto Health Care System also found that 35% of the anemia cases remained unexplained after a complete workup.[6] A similar study of outpatients aged 65 years and older referred to the University of Chicago Hematology Clinic without a known hematologic malignancy, cancer chemotherapy, or radiation therapy completed within the previous six months, reported 44% of patients had unexplained anemia after a hematologic workup.[7] Finally, in a study by Ania et al.[8], the cause of 16% of the anemia in men and women of Olmsted County, Minnesota was uncertain.

The primary purpose of this report was to examine the causes of anemia and prevalence of unexplained anemia in patients referred to a rural community hematology clinic for an initial evaluation of a primary diagnosis of anemia. A secondary aim was to compare the etiologies for anemia found at TWCC with the published findings of four major academic medical centers.

METHODS

A retrospective medical record review was conducted of all patients referred to Tammy Walker Cancer Center (TWCC) in Salina, Kansas from August 2015 through May 2019, specifically for the evaluation and treatment of anemia. Salina is a community of approximately 48,000 in rural north central Kansas.

Anemia was defined using the World Health Organization criteria: a hemoglobin (Hb) of less than 12.0 g/dL for women and less than 13.0 g/dL for men.[9] Records were excluded if anemia was not the initial cause for the referral or if the patient was referred for evaluation of anemia discovered after a prior diagnosis or treatment of a non-hematologic malignancy within the preceding five years.

Each patient's Hb, hematocrit, white blood cell count (WBC) and platelet count, mean corpuscular volume (MCV), red blood cell distribution width (RDW), and reticulocyte count determined by the referring physician, if available, were reviewed. The additional diagnostic laboratory studies deemed appropriate by the TWCC hematologist also were reviewed. A complete blood count (CBC) and a complete metabolic panel invariably were repeated by the TWCC hematologist. Depending on the initial presentation of the patient, additional studies included iron studies, B-12 and folate levels, serum protein electrophoresis, coagulation studies, and bone marrow aspiration/biopsy with flow cytometry and cytogenetic studies. Final diagnoses were

determined by the TWCC physician after completion of the hematologic workup. Some patients were diagnosed as having multiple contributory causes to their anemia.

The number and percentage of the total cases represented by each etiology were calculated and compared to the results of four previously published reports on the etiologies of anemia.[5-8] For each diagnosis, the percentage of males and females, median age, and age range were reported, as well as the median values and ranges of select hematologic values including WBC, Hb, platelet count, MCV, and RDW.

The study was approved by the Salina Regional Health Center Institutional Review Board.

RESULTS

The study population totaled 152 patients (56 males and 96 females), ranging in age from 16 to 95 years old. The median age of patients at their initial visit was 71.5 years old and 67.1% of the total study population was greater than 60 years old. The basic hematologic data of the study population are summarized in Table 1. The median hemoglobin seen in the patients reviewed in this study was 10.2 g/dL. Nineteen (12.5%) of the TWCC patients had severe anemia (Hb levels less than 8.0 g/dL). Anemia in the absence of leukopenia or thrombocytopenia was seen in 59.2% of patients.

Table 1. Demographic and basic hematologic values of TWCC population.

Parameter	Median	Range
Age (years)	71.5	16 - 95
Hemoglobin (g/dL)	10.2	5.7 - 13
WBC (109/dL)	6.7	1.4 - 60.3
Platelet count (109/dL)	252.5	8.4 - 677

The final etiologies for the cause of anemia are summarized in Table 2. Demographic information and basic hematologic values associated with each diagnosis are summarized in Tables 3 and 4, respectively. Iron deficiency was the most common etiology of anemia seen in the TWCC population (48.7% of patients). Nearly one-third of patients with iron deficiency anemia (15.8% of all patients in the study) were determined to have a gastrointestinal bleed by clinical history or after referral to gastroenterologist for further workup. Malabsorption due to a previously diagnosed condition, such as gastric bypass, and a history of heavy menstruation contributed to the iron deficiency in other cases. Unfortunately, the cause for iron deficiency anemia could not be determined in 25.7% of the patients in this group.

Table 2. Etiology of anemia in TWCC study population.

Etiology of Anemia	Males Number (%)	Females Number (%)	Total Number (%)
Iron deficiency	22 (39.3%)	52 (54.29%)	74 (48.7%)
Hematologic malignancy	11 (19.6%)	11 (11.5%)	22 (14.4%)
Anemia of chronic inflammation	5 (8.9%)	16 (16.7%	21 (13.8%)
Renal insufficiency	9 (16.1%)	8 (8.3%)	17 (11.2%)
B-12/folate deficiency	7 (12.5%)	4 (4.2%)	11 (7.2%)
Other	7 (12.5%)	7 (7.3%)	14 (9.2%)
Unknown	4 (7.1%)	11 (11.5%)	15 (9.9%)

Table 3. Demographics of patients with a given diagnosis.

Etiology of Anemia	Male (%)	Female (%)	Median Age (years)	Age Range (years)
Iron deficiency	29.7	70.3	63	16 - 91
Hematologic malignancy	50.0	50.0	75	58 - 95
Anemia of chronic inflammation	23.8	76.2	70	39 - 93
Renal insufficiency	52.9	47.1	75	51 - 90
B-12/folate deficiency	63.6	36.4	75	50 - 85
Other	50.0	50.0	59.5	27 - 91
Unknown	26.7	73.3	78	35 - 95

The median age of the iron deficiency group of patients was 63 years, considerably younger than the median age of the patients with other causes of anemia in this study, except for those in the "other" category. Furthermore, iron deficiency contributed to the anemia in 83.3% of patients that were 40 years old or younger. Iron deficiency was more common in women; 70.3% of those affected by iron deficiency were women. While iron deficiency was the most common cause of anemia in both males and females, it accounted for only 39.3% of the total cases of anemia in males compared to 54.2% of the total cases of anemia in females. This difference was most pronounced in iron-deficiency patients under the age of 50, which accounted for 20 women and only 4 men. Patients with iron deficiency tended to have a lower hemoglobin value (9.9 g/dL) than those patients determined to have other causes for their anemia, other than renal insufficiency.

Hematologic malignancy was the second leading cause for anemia, accounting for 14.5% of all cases. Myelodysplastic syndrome (MDS) was the most common neoplastic process seen (12 patients or 54.5% of hematologic malignancies). Less common types of hematologic malignancy included multiple myeloma (three patients), monoclonal gammopathy of unknown significance (two patients), chronic lymphocytic leukemia (two patients), acute myeloid leukemia (two patients; one of these patients had a prior history of MDS as well), B cell lymphoblastic leukemia (one patient), and T cell large granular lymphocyte leukemia (one patient). Hematologic malignancies contributing to anemia were more common in older individuals, with the median age of those affected being 75 years old. Hematologic malignancies showed a higher prevalence in males (16.1%) than females (8.3%). Most patients with a hematologic malignancy had abnormalities in their white blood cell count or platelet count, in addition to their anemia. The median WBC count and platelet counts were below normal in the TWCC patients, although the range was wide. Over 70% had an abnormality in either WBC or platelet count and 55% had abnormalities in both. The median RDW also was elevated in this group at 16.9. Sixteen of the 22 patients (73%) with a hematologic malignancy had an elevated RDW.

Anemia of chronic inflammation was diagnosed in 13.8% of all TWCC patients. Anemia of chronic inflammation showed the greatest female predominance of any etiology of anemia in this study,

Table 4. Median and ranges of basic hematologic values by diagnosis.

Etiology of Anemia		WBCs (109/L)	Hemoglobin (g/dL)	Platelets (109/L)	MCV (fL)	RDW (%)
Iron deficiency	Median	6.7	9.9	282	82.9	17
	Range	2.6-14.7	5.9-13.5	8.4-677	61.0-100.4	12.7-59.6
Neoplasm	Median	4.3	10.0	141	96.5	16.9
	Range	1.4-60.3	5.7-13.1	33-578	70.0-110.5	11.5-36.9
Anemia of chronic inflammation	Median	7.6	10.2	237	95.6	14.1
	Range	4.1-14.3	7.1-12.2	106-426	81.0-103.5	11.9-19.3
Renal insufficiency	Median	7.3	9.8	196	93.8	14.3
	Range	4.1-13.9	7.3-12.7	131-432	84.6-104.9	12.1-16.5
B-12/folate deficiency	Median	6.2	10.1	222	91.9	14.9
	Range	2.6-9.4	6.7-13.3	119-305	67.1-100.8	12.9-21.1
Other	Median	6.6	10.7	250	87.2	15.0
	Range	4.3-46.1	7.1-13.1	131-472	56.1-114.1	13.2-18.2
Unknown	Median	6.6	10.8	257	96.7	14.4
	Range	2.8-14.7	7.4-12.8	46-589	88.4-106.5	12.5-21.1

with females accounting for 76.2% of patients in this group. Most patients in this study with anemia of chronic inflammation had a normocytic anemia, as the median MCV was 95.6 μm^3 and the range was from 81.0 to 103.5 μm^3.

Renal insufficiency was a contributing cause of anemia for 11.2% of all TWCC patients. Nearly half (8 of 17 or 47.1%) of those with renal insufficiency also had additional contributing factors to their anemia such as iron deficiency and chronic inflammation. Males had a higher prevalence of renal insufficiency associated anemia in this study, with 16.1% of all male cases of anemia caused by renal insufficiency, compared to 11.5% of all female cases of anemia. Renal insufficiency resulted in the lowest median hemoglobin of any etiology in this study with a value of 9.8 g/dL (ranging from 7.3 to 12.7 g/dL). This group also tended to show a normocytic anemia with a median MCV of 93.8 fL (range from 84.6 to 104.9 fL).

Four patients were found to have isolated B-12 deficiency; three were subsequently diagnosed with pernicious anemia. Seven additional patients were shown to have B-12/folate deficiency in addition to iron deficiency. Males showed a higher prevalence of B-12 or folate deficiency in this study with 12.5% of all males affected and only 4.2% of all females. Although, B-12 and folate deficiency are causes of macrocytic anemia, defined as having MCV greater than 100 fL, surprisingly, in this study the median MCV was 91.9 fL (range of 67.1 to 100.8 fL).

Additional etiologies for anemia were found in a very small number of patients in this population, accounting for 14 (9.2%) of the patients with anemia. Three patients were diagnosed with hemoglobinopathies (one each with Hemoglobin C, Hemoglobin E, and Hemoglobin constant spring), two patients were diagnosed with beta thalassemia minor, and one patient was diagnosed with alpha thalassemia (same patient that also had Hemoglobin constant spring). Five patients had hemolytic anemia (one due to pyruvate kinase deficiency, three due to autoimmune hemolytic anemia, and one suspected to be caused by mechanical hemolysis across the patient's prosthetic aortic valve). Finally, the anemia in two patients was attributed to the acute blood loss.

The exact etiology of the anemia in 15 patients (9.9% of the study population) was not determined. The factors that precluded diagnosis varied. Three patients declined further workup after discussion of their mild level of anemia, lack of symptoms, and possibility for anemia resolution without intervention. Two patients declined further evaluation due to severe comorbidities and advanced age. In six patients, no diagnosis was reached despite extensive evaluation; four of these patients experienced only transient anemia (anemia eventually resolved), while two other patients were unable to be diagnosed despite evaluation. A loss to follow-up contributed to the inability to determine a final diagnosis in four patients.

DISCUSSION

Investigators at the four academic medical centers were chosen to compare the results of this study with limited their study populations to patients 65 years of age and older.[5-8] The TWCC study did not have this age limitation. Table 5 provides a brief comparison of the patient populations in the TWCC study and the four cited studies. Table 6 compares the etiologies for anemia found in the TWCC study with these previous studies. The TWCC study reported a nearly 50% incidence of iron deficiency anemia compared to the 12-25% in the four studies cited. The TWCC study also showed a higher contribution of confirmed GI bleeds (15.8%) to the anemia compared to the 9% reported by Ania et al.[8] Differences in study populations undoubtedly played a significant role in diverse results. For example, the higher incidence of iron deficiency anemia at TWCC may be the result of inclusion of young, menstruating women in the study.

Table 5. Comparative study populations.

Study	Population Studied
TWCC	Individuals referred to hematologists at TWCC, Salina, KS for workup of a new diagnosis of anemia between August 2015 and May 2019 (excluded, if prior diagnosis or treatment of non-hematologic malignancy).
Guralnik et al.[5]	Participants in Third National Health and Nutrition Examination Survey (NHANES III); older than 65 and anemic.
Price et al.[6]	Patients older than 65 and anemic referred between March 2006 and January 2010 to Stanford Hospital and Clinics and Veteran Affairs Palo Alto Health Care Systems outpatient hematology clinics; not institutionalized; ECOG performance ≥ 2; excluded, if had received any red cell transfusion or erythropoiesis-stimulating agent within prior three months, had end-stage liver disease, were dialysis-dependent, had known diagnosis of hematologic malignancy, had predicted survival less than three months due to other comorbidities, or were unlikely to comply with protocol.
Artz and Thirman[7]	Patients older than 65 seen in anemia referral clinic from January 2005 - June 2009 at University of Chicago Hematology Clinic; excluded for erythropoietin-stimulating agent hyporesponsiveness, known hematologic malignancy, or cancer chemotherapy or radiation therapy completed within prior six months.
Ania et al.[8]	Individuals in Olmstead County, Minnesota older than 65 years old with newly recognized cases of anemia during 1986.

Table 6. Comparison of the etiologies of anemia.

Parameter	TWCC Study	Guralnik et al.[5]	Price et al.[6]	Artz and Thirman[7]	Ania et al.[8]
Number of anemic patients evaluated	152	2,096	190	174	618
Male cases (%)/ female cases (%)	37/63	Not reported	85/15	69/31	39/61
Iron deficiency (% of total)	48%	20%	12%	25.3%	14%
Hematologic malignancy (% of total)	14%	Not reported	22%	7.5%	2%
Anemia of chronic inflammation (% of total)	14%	24%	6%	9.8%	4%
Renal insufficiency (% of total)	11%	12%	4%	3%	1%
B-12/folate deficiency (% of total)	7%	14%	0.5%	0.6%	1%

Although the four academic medical center reports showed some variability in the incidence of anemia due to hematologic malignancies, chronic inflammation, renal insufficiency, and B-12/folate deficiency, when reviewed, they are not too dissimilar from the TWCC results. Interestingly, the incidence of MDS in the TWCC study correlated well with the study performed by Artz and Thirman.[7] Additionally, the anemia of chronic inflammation predominately was seen in females in the TWCC report compared to approximately equal representation in the Ania study[8] or male predominance (61.8%) in the Guralnik study.[5]

The rate of unexplained anemia was much lower (9.9% of total patients studied) in the TWCC study compared with the other studies cited (19-39%). While the reason for the lower incidence of unexplained anemia in the TWCC study was not determined, the duration and extent of evaluation or the referral patterns of physicians may have contributed to differences.

Specifically, the patient population referred to TWCC was not identical to that seen in the other reported studies, and the TWCC hematologists may have taken more time and performed a more exhaustive evaluation to determine the cause of anemia.

The choice of how to classify patients with multifactorial disease differed from report to report. In the current study, patients deemed to have multifactorial disease were given multiple diagnoses. In Price et al.[6], study investigators determined which of the contributing factors was most clinically relevant. In the studies by Guralnik et al.[5] and Artz and Thirman[7], the cause of anemia was determined in a hierarchical fashion in which diagnoses were excluded in a systematic manner until the diagnosis was reached, though Guralnik additionally included some multifactorial diagnoses such as combined nutrient deficiency.

CONCLUSIONS

The TWCC study found similar etiologies for anemia as those previously reported by four academic medical centers; however, the incidences of the etiologies were dissimilar. While the incidence of anemia due to hematologic malignancy, chronic inflammation, renal insufficiency, and B-12/folate deficiency were similar to previous reports, significantly more iron deficiency and less unexplained anemia were found in the TWCC study. The differences in findings undoubtedly reflected dissimilarities in the demographics of referral/study populations, duration and extent of evaluation, and referral patterns.

This report provided important information to physicians, especially those caring for anemic patients, regarding the causes and incidence of different anemias in patients seen in a rural hematology clinic. Although consultation with the community hematologist may be an important step in the evaluation of the patient with anemia, it might not need to be the first step. The results of this study provide guidance to the primary care provider regarding the most common causes for anemia seen by community hematologists and a basic evaluation prior to referral. This study found that approximately 80% of patients were affected by one or more of four basic benign types of anemia: iron deficiency, anemia of chronic inflammation, renal insufficiency, and B-12/folate deficiency. Approximately half of patients were affected by iron deficiency anemia, and an additional 30% of patients by anemia of chronic disease, with renal insufficiency and B-12/folate deficiency as less common nonmalignant causes of anemia.

A complete history and physical exam and a CBC and reticulocyte count are important initial diagnostic measures for the primary care physician. The information gleaned enables the classification of the anemia as mild, moderate, or severe, microcytic, normocytic, or macrocytic, and hypoproliferative, normoproliferative, or hyperproliferative and can direct the necessity for further testing. Additional tests, such as

iron studies, inflammatory markers such as C-reactive protein or erythrocyte sedimentation rate, a complete metabolic panel, and vitamin B-12 and folate levels may provide the necessary information to confirm a diagnosis and guide a definitive treatment plan. If a hematologic consultation is desired or warranted, this information will go a long way in helping the consultant care for the patient.

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A Geo-Stratified Analysis of Associations Between Socio-Economic Factors and Diabetes Risk

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ABSTRACT

Introduction. In 2019, diabetes was the seventh leading cause of death in the United States. The association between diabetes risk and socio-economic factors in the U.S. has been examined primarily at the national level; little is known about this association at the regional level. This study examined and compared the association between diabetes risk and previously established socio-economic factors across four geographic regions (South, Midwest, West, and Northwest).

Methods. This study analyzed the 2014 Behavioral Risk Factor Surveillance System (BRFSS) data stratified by four geographic regions of the U.S. The risk estimates of diabetes associated with previously established socio-economic factors, as well as diabetes prevalence, were compared across four geographic regions.

Results. There was marked variation in association between diabetes risk and previously established risk factors across the four geographic regions. In the South, rural residency was associated with increased diabetes risk, whereas in the other geographic regions rural residency had a protective effect. In the South, the diabetes risk for males was 22% higher compared to females, whereas the risk for males was 41% higher than females in the Northeast. Independently, age had the strongest discriminative ability to distinguish between a person with diabetes and a person without diabetes, whereas ethnicity, race, and sex had the weakest discriminative abilities.

Conclusions. These findings suggested a higher prevalence of diabetes by race/ethnicity (non-Hispanic Black and Hispanic) and income across all four regions. Rural residency was highest in the South, but protective in other regions. Overall, age and income provided the highest predictive ability for diabetes risk. This study highlighted differences in diabetes prevalence in association between previously established socio-economic variables and diabetes risk across four geographic regions. These findings could help public health professionals and policy makers in understanding the dynamic relationship between diabetes and risk factors at the regional level.

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INTRODUCTION

In 2018, 34.2 million people were estimated to have diabetes mellitus (diabetes), and another 7.3 million were estimated to live with undiagnosed diabetes.[1] In 2019, type II diabetes mellitus was the eighth leading cause of death in the U.S., with more than 84,000 deaths.[2] Diabetes is associated with increased risk of a wide variety of diseases and health complications, such as cardiovascular disease, kidney disease, tuberculosis, obesity, ophthalmic disorders, nephrology complications, and periodontal disease.[3-8]

The economic toll of diabetes is equally catastrophic. In the U.S., the total estimated cost of diabetes in 2017 was $327 billion, 72% of which was accounted for by direct health care expenditures and 28% was associated with reduced productivity.[9] On average, the health care cost was estimated to increase by 230% for someone with diabetes. The increased cost associated with diabetes had more of a severe impact on low- and middle-income families. Considering the tremendous clinical and financial burden incurred, the increasing trend of diabetes prevalence, and the fact that diabetes has been viewed as a largely preventable disease, studies aimed at identifying the determinants of diabetes have become more important than ever.

Multiple demographic factors have been associated with the risk of diabetes, including gender, age, income, education, race, ethnicity, and rural residency.[10-12] Specifically, being male, non-Hispanic Black, Hispanic, low-income, having less education, and being older all put one at a higher risk of having diabetes.[10-16] However, understanding geographic disparities around diabetes is needed. Rural residents have a higher prevalence of diabetes compared to urban residents.[17-22] O'Connor and Wellenuis found disparities exist between rural and urban residents, with rural residents more likely to receive a diagnosis of diabetes mellitus compared to urban residents.[17] However, after controlling for risk factors, the prevalence of diabetes diminished for rural residents. Barker and colleagues[21] suggested the southern region of the U.S. is the "diabetes belt", meaning it had a higher prevalence of diabetes and most often was linked to non-Hispanic Blacks who were obese and led a sedentary lifestyle.[21] Additional studies have examined the differences in how rural residents receive treatment and manage their diabetes compared to urban residents.[22] Stark differences were discovered that left rural residents with a disadvantage because of several factors, such as being overweight, having less access to a primary care physician (e.g., living in a Health Professional Shortage Area), and cost of care.

There is a dearth of literature on the prevalence of diabetes based on geographical region within the U.S. Although several studies have addressed the prevalence of diabetes in terms of socio-economic variables, little is known about the association of diabetes risk by geographic region.[10,23] Voeks et al.[23] suggested there are regional differences in terms of diabetes prevalence within selected southern states. How diabetes prevalence differs across geographical regions of the U.S. is poorly understood. Therefore, the purpose of this study was to examine diabetes prevalence in regions across the U.S. and describe relationships between diabetes risk and previously established socio-economic determinants of diabetes by region.

METHODS

Dataset and Study Design. The Behavioral Risk Factor Surveillance System (BRFSS) survey is a collaborative effort between the states, participating U.S. territories, and the U.S. Centers for Disease Control and Prevention (CDC).[24] The BRFSS is an ongoing

surveillance system designed to measure behavioral risk factors for non-institutionalized adults in the U.S. The BRFSS survey is administered through landline or cellular telephone. The landline telephone survey involved data collection from a randomly selected adult in each household. Among the cellular telephone users, information was collected from participants who resided in private residences or college housing. Information collected during the interview included demographics, preventive health practices, and risk behaviors.[24] This study used data collected during the 2014 survey cycle from four U.S. geographical regions: South, Midwest, West, and Northwest. A stratified analysis for each geographic region was conducted (Figure 1). The BRFSS inclusion criteria included U.S. residents 18 years or older who owned a landline telephone or cellular telephone.

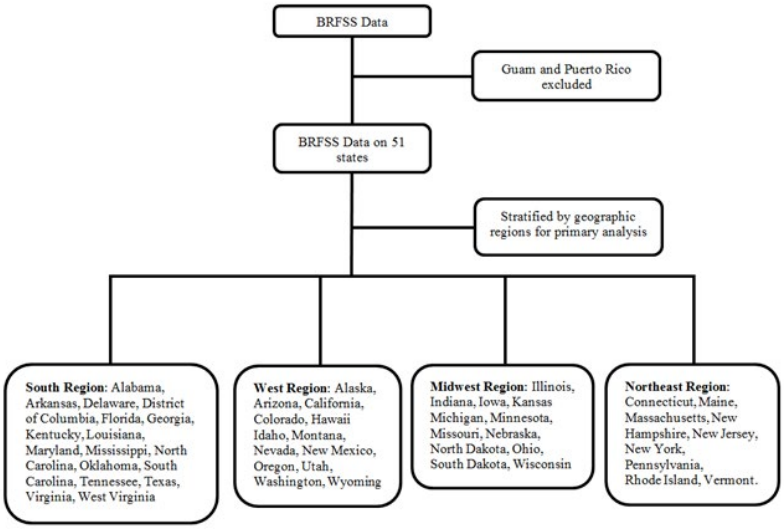

Figure 1. Study flowchart stratification.

Variables. The primary outcome of interest was if the respondent had ever been told by a doctor that they had diabetes. Although there are differences between type 1 and type 2 diabetes, the BRFSS database did not assess the type of diabetes; thus, the term "diabetes" referred to both types. Those who reported not having been diagnosed with diabetes or having been diagnosed only during pregnancy or with pre-diabetes or borderline diabetes were categorized as not having diabetes. Participants who refused to respond, were not asked, responded as being unsure, or left the question blank were excluded from analysis.

Based on residency, respondents were classified as rural residents if they reported their residency was not in a metropolitan statistical area (MSA). MSAs are defined by the U.S. Office of Management and Budget, and this definition has been applied by the U.S. Census Bureau for data collection.[25] Based on household income, participants were classified into one of the three categories: less than $25,000, between $25,000 and $50,000, and at least $50,000. Regarding race, participants were categorized as non-Hispanic White, non-Hispanic Black, and "other" (if race was reported as Asian, Native Hawaiian or other Pacific Islander, or other race). Regarding age, participants were categorized as 34 or younger, between 35 and 44, between 45 and 54, between 55 and 64, and 65 or older. To determine education level, participants were stratified into one of four groups: "did not graduate high school", "graduated high school", "attended college or technical school", and "graduated from college or technical school".[25]

Statistical Analysis. The association between diabetes risk and previously established socio-economic determinants of diabetes was explored by geographic region through modeling the relative risk ratio of probabilities in lieu of the more commonly reported odds ratio modeling. Zou's modified Poisson regression was used to obtain relative risk estimates.[26] Unlike odds ratios, relative risk estimates are more intuitive and comprehensible as they directly compare the probabilities of two mutually exclusive events: the presence and absence of diabetes.[27,28]

All variables included in this study were categorical. Descriptive statistics were reported as frequency (percentage). The association between diabetes status and each categorical variable was examined initially using Pearson's Chi-Square test of independence. Overall, diabetes prevalence was reported at each level of categorical variable. Zou's modified Poisson regression approach was used to obtain risk of diabetes associated with each variable.[26] Two-way interactions among variables were tested and adjusted for when the interaction was significant. Additionally, concordance index (C-index) was used to assess the predictive ability of a fitted model as well as the independent predictive ability of each variable. Reference categories for covariates were urban residency, female, income greater than $50,000, non-Hispanic ethnicity, non-Hispanic White, age younger than 34 years, and graduate from college or technical school. The analyses were performed using SAS 9.4 statistical software for Windows®. Statistical significance was based on two-sided tests, assuming a type I error rate of 0.05.

RESULTS

Descriptive Statistics. In the South (n = 71,441), 70% of respondents lived in an urban or semi-urban region; 61% were females; 43% had income greater than $50,000; 94% were non-Hispanic, 78% were non-Hispanic Whites, 14% were 34 years or younger, and 34% graduated from college or technical school. The prevalence of self-reported diabetes was higher in rural regions (20%) than in urban regions (17%); slightly higher among males (16%) than females (15%); highest among those with an income of less than $25,000 (22%) and least among those with incomes greater than $50,000 (10%); higher among Hispanics (16%) than non-Hispanics (14%); highest among non-Hispanic Blacks (21%) and least among "other" race (13%); highest among those 65 years or older (23%) and least among those 34 years or younger (2%); highest among those who graduated from high school but did not attend college or technical school (24%) and least among those who graduated from college or technical school (11%). The Chi-Square test of association suggested significant associations among all the covariates and diabetes status (Table 1).

In the West (n = 54,830), 63% of respondents lived in an urban or semi-urban region; 56% were females; 47% had income greater than $50,000; 89% were non-Hispanic; 86% were non-Hispanic Whites; 16% were 34 years old or younger; 38% graduated from college or technical school. The prevalence of self-reported diabetes was similar in rural and urban regions (13%); slightly higher among males (12%) than females (11%); highest among those with an income of less than $25,000 (16%) and least among those with incomes greater than

$50,000 (8%); higher among Hispanics (14%) than non-Hispanics (11%); highest among non-Hispanic Blacks and "other" race (14%) and least among non-Hispanic Whites (11%); highest among those who are at least 65 years old (18%) and least among those 34 years old or younger (2%); highest among those who did not graduate high school (18%) and least among those who graduated from college or technical school (8%). Gender, income category, ethnicity, race, age category, and education level were associated independently with diabetes status (Table 2). The association among rural residency and diabetes status was not significant.

In the Midwest (n = 62,443), 57% of respondents lived in an urban or semi-urban region; 57% were females; 46% had income greater than $50,000; 97% were non-Hispanic; 91% were non-Hispanic Whites; 15% were 34 years old or younger; 34% graduated from college or technical school (Table 3). The prevalence of self-reported diabetes was similar in rural and urban regions (15%); slightly higher among males (13%) than females (12%); highest among those with an income of less than $25,000 (19%) and least among those with incomes greater than $50,000 (8%); higher among Hispanics (13%) than non-Hispanics (11%); highest among non-Hispanic Blacks (20%) and least among non-Hispanic Whites (12%); highest among those with aged 65 years or older (20%) and least among those that are 34 years old or younger (2%); highest among those who did not graduate high school (20%) and least among those who graduated from college or technical school (9%). Gender, income category, ethnicity, race, age category, and education level were associated independently with diabetes status (Table 3). The association among rural residency and diabetes status was not significant.

Table 1. Prevalence of self-reported diabetes by socio-economic variables in southern region of the United States: BRFFS, 2014.

Variable	Response Options	Count (%)[1]	Prevalence (%)[2]	p Value[3]
Rural status	Urban	63,513 (70)	10,719 (17)	< 0.01
	Rural	27,790 (30)	5,491 (20)	
Gender	Male	53,383 (39)	8,499 (16)	< 0.01
	Female	82,838 (61)	12,646 (15)	
Income	< $25,000	36,120 (32)	7,908 (22)	< 0.01
	≥ $25,000 and ≤ $50,000	28,672 (25)	4,631 (16)	
	> $50,000	47,932 (43)	4,878 (10)	
Ethnicity	Not Hispanic	126,498 (94)	19,733 (16)	< 0.01
	Hispanic	8,482 (6)	1,196 (14)	
Race	Non-Hispanic White	103,488 (78)	14,809 (14)	< 0.01
	Non-Hispanic Black	23,768 (18)	5,107 (21)	
	Other	5,613 (4)	734 (13)	
Age	≤ 34	18,544 (14)	373 (2)	< 0.01
	≥ 35 and ≤ 44	15,294 (11)	906 (6)	
	≥ 45 and ≤ 54	22,460 (16)	2,649 (12)	
	≥ 55 and ≥ 65	30,854 (23)	5,977 (19)	
	≥ 65	49,069 (36)	11,240 (23)	
Education	Did not graduate high school	14,367 (11)	3,438 (24)	< 0.01
	Graduated high school	39,594 (29)	7,007 (18)	
	Attended college or technical school	35,121 (26)	5,583 (16)	
	Graduated from college or technical school	46,123 (34)	4,971 (11)	

[1]Count (%) is the frequency counts and percentage for each level of variable.
[2]Prevalence (%) represents prevalence of self-reported diabetes for each level of categorical.
[3]p value is based on Chi-Square test of association between diabetes status and the variables.

Table 2. Prevalence of self-reported diabetes by socio-economic variables in western region of the United States: BRFFS, 2014.

Variable	Response Options	Count (%)[1]	Prevalence (%)[2]	p Value[3]
Rural status	Urban	42,445 (63)	5,458 (13)	0.20
	Rural	25,345 (37)	3,350 (13)	
Gender	Male	48,416 (44)	5,780 (12)	< 0.01
	Female	62,747 (56)	6,643 (11)	
Income	< $25,000	25,485 (27)	4,140 (16)	< 0.01
	≥ $25,000 and ≤ $50,000	24,308 (26)	2,985 (12)	
	> $50,000	45,335 (47)	3,439 (8)	

Table 2. Prevalence of self-reported diabetes by socio-economic variables in western region of the United States: BRFFS, 2014. *cont.*

Variable	Response Options	Count (%)[1]	Prevalence (%)[2]	p Value[3]
Ethnicity	Not Hispanic	9,7248 (89)	10,474 (11)	< 0.01
	Hispanic	12,563 (11)	1,769 (14)	
Race	Non-Hispanic White	92,977 (86)	9,870 (11)	< 0.01
	Non-Hispanic Black	2,333 (2)	359 (14)	
	Other	12,978 (12)	1,835 (14)	
Age	LE 34	17,627 (16)	279 (2)	< 0.01
	≥ 35 and ≤ 44	13,948 (13)	611 (4)	
	≥ 45 and ≤ 54	17,715 (16)	1,597 (9)	
	≥ 55 and ≥ 65	24,609 (22)	3,234 (13)	
	≥ 65	37,264 (33)	6,702 (18)	
Education	Did not graduate high school	7,707 (7)	1,410 (18)	< 0.01
	Graduated high school	27,775 (25)	3,535 (13)	
	Attended college or technical school	32,470 (30)	3,864 (12)	
	Graduated from college or technical school	42,130 (38)	3,496 (8)	

[1]Count (%) is the frequency counts and percentage for each level of variable.
[2]Prevalence (%) represents prevalence of self-reported diabetes for each level of categorical.
[3]p value is based on Chi-Square test of association between diabetes status and the variables.

Table 3. Prevalence of self-reported diabetes by socio-economic variables in midwestern region of the United States: BRFFS, 2014.

Variable	Response Options	Count (%)[1]	Prevalence (%)[2]	p Value[3]
Rural status	Urban	43,277 (57)	6,375 (15)	0.74
	Rural	32,916 (43)	4,817 (15)	
Gender	Male	53,620 (43)	7,105 (13)	< 0.01
	Female	72,386 (57)	8,745 (12)	
Income	< $25,000	27,968 (26)	5,322 (19)	< 0.01
	≥ $25,000 and ≤ $50,000	30,436 (28)	4,106 (13)	
	> $50,000	50,035 (46)	4,109 (8)	
Ethnicity	Not Hispanic	121,334 (97)	15,301 (13)	< 0.01
	Hispanic	3,781 (3)	407 (11)	
Race	Non-Hispanic White	113,442 (91)	13,692 (12)	< 0.01
	Non-Hispanic Black	5,759 (5)	1,165 (20)	
	Other	4,937 (4)	765 (15)	
Age	≤ 34	18,899 (15)	305 (2)	< 0.01
	≥ 35 and ≤ 44	14,533 (12)	651 (4)	
	≥ 45 and ≤ 54	20,933 (17)	1,963 (9)	
	≥ 55 and ≥ 65	28,836 (23)	4,220 (15)	
	≥ 65	42,805 (34)	8,711 (20)	
Education	Did not graduate high school	8,033 (6)	1,590 (20)	< 0.01
	Graduated high school	38,967 (31)	5,816 (15)	
	Attended college or technical school	36,289 (29)	4,601 (13)	
	Graduated from college or technical school	42,027 (34)	3,746 (9)	

[1]Count (%) is the frequency counts and percentage for each level of variable.
[2]Prevalence (%) represents prevalence of self-reported diabetes for each level of categorical.
[3]p value is based on Chi-Square test of association between diabetes status and the variables.

In the Northeast (n = 46,571), 81% of respondents lived in an urban or semi-urban region; 59% were females; 50% had income greater than $50,000; 94% were non-Hispanic; 88% were non-Hispanic Whites; 13% were 34 years or younger; 42% graduated from college or technical school (Table 4). The prevalence of self-reported diabetes was slightly higher in urban regions (14%) than rural regions (13%); higher among males (14%) than females (11%); highest among those with an income of less than $25,000 (19%) and least among those with incomes greater than $50,000 (8%); higher among Hispanics (14%) than those who identified as non-Hispanic (12%); highest among non-Hispanic Blacks (18%) and least among non-Hispanic Whites and "other" race (12%); highest among those 65 years or older (20%) and least among those aged 34 years or younger (4%); highest among those who did not graduate high school (22%) and least among those who graduated from college or technical school (8%). Gender, income category, ethnicity, race, age category, and education level were associated independently with diabetes status (Table 4). The association among rural residency and diabetes status was moderately significant (p = 0.02).

Relative Risk Modeling. For each of the geographic regions, the interaction between income and age, and income and education level were significant. The relative risk modeling results presented in Table 5 provide risk estimates after adjusting for the interactions. The interpretation of risk estimates associated with any covariate in the subsequent paragraphs implicitly assumed values of all covariates, besides the covariate whose risk was being interpreted, were held fixed.

Table 4. Prevalence of self-reported diabetes by socio-economic variables in northeastern region of the United States: BRFFS, 2014.

Variable	Response Options	Count (%)[1]	Prevalence (%)[2]	p Value[3]
Rural status	Urban	46,877 (81)	6,595 (14)	0.02
	Rural	10,957 (19)	1,447 (13)	
Gender	Male	3,4284 (41)	4,652 (14)	< 0.01
	Female	48,484 (59)	5,535 (11)	
Income	< $25,000	18,161 (26)	3,537 (19)	< 0.01
	≥ $25,000 and ≤ $50,000	16,752 (24)	2,328 (14)	
	> $50,000	34,849 (50)	2,725 (8)	
Ethnicity	Not Hispanic	76,955 (94)	9,355 (12)	< 0.01
	Hispanic	4,878 (6)	691 (14)	
Race	Non-Hispanic White	70,751 (88)	8,351 (12)	< 0.01
	Non-Hispanic Black	5,552 (7)	992 (18)	
	Other	4,117 (5)	496 (12)	
Age	≤ 34	10,782 (13)	202 (2)	< 0.01
	≥ 35 and ≤ 44	9,441 (11)	402 (4)	
	≥ 45 and ≤ 54	14,934 (18)	1,303 (9)	
	≥ 55 and ≥ 65	19,748 (24)	2,768 (14)	
	≥ 65	27,863 (34)	5,512 (20)	
Education	Did not graduate high school	5,396 (7)	1,173 (22)	< 0.01
	Graduated high school	22,585 (28)	3,533 (16)	
	Attended college or technical school	19,699 (24)	2,553 (13)	
	Graduated from college or technical school	34,190 (42)	2,811 (8)	

[1]Count (%) is the frequency counts and percentage for each level of variable.
[2]Prevalence (%) represents prevalence of self-reported diabetes for each level of categorical.
[3]p value is based on Chi-Square test of association between diabetes status and the variables.

Table 5. Associations between diabetes and socio-economic variables, BRFSS, 2014.

Variables	Variable Category*	Variable Category*	Relative Risk (95% CI)			
			South (n = 71,441)	West (n = 54,830)	Midwest (n = 62,443)	Northeast (n = 46,571)
Rural status	Rural		1.09 (1.06 - 1.13)	0.96 (0.92 - 1)	0.95 (0.91 - 0.98)	0.91 (0.86 - 0.96)
	Urban		Reference category	Reference category	Reference category	Reference category
Gender	Male		1.22 (1.18 - 1.25)	1.29 (1.24 - 1.35)	1.30 (1.25 - 1.35)	1.41 (1.35 - 1.47)
	Female		Reference category	Reference category	Reference category	Reference category
Income	< $25,000		3.69 (2.28 - 5.97)	2.40 (1.43 - 4.02)	1.99 (1.17 - 3.37)	2.81 (1.62 - 4.88)
	≥ $25,000 and ≤ $50,000		1.92 (1.08 - 3.39)	1.28 (0.68 - 2.41)	1.19 (0.64 - 2.21)	1.76 (0.93 - 3.33)
	> $50,000		Reference category	Reference category	Reference category	Reference category
Ethnicity	Hispanic		1.26 (1.16 - 1.36)	1.34 (1.25 - 1.44)	1.08 (0.92 - 1.25)	1.29 (1.16 - 1.43)
	Not Hispanic		Reference category	Reference category	Reference category	Reference category
Race	Non-Hispanic Black		1.54 (1.49 - 1.60)	1.72 (1.53 - 1.95)	1.63 (1.52 - 1.74)	1.51 (1.40 - 1.63)
	Other		1.25 (1.14 - 1.36)	1.48 (1.39 - 1.57)	1.70 (1.56 - 1.86)	1.30 (1.16 - 1.46)
	Non-Hispanic White		Reference category	Reference category	Reference category	Reference category
Age	≥ 35 and ≤ 44		3.00 (1.93 - 4.68)	1.48 (0.93 - 2.37)	1.70 (1.10 - 2.64)	2.34 (1.45 - 3.76)
	≥ 45 and ≤ 54		6.00 (3.93 - 9.17)	3.93 (2.57 - 5.99)	4.32 (2.89 - 6.46)	3.94 (2.51 - 6.18)
	≥ 55 and ≤ 65		11.37 (7.48 - 17.27)	7.13 (4.72 - 10.78)	7.80 (5.26 - 11.56)	7.70 (4.95 - 11.97)
	≥ 65		15.06 (9.92 - 22.86)	10.59 (7.03 - 15.97)	11.76 (7.95 - 17.41)	11.47 (7.39 - 17.79)
	≤ 34		Reference category	Reference category	Reference category	Reference category
Education	Attended college or technical school		1.44 (1.35 - 1.55)	1.48 (1.36 - 1.62)	1.33 (1.23 - 1.45)	1.44 (1.3 - 1.59)
	Did not graduate high school		1.81 (1.48 - 2.21)	1.83 (1.37 - 2.45)	1.72 (1.34 - 2.21)	1.96 (1.48 - 2.58)
	Graduated high school		1.48 (1.36 - 1.60)	1.49 (1.34 - 1.66)	1.33 (1.22 - 1.46)	1.54 (1.39 - 1.71)
	Graduated from college or technical school		Reference category	Reference category	Reference category	Reference category
Income *age	≥ $25,000 and ≤ $50,000	≥ 35 and ≤ 44	1.10 (0.59 - 2.04)	2.16 (1.06 - 4.38)	2.11 (1.07 - 4.17)	0.85 (0.41 - 1.78)
	≥ $25,000 and ≤ $50,000	≥ 45 and ≤ 54	0.95 (0.53 - 1.69)	1.47 (0.77 - 2.82)	1.43 (0.76 - 2.70)	1.14 (0.59 - 2.20)
	≥ $25,000 and ≤ $50,000	≥ 55 and ≤ 65	0.8 (0.45 - 1.42)	1.19 (0.63 - 2.24)	1.3 (0.70 - 2.42)	0.98 (0.52 - 1.86)
	≥ $25,000 and ≤ $50,000	≥ 65	0.71 (0.4 - 1.25)	1.09 (0.58 - 2.04)	1.12 (0.60 - 2.07)	0.84 (0.45 - 1.59)
	< $25,000	≥ 35 and ≤ 44	0.92 (0.55 - 1.54)	1.64 (0.91 - 2.96)	1.90 (1.05 - 3.44)	0.95 (0.51 - 1.77)
	< $25,000	≥ 45 and ≤ 54	0.79 (0.48 - 1.28)	1.30 (0.77 - 2.21)	1.68 (0.98 - 2.88)	1.16 (0.66 - 2.04)

Table 5. Associations between diabetes and socio-economic variables, BRFSS, 2014. *cont.*

Variables	Variable Category*	Variable Category*	Relative Risk (95% CI)			
			South (n = 71,441)	West (n = 54,830)	Midwest (n = 62,443)	Northeast (n = 46,571)
Income *age	< $25,000	≥ 55 and ≤ 65	0.58 (0.36 - 0.93)	0.88 (0.53 - 1.48)	1.23 (0.73 - 2.09)	0.80 (0.46 - 1.39)
	< $25,000	≥ 65	0.45 (0.28 - 0.73)	0.73 (0.44 - 1.21)	0.87 (0.52 - 1.47)	0.60 (0.35 - 1.03)
Income * Education	≥ $25,000 and ≤ $50,000	Attended college or technical school	0.82 (0.74 - 0.91)	0.86 (0.76 - 0.98)	0.86 (0.76 - 0.97)	0.81 (0.7 - 0.94)
	≥ $25,000 and ≤ $50,000	Did not graduate high school	0.67 (0.53 - 0.85)	0.71 (0.51 - 1.00)	0.84 (0.63 - 1.12)	0.70 (0.5 - 0.97)
	≥ $25,000 and ≤ $50,000	Graduated high school	0.77 (0.68 - 0.86)	0.80 (0.69 - 0.93)	0.85 (0.75 - 0.96)	0.80 (0.69 - 0.92)
	< $25,000	Attended college or technical school	0.78 (0.7 - 0.87)	0.80 (0.7 - 0.92)	0.82 (0.72 - 0.93)	0.87 (0.75 - 1.02)
	< $25,000	Did not graduate high school	0.67 (0.54 - 0.83)	0.76 (0.56 - 1.04)	0.69 (0.53 - 0.91)	0.76 (0.56 - 1.03)
	< $25,000	Graduated high school	0.75 (0.67 - 0.84)	0.77 (0.66 - 0.89)	0.79 (0.7 - 0.91)	0.86 (0.74 - 1.00)

n = Number of observations used in analysis.
Reference Group: Female (Sex) - Urban (Rural) - Greater than 50,000 (Income Status) - Not Hispanic (Ethnicity) -Less than 34 years (Age category) -and graduated from college or technical school (Education)
Results that are statistically significant are highlighted in yellow.

Equipoise exists with respect to risk estimates associated with rural residency as both protective and harmful effects of rural residency were observed across the four geographic regions. Rural residents had a 9% higher diabetes risk in the South. However, in the other regions, rural residency appeared to have a protective effect. Diabetes risk among rural residents was 5% lower in the Midwest, 9% lower in the Northeast, and 4% lower in the West. Compared to females in the following regions, the diabetes risk among males was 41% higher in the Northeast, 30% higher in the Midwest, 29% higher in the West, and 22% higher in the South. Hispanic Americans were at consistently higher diabetes risk across all four geographic regions. Compared to non-Hispanic Whites in the following regions, the risk of diabetes for Hispanics was 34% higher in the West, 29% higher in the Northeast, 26% in the South, and 8% higher in the Midwest. Similarly, compared to non-Hispanic Whites in the following regions, the risk of diabetes for non-Hispanic Blacks was 72% higher in the West, 63% higher in the Midwest, 54% higher in the South, and 51% higher in the Northeast.

Owing to interaction between age and income, and between age and education, the increased risk estimates for each stratification of age, income, and education were not directly interpretable. For the sake of presentation, the risk estimates of an individual were computed with "an income between $25,000 and $50,000, age between 45 and 54 years, and graduated high school". Compared to the reference category (income greater than $50,000, 34 years or younger, and graduated from college or technical school), this risk estimate was 12.5 times higher in the South, 9 times higher in the Northeast, 8.8 times higher in the West, and 8.3 times higher in the Midwest.

Additional Analysis. The discriminative (predictive) ability of the model in correctly classifying respondents with diabetes and those without diabetes was estimated by C-index. The C-index for the fitted models ranged from 0.72 (for the South) to 0.73 (for the West, Midwest, Northeast; Figure 2). Traditionally, the threshold of 0.8 has been used to identify models with strong predictive abilities.[29] The fitted models are thus moderately strong in terms of their predictive abilities. The predictive ability of each variable also was examined independently. Age had the greatest predictive ability across all geographical regions, followed by income (Figure 2). Ethnicity, sex, and race had the least predictive ability with C-indices marginally above 0.5, thus performing no better than a random coin flip.

DISCUSSION

This study examined associations between socio-economic factors and diabetes risk across the four geographic regions in the U.S. Unlike previous studies, these associations were examined while considering the possible interactions among socio-economic factors. The independent predictive ability of each of these factors also were evaluated. It was seen that the magnitude of the effect of these factors on the diabetes risks varied markedly across the four geographic regions; and for rural residency the direction of the effect in the South (increased risk) and the rest of the geographic regions (protective effect) were in the opposite direction. These results suggested the relationship between socio-economic factors and diabetes risk could differ significantly across the four geographic regions. These findings were similar to Barker and colleagues who found there to be a diabetes belt in the Southern region of the U.S. linked to non-Hispanic Black residents.[22]

Other studies have found similar results related to the Southern and Midwestern region of the U.S., where a significant prevalence of diabetes and metabolic syndrome exists.[30-31] In this study, a significant difference in self-reported prevalence among rural and urban regions was found in the South, with rural regions reporting a higher prevalence of diabetes and non-Hispanic Blacks having a higher risk of diabetes. Even with regional differences when looking at relative risk of diabetes, the interaction between income and education is the strongest predictor of diabetes prevalence. More tools need to be implemented to lower the prevalence of diabetes among low income and those with a lower educational attainment to improve areas such as a "diabetes belt". Myers and colleagues also investigated community level factors to better understand their results.[31] Myers found the "diabetes belt" region lacked sufficient recreational opportunities, more so than economic. What is unclear is if the county level factors were impacted by the community economic factor rather than the individual. Understanding environmental determinants that contribute to diabetes at a county and city level would be beneficial.

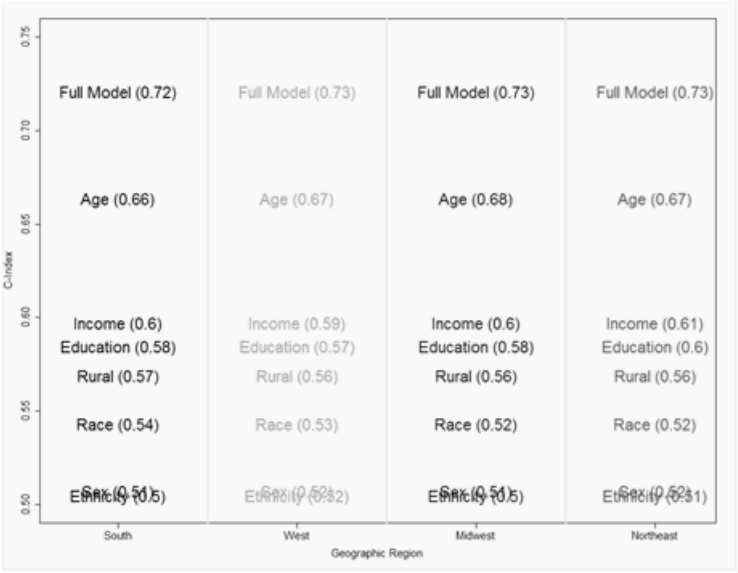

Figure 2. Discriminative (predictive) ability of diabetes classification by geographic region by estimated C-index.

There were also protective factors to consider in this work. Rural residency can be a protective factor in the Midwest, West, and Northeast, but not the South. Interestingly, a respondent's age and income were stronger predictors of diabetes risk. This study did not find race, ethnicity, or sex to be a dependable predictor of diabetes risk. This was important because of the overwhelming disparity in the prevalence of diabetes for specific racial/ethnic groups (non-Hispanic Black, Native American, Hispanic).

Limitations. The study had several limitations that were primarily attributable to the nature of the study design and the collected data. Limitations such as recall bias, inclusion of participants with access to phone services, missing information, lack of distinction between type 1 and type 2 diabetes, and biases associated with self-reporting (i.e., social desirability bias) limit the generalizability of our findings. The focus of our work was socio-economic factors, and influential variables (i.e., physical activity, food and beverage consumption, tobacco use) have not been included which likely would affect the risk estimates. Finally, retrospective studies can only identify associations and make it impossible to infer causality between the variables and diabetes risk.

CONCLUSIONS

This study highlighted novel findings, primarily, the variation in effect of socio-economic factors on diabetes risk across four geographic regions. This suggested that the dynamics between diabetes and the risk factors examined in the study differed by geographic region. The concordance index suggested that although variables could be associated significantly, their predictive ability may only be modest, essentially affirming the statistical adage that strongly associated variables may not be strongly predictive. There is a great need to develop a model with stronger predictive ability. Owing to interplay between social, economic, environmental, and genetic factors in establishing diabetes risk, the authors believe a strongly predictive model must incorporate individual and community-level information at the genetic, social, economic, and environmental levels. In conclusion, this study highlighted the differences in diabetes prevalence and the association between previously established socio-economic variables and diabetes risk across the four geographic regions of the U.S.

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Aspiration Risk Factors in Hospitalized Patients Following Trauma

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ABSTRACT

Introduction. Risk factors for aspiration are not well characterized in the trauma patient population. Improved understanding is important due to features of this patient population that place them at high risk for morbidity and mortality with aspiration.

Methods. In a retrospective analysis of patients who suffered a traumatic injury from 2016 to 2018, potential risk factors were recorded and analyzed with logistic regression to evaluate the trauma patient at risk for aspiration.

Results. Of the 146 patient charts analyzed, 56 (38%) had at least one documented aspiration event, while 90 (62%) patients had none. Multivariate logistic regression found a significant association between impaired consciousness and aspiration events ($p = 0.012$).

Conclusions. This study was a novel characterization of trauma patients likely to have experienced an aspiration event while hospitalized. The results suggested candidate risk factors for aspiration exist in a trauma-specific population. Impaired consciousness is likely to show a significant association with aspiration in trauma patients in future studies. ***Kans J Med 2022;15:184-188***

INTRODUCTION

Pulmonary aspiration is defined as the entry of foreign bodies or substances into the lungs.[1] The clinical sequelae following aspiration events are wide-ranging with the potential for serious morbidity and mortality. The most significant of these complications appeared to be acute lung injury, ventilator-associated pneumonia, and acute respiratory distress syndrome.[2-4] Risk factors for aspiration and its associated complications were well characterized in a variety of patient populations, but the trauma population has not been examined thoroughly.[2,5]

Trauma has been suggested to predispose patients to suffer an aspiration event, but there was little evidence in the literature that details the mechanisms driving this increased risk.[6,7] Furthermore, there was a distinct lack of evidence detailing which trauma patient would be most likely to aspirate. Improved understanding is vital due to the unique features and circumstances of the trauma population that potentially place them at high risk for morbidity and mortality associated with aspiration. It is not an unlikely scenario for patients suffering from traumatic injury to have compromised anatomical barriers, lower levels of consciousness (injury-related or therapeutic), or direct insult of foreign bodies within the thorax. It is unclear how these features affect the incidence of aspiration and its clinical sequelae in the trauma population.

In trauma patients, aspiration has been associated with increased hospital lengths of stay and an increased risk for ventilator-associated pneumonia.[8] The importance and significance of aspiration events were not well established in the literature and focused mostly on morbidity and mortality associated with aspiration. Current guidelines and information regarding aspiration from the American Association for the Surgery of Trauma were based largely on evidence from critical care populations not specific to the trauma patient.[7] These studies addressed aspiration from a broader perspective identifying and classifying the syndromes and sequelae associated with aspiration in critically ill patients.[1-3]

Two studies specific to the trauma patient population shared our outcome of interest. A retrospective study conducted in South Korea identified patient characteristics likely to be present in the setting of computed tomography findings suggestive of aspiration pneumonia.[9] They concluded the median head Abbreviated Injury Scale (AIS) scores, and severe Glasgow Coma Scores (GCS) were predictive for aspiration events. The second was a comprehensive prospective study which addressed the mortality associated with aspiration in trauma patients and identifies risk factors likely to be present as a secondary outcome.[10] This study was an important contribution in characterizing the trauma patient at risk for aspiration, but their primary focus was to address mortality associated with aspiration events. They concluded that patients who aspirated were injured more severely, had lower GCS scores, and were more likely to have required multiple intubation attempts.

Given the relative paucity of evidence surrounding aspiration in traumatic injuries, it was important to characterize the patient at risk for suffering an aspiration to inform future studies and patient care plans. This study sought to inform future studies by identifying potential risk factors for aspiration. It was hypothesized that risk factors for aspiration could be identified in patients hospitalized following traumatic injury.

METHODS

This study was a retrospective chart review approved by the Institutional Review Board at the University of Kansas Medical Center. The University of Kansas Trauma Registry was used to generate the initial patient list covering admissions to the Level I Trauma Center following traumatic injury from 2016 to 2018. Charts of adult patients who had an unplanned intubation, ventilator-associated pneumonia, respiratory failure, acute respiratory distress syndrome (ARDS), or unplanned/readmission to the intensive care unit (ICU) were examined as a filter to identify patients with respiratory distress and identify those with aspiration events. Those excluded from the study included patients who initially received care at an institution other than the University of Kansas, children, and readmissions. Documented aspiration events were recorded, and patients were divided into those with and without at least one documented aspiration event. To record an aspiration event, one of the following had to be present: (1) a diagnosis of aspiration

pneumonia or decompensation secondary to aspiration (ICD J69.0 or Y84.4)[11], staff witnessed or charted, (2) bronchoalveolar lavage with culture positive for mixed anaerobic organisms, or (3) speech-language pathology report positive for aspiration.

Data collected from the trauma registry included age, sex, race, ethnicity, body mass index (BMI), substance use, past medical history, mechanism of injury, type of injury, AIS score, Injury Severity Score (ISS), admission GCS.

The remaining data were collected from the patients' clinical charts. These data included past surgical history, smoking history and status, presence of feeding tubes (nasogastric, nasoenteric, or gastrostomy), number of surgeries for treatment, and documented aspiration events. For those with at least one aspiration event, additional collected data were type of aspiration, time from admission to first aspiration event, time from aspiration to death if applicable, reason documented for aspiration, and aspiration event confirmation with swallow studies.

Past medical history was recorded in the following categorical groupings: coronary heart disease, diabetes mellitus, chronic respiratory disease, stroke, liver disease, obesity, neurologic disorder, obstructive sleep apnea, and other. Similarly, medical complications were categorically grouped as: dysphagia, neurologic, impaired consciousness, anatomical disruption, gastroesophageal reflux disease, post-operative nausea and vomiting, and an optional fill-in text. Impaired consciousness was recorded as reflex impairment in coughing, swallowing, or a failure to respond adequately to external stimuli.

A bivariate analysis initially evaluated the entirety of our collected variables. From these data, only those variables which were found to be significant on bivariate analysis were reported. Cutoff for statistical significance was a p value < 0.05 and the data were analyzed with IBM SPSS®.

RESULTS

A total of 6,364 patients were admitted to the University of Kansas Hospital trauma service during the study period of 2016 to 2018. Of these patients, 147 met inclusion criteria; ultimately, 146 patients were used in our data analysis, with one patient excluded due to a recording error. Table 1 summarizes the baseline characteristics of the patients included in the study.

The average age of the patient population was 57 years and was predominantly non-Hispanic or Latino, Caucasian males. Dysphagia was the most prevalent medical complication with 52/146 (36%). It was excluded from the analysis as the time of diagnosis for recording a documented aspiration event was not reliably present. Regarding the general health of the population, 106 patients (73%) were classified as having some form of obesity with the overweight category being the most prevalent with 45 documented patients. The two most common medical complications post-admission were 52 recorded cases of dysphagia and 30 recorded cases of impaired consciousness. Substance abuse had variable reporting on data from the electronic health record with data being unavailable on 67 patients in our study.

Table 2 summarizes the details of traumatic injury in our study population. Falls were the most common cause of injury with 74/146 (51%) patients, followed by motor vehicle collisions at 49/146 (34%) patients. The most common type of injury reported was blunt trauma with 132/146 (90%) patients followed by fracture with 34/146 (23%) patients. Most of the study group required one surgery or less during their admission.

Table 1. Baseline characteristics of included patients.

Age (in years)	
Mean	57.4
Sex	
Male	71%
Race	
Caucasian	76%
African American	8%
Other	9%
Not available	8%
Ethnicity	
Hispanic or Latino	4%
Not Hispanic or Latino	93%
Unknown	3%
Mean Body Mass Index (BMI)	29
Substance Use	
None	39
Alcohol	15
Illicit drugs	25
Not available	67
Comorbidities and Complications	
Coronary heart disease	10%
Diabetes mellitus	33%
Chronic respiratory disease	22%
Stroke	1%
Liver disease	1%
Obesity	73%
Overweight (BMI: 25.0 - 29.9)	45%
Class I (BMI: 30.0 - 34.9)	29%
Class II (BMI: 35.0 - 39.9)	17%
Class III (BMI: 40.0 and greater)	9%
Neurological disorder	5%
Obstructive sleep apnea	6%
Other	79%
Prevalence of Documented Medical Complications	
Dysphagia	52
Impaired consciousness	30
Anatomical disruption, upper airway	8
Gastroesophageal reflux disease	9
Post-operative emesis	0
Other	99
Stroke	2
Neurologic injury	23

Table 2. Details of traumatic injury.

Mechanism of Injury	
Motor vehicle collision	34%
Firearm	7%
Fall	51%
Penetrating	3%
Motor vehicle vs. pedestrian	3%
Type of Injury	
Penetrating	10%
Fracture	23%
Blunt	90%
Mean Maximum Abbreviated Injury Scale	
Head	3.4
Face	1.6
Neck	2.0
Thorax	3.0
Abdomen	2.7
Upper extremity	1.7
Number of Surgeries Required for Treatment	
0	30%
1	40%
2	11%
3	7%
4	6%
5	0%
> 5	5%

Details concerning aspiration events are listed in Table 3. Of the 146 patients analyzed, 56 (38%) had at least one documented aspiration event while 90 (62%) patients had none. Most documented aspiration events occurred after 120 hours post-admission, with dysphagia being the most documented reason for aspiration. As stated above, dysphagia was excluded from the analysis, so this was an observational finding. Overt aspiration events were the most recorded with 36/56 (64%). There were 19 individuals whose deaths were attributed to complications from aspiration. In all 19 deceased individuals, the time from a documented aspiration event to death was greater than 72 hours.

Using a bivariate analysis, significant risk factors for aspiration were identified including race, maximum head AIS, ISS, intubation, presence of feeding tubes (e.g., nasogastric, nasoenteric, or gastrostomy), and impaired consciousness. A multivariate logistic regression was used to evaluate the influence of our selected potential risk factors on the likelihood of patients suffering an aspiration event. There was a significant association between impaired consciousness ($p = 0.012$) and patients having suffered an aspiration event. Ptients who suffered an aspiration event were 3.69 (95% CI 2.67, 4.71) times more likely to have had impaired consciousness following traumatic injury. Tables 4 and 5 display these results.

Table 3. Aspiration event details.

Documented Aspiration Events	
1	15%
2	8%
3	7%
4	2%
5	3%
> 5	3%
0	62%
Time from Admission to First Aspiration Event	
< 6 hours	5%
6 - 24 hours	4%
25 - 48 hours	7%
49 - 72 hours	9%
73 - 96 hours	5%
97 - 120 hours	7%
> 120 hours	57%
Unknown	5%
Type of Aspiration	
Overt	64%
Silent	11%
Both	16%
Unknown	9%
Documented Reason for Aspiration	
Dysphagia	84%
Supine position	11%
Neurologic disorder	11%
Impaired consciousness	29%
Anatomical disruption	7%
Post-operative emesis	2%
Other	34%

Table 4. Bivariate analysis.

Risk Factors Significant on Bivariate Analysis	
Race	0.019
Maximum head Abbreviated Injury Scale	0.045
Intubated	< 0.001
Feeding tube	< 0.001
Nasogastric tube present	< 0.001
Nasoenteric tube present	< 0.001
Gastrostomy present	0.009
Impaired consciousness	0.005
Injury Severity Score	0.003

*p values shown in right column with significance level of < 0.05.

Table 5. Multivariate logistic regression.

	Odds Ratio (95% CI)	p Value
Race	1.197 (1.0, 1.39)	0.066
Maximum head Abbreviated Injury Scale	1.010 (0.78, 1.24)	0.935
Intubated	2.643 (1.43, 3.86)	0.118
Feeding tube	0.00	0.999
Nasogastric tube present	0.00	0.999
Nasoenteric tube present	2.152 (1.23, 3.08)	0.105
Gastrostomy present	1.108 (0.16, 2.05)	0.831
Impaired consciousness	3.689 (2.67, 4.71)	0.012
Injury Severity Scale	0.999 (0.95, 1.04)	0.973

DISCUSSION

This study was a relatively novel characterization of trauma patients at risk for suffering an aspiration event. It was conducted in the hopes that the findings could inform future studies. The results suggested candidate risk factors for aspiration exist in a trauma-specific patient population. The primary takeaway from this exploratory study was that impaired consciousness is likely to show continued and significant association with aspiration in trauma patients in future studies. Secondarily, factors found to be significant on bivariate analysis should be examined more closely in future studies as they likely are underrepresented in this study.

Our findings were supported by the work of Benjamin et al.[9] and Heo et al.[10] which both identified impaired consciousness and injury severity scores being significantly associated with aspiration. Additionally, Heo et al.[10] found that a higher number of attempted intubations in the trauma bay was predictive of patients suffering an aspiration event. Witnessed aspirations, multiple intubation attempts, and emergency medical service reports of aspiration were key variables in these previous studies which focused primarily on the initial evaluation and treatment of this population. A notable difference between prior studies' populations and our selected populations was that our patients tended to have a longer mean time to the first aspiration event. In this context, it may be appropriate in future studies to delineate aspiration between early and late events as the mechanism of aspiration may be significantly different.

Benjamin et al.[9] and Heo et al.[10] evaluated the prevalence of evidence of aspiration on computed tomography in the setting of a witnessed aspiration event. Our study did not include this, as imaging was not consistently available retrospectively. Both prior studies suggested that it was not uncommon for patients to have a clinically significant aspiration event with no evidence of aspiration on computed tomography. This could be a result of imaging studies being ordered too early in the disease process or inappropriately attributing clinical sequelae to witnessed aspiration events. Regardless, these results highlighted the difficult nature in the identification and diagnosis of aspiration.

Patients included in our study were filtered around clinically significant respiratory complications to generate a patient population likely to have suffered an aspiration event. This was done to examine trauma patients' clinical progression and identify significant associations with aspiration following admission. This was a distinction from prior studies which addressed pre-hospital factors and immediate aspiration associated with the trauma itself.[9,10] By doing this, the aim was to identify potential hindrances in patient recovery.

Aspiration was not an uncommon experience in the study's patient population, yet there is no clear body of evidence outlining the clinical risks, significance, or even prevalence of aspiration in trauma patients. Significant limitations existed in a retrospective analysis of clinical charts when trying to establish a causal relationship between an exposure and an outcome. This was further complicated by the lack of consistent clinical charting surrounding aspiration events. Due to the nature of aspiration, its clinical presentation often is inferred based on bronchoalveolar lavage findings, speech-language pathology studies, and clinical presentations. Witnessed aspiration events were rare when examining documentation, but this is anecdotal and could represent a lack of reporting and documentation. In clinical documentation, aspiration often was referred to as "suspected aspiration" following the diagnosis of pneumonia, suggesting that aspiration may be inferred only in retrospect. This is important contextually when considering what little evidence exists on aspiration in trauma patients. These limitations in documentation surrounding aspiration raised concerns for existing evidence regarding aspiration and warrants further study with a focus on identification and accurate reporting of aspiration events throughout the patients' hospital course. By extension, clinically relevant evidence is likely to be revealed if these issues are addressed and a higher-powered study is performed.

CONCLUSIONS

In a retrospective analysis of a select group of patients who suffered a traumatic injury, candidate and significant risk factors were identified for aspiration events. Impaired consciousness appeared to have the strongest association with aspiration when accounting for other potential causative factors. With the results of this bivariate analysis, there existed likely risk factors for aspiration unique to the trauma patient population. Clinically, it may be that aspiration is an under reported complication, often identified retrospectively, that could have significant implications for morbidity and mortality in the trauma patient. Given the significant morbidity associated with these events, these data will play an important role in the development of care pathways to prevent their occurrence and inform future studies.

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Keywords: respiratory aspiration, risk factors, trauma, altered level of consciousness

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Perceived Barriers to Pediatric Clinical Trials Implementation: A Survey of Health Care Staff

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ABSTRACT

Introduction. Clinical trials are the gold standard for assessing the effectiveness and safety of treatments. The objective of this study was to assess provider opinions regarding implementing pediatric clinical trials in various practice settings across Kansas.

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). A cross-sectional, 36-item survey was administered to a state-wide convenience sample targeting health care providers and clinic staff.

Results. A total of 115 health care providers and clinic staff completed surveys; 31% were physicians. Physicians were more likely than other clinic staff to have experience with clinical trials (correlation coefficient [CC] = 0.270, p = 0.004). When compared to urban respondents, rural providers were less supportive of recruitment for clinical trials in their practices (CC = -0.251, p = 0.008) and more likely to feel comfortable referring patients for clinical trials involving treatments that their insurance did not cover (CC = 0.302, p = 0.001).

Conclusions. A range of rural and urban health care professionals supported conducting pediatric clinical trials but identified several barriers as well. These results will support future pediatric clinical trials across the country including Kansas. ***Kans J Med 2022;15:189-193***

INTRODUCTION

Clinical trials are the gold standard for assessing the effectiveness and safety of treatments in health care.[1] Dramatic improvements in health care outcomes have resulted from clinical trials, such as reduced mortality in childhood leukemia.[2] Despite the benefits of pediatric clinical trials to health outcomes, children routinely receive medical therapies that have not been studied in clinical trials involving pediatric subjects.[3] For example, over 75% of hospitalized children may receive a medication "off-label", in a manner not explicitly approved in children.

Numerous factors may restrict broader implementation of clinical trials in pediatric settings. Prior studies have reported patient and provider time constraints, lack of trained staff, and scarcity of appropriate facilities for clinical trials procedures as potential barriers.[4,5] These barriers point to a lack of dedicated resources for pediatric clinical trials.[6] In an attempt to increase the availability of pediatric clinical trials resources, the National Institutes of Health funded the IDeA States Pediatric Clinical Trials Network (ISPCTN).[7] The ISPCTN's primary objectives are to: 1) extend clinical trials opportunities to children and communities, and 2) increase the capacity of participating states to conduct pediatric clinical trials.

Participating sites within the ISPCTN are located in states that are part of the Institutional Development Award (IDeA) Program. The IDeA Program, which was established by congressional mandate in 1993, seeks to broaden the geographic distribution of NIH funding through faculty development and institutional research infrastructure enhancements in states with historically low NIH funding.[7] As the program for the ISPCTN in the state of Kansas, the Sunflower Pediatric Clinical Trials Network (SPeCTRE) deployed targeted surveys to assess barriers and facilitators to clinical trials participation faced by parents/caregivers and health care providers residing in rural and urban communities across one rural IDeA state, Kansas. The objective of the current study was to identify and determine the relative importance of specific factors relating to implementation of pediatric clinical trials in various practice settings across the state.

METHODS

The study team administered a 36-item survey online and in person to a convenience sample of health clinic providers, nurses, and non-clinical administrative staff (administrative assistants and schedulers). Clinic managers were excluded from the survey. Subjects were recruited into the study in person by research staff who visited clinical sites or community events or via targeted email. Participants were surveyed over a two-year period (2017-2018).

Sampling strategy focused on ensuring that health care providers and staff working in a variety of settings were included. Participating subjects were recruited from one of three settings: 1) community-based outpatient clinics, 2) county health departments, and 3) academic medical centers and affiliated clinics. Emails were distributed to health care providers and staff who had signed up for education and outreach activities through the University of Kansas Medical Center Area Health Education Centers (AHECs). The AHECs' mission is to enhance the quality and accessibility of health care services in Kansas through partnerships with communities, health care professionals, and organizations across the state.

The study team used distinct procedures for in-person and online enrollment. For in-person enrollment, written documentation of risks and benefits was provided to respondents with questions answered by the study team. Recruitment occurred at clinical sites as noted above or at community events such as health fairs and county fairs. Following verbal informed consent, respondents completed surveys by paper or on an electronic tablet based on participant preference. Online enrollment was completed via email with initial content including an informed consent statement. Affiliated clinical sites invited their staff to participate and the individuals with recent participation in education

activities at the AHEC.

Survey items were adapted from established tools[4,8] and beta tested for understandability with five research and clinical staff at clinical sites affiliated with project. Beta testing suggested small wording changes, primarily grammatical, that would be helpful to aid health care provider understanding of items. Content and themes were retained from items in previous published surveys[4,8] as well as the 5-point Likert scale (1 = Strongly Disagree, 2 = Disagree, 3 = Neutral, 4 = Agree, 5 = Strongly Agree) although verbiage varied slightly on some survey items. Additional items addressing basic demographic information, practice type, experience with clinical trials, and preferences for learning more about clinical trials also were included. Survey responses were recorded in REDCap®[9] either directly from participants or entered from paper surveys.

The University of Kansas Medical Center Institutional Review Board approved and monitored the study. Survey participation was voluntary and provided without incentive. Data analyses were completed in IBM SPSS Statistics 23 (Armonk, NY) using t-test or non-parametric statistical methods, including Spearman's correlation coefficient (CC) and Kruskal-Wallis H test, as appropriate.

RESULTS

A total of 145 participants completed at least one survey item and 115 completed all survey items, for a completion rate of 79%. Response rate from site visits was 100%; response rate from email could not be determined due to changes in the listserv membership during the study period. Demographics of participants are detailed in Table 1. Physicians and nurses represented the most frequent professional roles for participants (31% and 32%, respectively). The largest proportion of respondents was recruited from clinic-based practice (39%), with a smaller number of respondents engaged in hospital-based practice (14%). The majority of respondents (68%) served urban and suburban communities while 32% of respondents were from areas considered rural. The majority of surveys were completed online (53.4%).

Only 23% of respondents had ever enrolled a patient into a clinical trial; 43% had referred a patient to participate in a clinical trial. Clinical experience by years of practice was associated significantly with respondents' level of experience with clinical trials (no experience, experience referring, and experience enrolling; H = 17.233 (Kruskal-Wallis Test), $p < 0.05$). Physicians were significantly more likely than other clinic providers to have experience with clinical trials (CC = 0.270, p = 0.004).

Most respondents (55%), regardless of clinic role, were interested in learning more about clinical trials. Respondents most often reported interest in learning about available clinical trials in their area (35%). A comparable number of respondents preferred receiving information on clinical trials through in-person (68%, 99/145) and online (96%, 139/145, e.g., Skype, webinar, telemedicine) educational activities. Roughly one third of respondents (64%, 93/145) requested continuing medical education (CME) credit for such sessions. Physicians (CC = 0.210, p = 0.23) were significantly more likely to prefer CME learning opportunities than were other clinic roles. Of note, no learning modalities neared 50% preference from respondents.

Table 2 describes beliefs regarding clinical trials according to the 5-point Likert scale (1 = Strongly Disagree, 2 = Disagree, 3 = Neutral, 4 = Agree, 5 = Strongly Agree). Because responses were distributed non-normally, data were reported as medians (interquartile range [IQR]). Respondents considered clinical trials safe and effective (Med 4 [IQR 3-5]) and agreed that clinical trials help discover new treatments (Med 5 [IQR 4-5]). Participants differed on the impact of available time on implementation of clinical trials (Med 3 [IQR 3-4]). Respondents agreed that limiting costs incurred by patients (Med 4 [IQR 4-5]) and the clinic (Med 4 [IQR 3-5]) would increase their desire to offer and/or participate in clinical trials. Respondents endorsed that reducing the burden of paperwork would be important for their practice to participate in clinical trials (Med 4 [IQR 4-5]) but were equivocal that their practices were not ready for a clinical trial (Med 3 [IQR 2-4]). An understandable and accessible protocol was attractive to practices considering clinical trials (Med 4 [IQR 4-5]). Respondents expressed disagreement with statements that they would not offer a clinical trial to participants if it involved use of a placebo in a study arm or randomization (Med 3 [IQR 2-3]).

Table 1. Participant demographics (n = 145).*

	N (%)
Gender (n= 116)	
Male	22 (19%)
Female	94 (81%)
Ethnicity (n= 115)	
White	95 (83%)
Black	13 (11%)
Other	7 (6%)
Age (years) (n=117)	
18-34	44 (38%)
35-44	27 (23%)
45-54	21 (18%)
55+	25 (21%)
Professional Role (n = 118)	
Physician	37 (31%)
Advanced Practice Provider	16 (14%)
Nurse	38 (32%)
Other	27 (23%)
Practice Location (n = 117)	
Urban/Suburban	79 (68%)
Rural	38 (32%)

*Efforts attempted to reflect the health care workforce in the state of Kansas with the largest proportion (30.3%) of respondents being under 35 years of age and most respondents (52.4%) identified as White and Female. Other for ethnicity and professional role was not defined by respondents although professional was presumed to include administrative assistant and clinic schedulers.

Table 2. Respondent beliefs rearding clinical trials.

	N	Median[1]	Question 1	Question 3
I consider clinical trials a safe and effective treatment option for my patients.	119	4.00	3.00	5.00
I feel comfortable offering a clinical trial as a treatment option to my patient.	118	4.00	3.00	5.00
I would not feel comfortable if my patients were not assigned to receive a treatment in a clinical trial (i.e., is assigned to receive a placebo, sugar pill).	118	3.00	2.00	3.00
I would offer a clinical trial treatment option to my patients if I had more time.	119	3.00	3.00	4.00
I would offer a clinical trial as a treatment option to my patients even if the standard treatment has not failed.	119	3.00	2.00	4.00
I would recruit my patients into a clinical trial if the protocol was easy to understand.	122	4.00	4.00	5.00
I would recruit my patients into a clinical trial if it didn't cost my practice/clinic.	124	4.00	3.00	5.00
I would offer a clinical trial treatment option to my patients if their insurance could cover tests/medications for them related to the trial.	123	4.00	4.00	5.00
I support clinical trial recruitment and enrollment at my practice/clinic.	124	4.00	3.00	5.00
I do not feel comfortable offering a clinical trial as a treatment option to my patients.	119	2.00	1.00	3.00
I would recruit my patients into a clinical trial if I had a training to complete the necessary paperwork.	120	4.00	3.00	4.00
I would recruit my patients into a clinical trial if I had trained staff to complete the necessary paperwork.	120	4.00	4.00	5.00
I would only offer a clinical trial as a treatment option to my patients if the standard treatment has failed.	119	3.00	2.00	4.00
I feel my practice/clinic is not ready to conduct a clinical trial.	119	3.00	2.00	4.00
I would not feel comfortable offering a clinical trial to my patients if the research involves randomization (where they receive one of two treatments).	119	2.00	2.00	3.00
I would recruit my patients into a clinical trial if the informed consent was easy to understand.	118	4.00	4.00	5.00
I believe clinical trials help us discover new treatment options to improve patient care.	121	5.00	4.00	5.00

[1]Median and interquartile (Question 1= 25% and Question 3= 75%) range on 5-point Likert scale (1 = Strongly Disagree, 2 = Disagree, 3 = Neutral, 4 = Agree, 5 = Strongly Agree.) Respondents endorsed an interest in clinical trials although preparedness remains a challenge for participating practices.

There were no significant differences in providers' perceived barriers to referring patients to clinical trials based on their years in practice (Table 3), except the perceived cost to their practice ($H = 11.283$, $p = 0.024$.) A significant positive correlation was observed between perceived cost to their own practice and providers' age ($CC = 0.247$, $p = 0.007$), years in practice ($H = 11.283$, $p = 0.024$), and level of experience with clinical trials ($H = 0.192$, $p = 0.038$). Negative correlations were observed between providers' perception that their practice is "not ready", their age ($CC = -0.230$, $p = 0.013$), and level of experience with clinical trials ($CC = -0.347$, $p < 0.05$). Additionally, providers' level of experience with clinical trials was correlated positively with perceived barriers, including time ($CC = 0.243$, $p=0.008$,) complexity of the protocol ($CC = 0.194$, $p=0.036$,) lack of trained staff ($CC = 0.337$, $p< 0.001$,) and complexity of informed consent ($CC = 0.259$, $p = 0.006$.)

Table 3. Correlation between provider perceived barriers to recruiting based on their years in practice, age group, and level of experience with clinical trials.

	Years in Practice		Provider's Age Group		Level of Experience with Clinical Trials	
	H#	p value	CC#	p value	CC#	p value
Lack of provider time	2.459	0.652	0.115	0.223	0.243*	0.008
Complexity of the protocol	3.483	0.480	0.107	0.252	0.194*	0.036
Cost to the practice/clinic	11.283*	0.024	0.247*	0.007	0.192*	0.038
Lack of trained staff	4.374	0.358	-0.031	0.739	0.337*	0.000
Complexity of informed consent	2.964	0.564	0.141	0.134	0.259*	0.006
Overall, practice is not ready	8.712	0.069	-0.230*	0.013	-0.347*	0.000
Patients' medical insurance coverage	8.850	0.065	0.179	0.055	0.064	0.491
Lack of access to standard treatment	3.448	0.486	0.16	0.09	0.122	0.189
Lack of training	2.453	0.653	-0.043	0.642	0.043	0.652

*Denotes values with p value less than 0.05.
#CC = correlation coefficient, H = Kruskal-Wallis H test.

The three benefits most cited as potential incentives for pediatric clinical trials participation included compensation for time and travel (72%), providing tests and medications not covered by insurance (64%), and providing the opportunity at a local practice or clinic rather than traveling to the research site (64%). Additional logistical considerations such as option for telephone participation (63%) or telehealth visit (40%) as well as childcare support (68%) were noted by many respondents.

DISCUSSION

Consistent with past studies,[4,10] this survey of health care providers and non-clinical office staff found that a majority of respondents were interested in participating in clinical trials, but only a small fraction had enrolled patients in such studies. The findings additionally supported previous studies[6,8] that identified an interest in clinical trials among providers and staff but also found a lack of familiarity with their availability and conduct. The present study provided new insights into the perceived barriers to clinical trials participation reported by non-physician health care staff including advanced practice providers, nurses, and non-clinical office staff. While prior literature supported the assertion that primary care physicians are the preferred person of contact for clinical trials participants,[11-13] successful implementation of clinical trials requires engagement and, at least, basic knowledge/skills for non-clinical and support staff to identify potentially eligible subjects in an efficient manner and otherwise carry out a trial.

Respondents reported agreement with survey items that addressed resource constraints and clinic preparedness as barriers to clinical trials participation. Particularly, the need to have clinical trials protocols that were easy to understand, the desire to minimize expense to the clinic for participation, and the need to have adequate training in the protocol before participation were supported strongly by respondents. Previous studies also have reported that knowledge, logistical, and financial constraints prevent participation.[12] Training and financial support of on-site research staff at all locations could address these concerns.

Time constraints were less often reported as a barrier to clinical trials participation in contrast to prior studies.[6,10] In particular, preparedness presented an obstacle to clinical trial implementation with a minority of health care staff ready to engage in such research. Compared to caregiver perceptions, health care staff reported less concern regarding the structural components of experimental design such as randomization to placebo.[5,10] Health care staff were supportive of enrollment in clinical trials when effective alternative treatment existed but expressed more reservation to offer higher-risk studies. This reservation was like what parents report related to risk-benefit.[5,14]

To address knowledge gaps, results from the survey suggested that multi-modal educational interventions that include in-person and online options with offered CME were preferred methods for disseminating information on clinical trials. Health care staff drawn from rural, urban, academic, and community practices showed interest in online and in-person education. Additional qualitative evaluation of staff perspectives on educational activities could identify preferred modalities better. Surveying a greater number of participants from provider, nursing, and clinical roles also could better characterize knowledge gaps in each group. Closing such gaps is critical to expanding clinical research in lower resource regions.[15] Few health care staff believed that remote options via telephone or telehealth would encourage patient participation in clinical trials. With the increasing use of telehealth across Kansas, such attitudes may change.[16]

The study provided specific insight into the most common and most important perceived barriers to pediatric clinical trials participation faced by health care providers and staff in Kansas. Strategies could provide an evidentiary basis for their use in other rural and/or underserved settings nationally. Expansion of this study to other IDeA States Pediatric Clinical Trials Network (ISPCTN) member states could generalize barriers and perceptions better in states with more limited research infrastructure and guide future policy. Future qualitative research may include the addition of technological options for sharing information that was absent in the current study, such as text messaging and smartphone applications.

Several limitations affected this study. Convenience sampling from a limited number of sites could result in selection bias. The sample size precluded conducting some important sub-analyses, particularly comparisons between rural and urban settings. Broader engagement of rural practices throughout the state could allow such comparisons in the future. Respondents from Kansas may not be representative of other ISPCTN communities; future studies are planned that will engage other sites. Adjustments to the wording of survey items may reduce their comparability to the source tools. However, beta testing for item comprehension was deemed necessary to maximize internal validity. Finally, non-clinical staff roles were not specified; further characterization of these roles could identify targeted concerns that need to be addressed to enhance clinical trials participation.

CONCLUSIONS

Physicians and other healthcare providers and staff across a broad range of disciplines and geography in Kansas support the performance of pediatric clinical trials but identify logistical barriers that reduce their willingness to refer potential subjects to or participate in such studies. Poor self-efficacy, cost, logistics, insufficient time, and administrative challenges were potential targets for intervention to increase pediatric clinical trials participation. These results will help to inform future, larger-scale assessments of barriers and facilitators to clinical trials participation planned for the ISPCTN and will aid the introduction and successful implementation of pediatric clinical trials in Kansas and similar regions.

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Keywords: clinical trials, pediatrics, providers, engagement, enrollment

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Intramural Duodenal Hematoma Secondary to Necrotizing Pancreatitis Leading to Gastric Outlet Obstruction

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INTRODUCTION

Intramural duodenal hematoma (IDH) is a rare condition most associated with blunt abdominal trauma.[1-10] The first reported case was by McLauchlan in 1838.[2,5,8,10-11] Most reported cases have been associated with coagulopathy, iatrogenic procedures (i.e., endoscopic biopsy), and rarely, acute pancreatitis. The rare patient with IDH associated with acute pancreatitis develops a complication of pancreatic necrosis in 20 to 30% of cases. This can be complicated by the development of organized and unorganized peripancreatic edema leading to pseudocysts that become infected and lead to sepsis, increasing the overall mortality by 80%.[4]

Although IDH most commonly is due to trauma, about 30% of cases are attributable to nontraumatic causes.[3] Nontraumatic cases include coagulation abnormalities, anticoagulation therapy such as warfarin, malignancy, and blood disorders.[2-5,8,10-11] Although especially rare, it is possible to encounter nontraumatic IDH as a complication of acute necrotizing pancreatitis.[4] Therefore, if a coagulation profile is normal with no history of anticoagulation drug use or blood disorder, other etiologies such as pancreatic origin should be considered in nontraumatic IDH.[11] This report highlighted a case of acute necrotizing pancreatitis complicated by nontraumatic IDH leading to gastric outlet obstruction.

CASE REPORT

A 41-year-old male with history of chronic pancreatitis secondary to alcohol abuse presented with acute onset abdominal pain, nausea, and vomiting. He reported daily, heavy alcohol use without any evidence of previous trauma. He denied any recent use of non-steroidal anti-inflammatory drugs or anti-coagulants. His medical history was significant for multiple hospital admissions for alcohol-induced pancreatitis, including three admissions within the prior 60 days. He was discharged most recently two weeks prior to the current admission.

On physical exam, the patient was febrile, tachycardic, tachypneic, and normotensive. He was in mild distress and diaphoretic. Respiratory exam revealed clear lung sounds, and tachypnea with a rate of 26 breaths per minute. However, he was not in any respiratory distress. Abdominal exam revealed epigastric tenderness with guarding and normal bowel sounds. The rest of the examination was unremarkable.

A complete blood count revealed macrocytosis with a hemoglobin of 15 g/dL as well as thrombocytopenia with platelets at 107 UL. Complete metabolic panel revealed bicarbonate of 7 mEq/L, creatinine of 1.33 mg/dL, and BUN of 30 mg/dL. Liver panel showed aspartate transaminase 334 U/L and alanine transaminase 90 U/L, alkaline phosphatase of 143 U/L, total bilirubin of 2.5 mg/dL, and lipase of 1015 U/L. Coagulation profile was within the normal range.

Urinalysis showed ketones with no signs of infections. A previous computed tomography (CT) of the abdomen with contrast done 14 days prior showed hepatic steatosis with no biliary dilation, status post cholecystectomy, peripancreatic fat stranding around the pancreatic head consistent with acute pancreatitis, as well as possible duodenal edema seen at the descending and transverse level (Figure 1). The patient met the criteria for admission based on laboratory and physical findings for acute pancreatitis and alcohol ketoacidosis, but no additional imaging was done on admission. Initial treatment consisted of nil per os, aggressive fluid replacement, pain control, and monitoring for alcohol withdrawal symptoms.

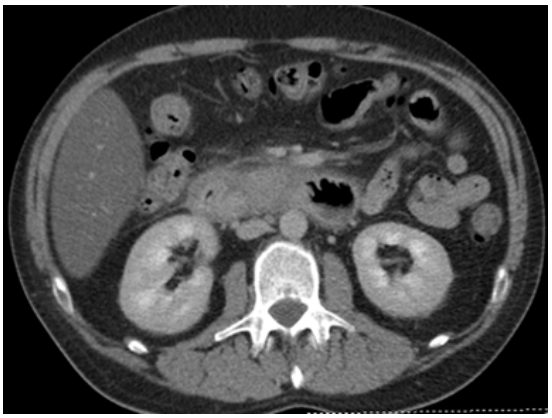

Figure 1. Computed Tomography of abdomen: Duodenum wall edema.

On hospital day two, the patient's respiratory status worsened with acute hypoxic respiratory failure. The patient subsequently was intubated. Chest x-ray showed diffuse bilateral alveolar opacities and broad-spectrum intravenous (IV) antibiotics were initiated for septic shock due to presumed aspiration pneumonia. Three days later, the patient had a 6 g/dL decrease in hemoglobin which warranted an urgent CT of the abdomen to evaluate for possible peritoneal bleed. CT angiography showed a large intramural hematoma of the third and fourth part of duodenum and pancreatic necrosis (Figure 2). The patient was transfused with two units of packed red blood cells and started on IV proton pump inhibitor therapy. Following these interventions, he remained stable during the hospitalization with no progression of his anemia.

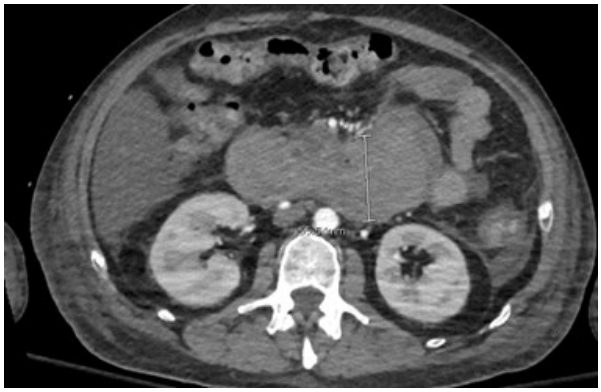

Figure 2. Computed tomography of abdomen: Showing duodenal hematoma.

On hospital day seven, the patient was extubated. He complained of persistent nausea and was not able to tolerate anything orally. An upper gastrointestinal series revealed severe constriction of duodenum consistent with gastric outlet syndrome secondary to the IDH (Figure 3). The patient was treated conservatively with resolution of symptoms and was discharged on hospital day 26 on a liquid diet with close outpatient follow up.

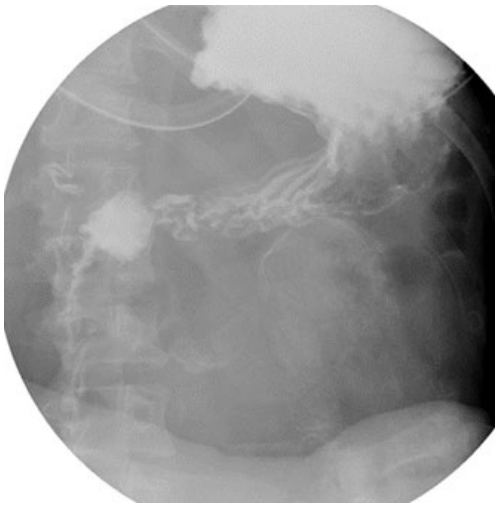

Figure 3. Upper Gastrointestinal series: gastric duodenal obstruction is confirmed as no contrast is seen pass duodenum.

DISCUSSION

Few cases of nontraumatic IDH associated with acute pancreatitis have been reported. Its exact mechanism remains unknown.[2-5,7-12] However, two important mechanisms have been proposed that work simultaneously in the formation of duodenal edema and nontraumatic IDH. The first includes leakage of pancreatic enzyme during an episode of acute pancreatitis causing inflammation, leading to local necrosis, and, subsequently, duodenal wall hematoma formation. The second mechanism is from pressure necrosis caused by pancreatitis, especially in the setting of pseudocyst or walled-off pancreatic necrosis. This leads to the leakage of pancreatic enzymes causing autodigestion that increases permeability of local tissues and blood vessels. Both mechanisms contribute to duodenal wall thinning that causes damage to duodenal blood vessels, eventually leading to duodenal edema and hematoma formation.[2-7,9-10] A periampullary IDH in the second portion of the duodenum may cause obstruction of the pancreatic duct and may be a cause of acute pancreatitis in this setting, as this is a common complication of nontraumatic IDH. This acute episode activates a massive inflammatory response that contributes to formation of organized and unorganized peripancreatic fluid that could lead to peripancreatic edema and the development of pseudocysts and pancreatic necrosis.

Other causes of hematoma formation are iatrogenic and due to duodenal biopsy via esophagogastroduodenoscopy.[2-5,8,10-11] Ultimately, the distinction between nontraumatic IDH leading to acute pancreatitis or pancreatitis leading to nontraumatic IDH is difficult to assess solely based on imaging, therefore correlating with the patient's history becomes an important factor to speculate on the specific mechanism. Shiozawa et al.[2] included 33 cases from 1981-2010; 11 cases of IDH were secondary to pancreatic disease. Furthermore, about one-third of reported IDH cases had concomitant heavy alcohol use, which raised questions of the impact alcohol may have on the development of IDH. However, the exact mechanism was unclear and poorly reported in literature.

The diagnosis of IDH is best made with CT with contrast.[2-3,12] However, abdominal ultrasound or endoscopy also can be used. A major complication of nontraumatic IDH seen in the reported case was leading to severe gastric outlet obstruction, which is a common complication of IDH.[1,7,10-11] Previous episodes of pancreatitis may have contributed to an early formation of IDH by the mechanism discussed above, however, this was not consistent with the initial CT. Furthermore, stable hemoglobin on admission as well as the late presentation of the gastric outlet obstruction led to a low suspicion of IDH initially. In this case, the sequence of events may have presented inversely of what is seen typically. It was speculated that the late presentation of IDH likely resulted from the release of pancreatic enzymes causing vascular disruption, subsequently leading to pressure necrosis and autodigestion, leading to the formation of the duodenal hematoma which ultimately caused the gastric outlet obstruction. In this case, acute pancreatitis was likely a contributing factor to nontraumatic IDH rather than a result of IDH, especially given the location of the hematoma in the third and fourth portion of the duodenum and the time course of the presentation.

CONCLUSIONS

IDH complicated with gastric outlet syndrome is treated conservatively by keeping the patient on nil per os and providing intravenous fluid hydration, nasogastric tube for decompression, and parenteral nutrition.[1,7,10-11] Surgical interventions and/or surgical decompression of the hematoma are reserved for complicated cases or following failure of conservative measures.[1] It is important to explore other uncommon causes of nontraumatic IDH such as pancreatic origin if initial imaging and laboratory results are within normal limits. Clinicians should monitor for a sudden decrease in hemoglobin as well as signs of gastric outlet obstruction in patients who present with recurrent alcoholic pancreatitis as this may be due to IDH. Therefore, establishing the diagnosis of nontraumatic IDH requires a good medical history, imaging, and complete laboratory work-up to narrow the differential diagnosis.

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Keywords: duodenal obstruction, acute necrotizing pancreatitis, alcohol-related disorders, gastric outlet obstruction, case study

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Role of Buprenorphine in an Adolescent with Opioid Abuse

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INTRODUCTION

Along with methadone and naltrexone, buprenorphine is one of three medications for opioid use disorder (MOUD) treatment options available for opioid use disorder (OUD).[1] Although approved by the U.S. Food and Drug Administration (FDA) for use in patients aged 16 and older, it can be prescribed by less than one percent of pediatricians and few child psychiatrists. Subsequently, adolescents with OUD are more likely to be treated by detoxification than MOUD.[1] The following case report demonstrated how buprenorphine treatment can be initiated effectively in a hospitalized adolescent patient with OUD.

CASE REPORT

A 15-year-old female with a history of severe OUD, generalized anxiety disorder, major depressive disorder, and trauma was admitted to a children's psychiatric hospital for suicidal ideation after her parent's discovered oxycodone in her room. Her opioid use consisted of daily inhalation of 60 to 90 mg of crushed M-30 pills for the preceding eight months, known to contain varying amounts of oxycodone and fentanyl. During this time, she had experienced one episode of withdrawal and subsequently returned to daily use. The patient had been experiencing suicidal ideation for the past three to four years, and opioid use suppressed those thoughts. Additional substances and routes reported by the patient included smoking marijuana from ages 13 to 14 and vaping nicotine from age 13 to presentation.

Psychiatric history included a hospitalization one year prior to presentation from which she was discharged on escitalopram but discontinued its use after six months. Family history was significant for bipolar disorder in her mother, opioid use in an older brother, and substance use disorder, in remission, in both her mother and father. Social history was significant for two close friends who also were opioid users.

At the time of admission, the patient was experiencing both nicotine and opioid withdrawal symptoms of bone pain, diaphoresis, restlessness, headache, mild tremors, nausea, rhinorrhea, and abdominal pain. She began treatment with clonidine, a lorazepam taper, and nicotine replacement. On hospital day two, the addiction psychiatry service received a telehealth consult for assistance in managing the patient's withdrawal. Her last opioid use was four days prior to the day of consultation, and she was continuing to experience the symptoms that were present on admission. Buprenorphine 2 mg was initiated, administered as a half-tablet (1 mg) four times daily due to concerns that a higher dose may worsen her withdrawal. This regimen did not provide significant alleviation; buprenorphine was titrated to 2 mg three times daily on hospital day six, and clonidine was discontinued due to hypotension. She continued to experience mild withdrawal symptoms, but by discharge she was reporting significant improvement.

After nine days in the hospital, the patient was discharged on buprenorphine 6 mg daily and escitalopram 10 mg daily, with recommendations to follow with the addiction clinic. Buprenorphine would be converted to buprenorphine/naloxone at her first outpatient appointment. However, her family opted instead to send her to an inpatient substance abuse rehabilitation program where she continued to receive buprenorphine and was doing well.

DISCUSSION

Prescription opioid and heroin use is most prevalent between the ages of 18 and 25, with the age at first opioid use decreasing.[2] Age at first opioid use and rates of dependence and severity are correlated inversely. Between 2001 and 2014, 26.8% of adolescents and young adults were treated with either buprenorphine or naltrexone within six months of receiving a diagnosis of OUD, but the percentage of youth receiving pharmacotherapy decreases directly with age.[3] Among patients aged 13 to 15, only 1.4% received MOUD. Of adolescents and young adults enrolled in Medicaid who overdosed on an opiate between 2018 and 2019, only 1.9% were treated with medication within 30 days after overdose.[4] These figures contrasted with the percentage of adults with OUD who receive MOUD: 26.3% of adults admitted for treatment of heroin use, compared to 2.4% of adolescents.[1]

A clear gap existed in the treatment of adolescent OUD. MOUDs are evidence-based, and there is an opportunity to increase their use among adolescents with OUD. The American Academy of Pediatrics recommended incorporating pharmacotherapy treatment for OUD in primary care settings.[5] The age of FDA approval presented a barrier to adolescents receiving buprenorphine therapy, and appropriate medications may be more available to adolescents if the age of approval is lowered. Treating OUD at younger ages likely would reduce addiction burden and disease morbidity across the lifespan.

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Keywords: buprenorphine, opioid use disorder, opioid overdose, adolescent, M-30 compound

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Prophylactic Laser Treatment Posterior to Pars Plana Vitrectomy Sclerotomy Wounds During Macular Surgery

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ABSTRACT

Introduction. Sclerotomy related retinal breaks (SRRBs) are a risk factor for postoperative retinal detachment (RD). Endolaser posterior to sclerotomy wounds decreased the risk of SRRBs after 20G pars plana vitrectomy (PPV) for macular disease. However, similar data do not exist for 25G and 23G wounds.

Methods. A retrospective cohort study of patients after 23G and 25G PPV for macular pathology was conducted between August 2017 and August 2020. The primary outcome was the postoperative rate of SRRBs or RDs. The secondary outcome was the postoperative rate of pupillary dysfunction and neurotrophic keratopathy. All participants had a minimum postoperative follow-up of one year.

Results. One hundred seventeen patients were included in the study (62 in the laser group and 55 in the control group). Mean age was 65.4 ± 11.3 years (56.4% female and 43.6% male). Most of the laser group underwent 23G PPV (90%) while most of the control group underwent 25G PPV (96%). One patient in the control group developed RD secondary to a SRRB. No SRRBs or RDs developed in the laser group. None of the secondary outcomes developed in either group after one year.

Conclusions. To the best of the authors' knowledge, this is the first report in the literature on prophylactic laser posterior to small gauge sclerotomies (25G and 23G) during macular surgery. Laser treatment posterior to small gauge sclerotomies (25G and 23G) had a similar incidence of SRRBs as with 20G sclerotomies. Larger prospective studies are needed to further understand the role of laser in lowering SRRB risk.

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INTRODUCTION

Retinal detachment (RD) after pars plana vitrectomy (PPV) for macular surgery is a devastating vision threatening condition. A significant risk factor for RD development after macular surgery is surgical wound related retinal breaks, also known as sclerotomy related retinal breaks (SRRBs).[1] SRRBs incidence reach up to 5.1% with 25-gauge (25G) and 7.2% with 20-gauge (20G) macular surgeries. SRRBs have been associated with 22.2% of RDs after idiopathic macular hole surgery and 44.4% of RDs after epiretinal membrane peel.[2] A key factor in the development of SRRBs includes vitreous incarceration into the surgical wound, which subsequently contracts and creates SRRBs.[3]

Wound structure modifications attempt to decrease vitreous incarceration by creating a self-sealing wound (e.g., two step oblique wounds), using smaller surgical instruments (e.g., 25G versus 20G), and utilizing valved pars plana cannulas. Despite these measures, postoperative vitreous incarceration occurs similarly between 23G, 25G, and 27G surgeries.[4] There have been other attempts aimed towards supporting the retina at traction sites, including prophylactic scleral buckling, 360-degree cryotherapy, and 360-degree laser. These have been shown to decrease successfully postoperative SRRBs,[5-7] but they can cause undesirable side effects (e.g., pupillary dysfunction, refractive error, and ocular inflammation).[8,9]

Laser posterior to sclerotomy sites in 20G vitrectomy has been shown to decrease postoperative SRRBs and avoids the risks associated with 360-degree endolaser.[10] However, the benefits of localized prophylactic laser treatment in smaller 23G and 25G macular surgeries remain unknown. To fill the current gap in knowledge, this study was conducted to identify the effect of localized prophylactic laser treatment in 23G and 25G macular vitrectomies.

METHODS

The authors implemented a retrospective cohort study design. To identify study participants, 23G and 25G macular surgeries performed between August 2017 and August 2020 at the tertiary referral center were reviewed. Screening extended until August 2020 to allow for one year of postoperative follow up. Study population included adults who were compliant with their postoperative care, and excluded patients with proliferative vitreoretinopathy (PVR), proliferative diabetic retinopathy (PDR), open globe injuries, loss of follow up, or were less than 18 years old.

The study had two groups: the control group did not have prophylactic laser performed while the treatment group had prophylactic laser performed posterior to sclerotomy wounds. The primary outcome of the study was to determine the rate of SRRBs and RDs after macular vitrectomy surgery. The secondary outcome was to determine the rate of pupillary dysfunction and neurotrophic keratopathy. The end point of this study's primary and secondary outcomes was one year after surgery.

All participants' operative reports included documentation of careful peripheral vitreous shaving and an intraoperative scleral depressed fundus exam to exclude intraoperative SRRBs. Surgeries were performed using the Constellation® vitrectomy system (Alcon, Inc., USA). In the laser group, prophylactic laser treatment consisted of three rows of confluent medium intensity endolaser posterior to the sclerotomy wound, with laser extending for approximately one-half clock hour on either side of each wound (Figure 1).

Statistical analysis was performed using RStudio® (version: 1.1.453; Boston, MA). Categorical variables were described using proportions. Continuous variables were described as means ± standard deviations. A series of independent sample t-tests, dependent sample t-tests, and independent sample tests of proportion were conducted. A sub-analysis of outcomes and complications between groups was conducted. A p value of 0.05 was used as the threshold value for statistical significance, and a confidence interval of 95% was chosen. Microsoft Office® Excel® 2020 was used for data collection (e.g., age, gender, vitrectomy gauge, reason for surgery, and postoperative adverse events). The institutional ethics review board (IRB) approved this study.

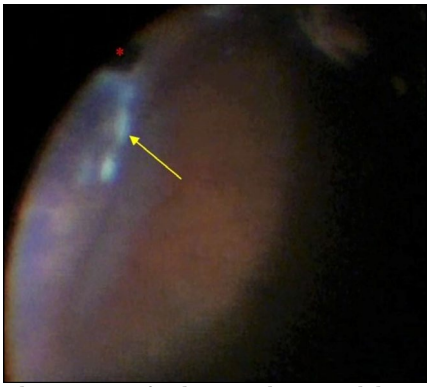

Figure 1. Surgical microscope fundus view during endolaser treatment posterior to sclerotomy wound. White laser marks (yellow arrow) posterior to sclerotomy wound and infusion cannula (red asterisk).

RESULTS

The study demographics included 117 patients who met the inclusion criteria. Patients' ages ranged from 23 to 90 years old (mean age of 65.4 ± 11.3 years old). The study cohort was 56.4% female and 43.6% male. Of the 117 patients, 90% of the laser treatment group underwent 23G vitrectomy while 96% of the control group underwent 25G vitrectomy. Study cohort demographics and results are summarized in Table 1.

Table 1. Cohort demographics and results summary.

	Control Group	Laser Group	p Value
Sample size	55	62	0.58
Age	66.15 ± 10.66	64.69 ± 11.93	0.49
Gender			
Females	27 (49%)	39 (63%)	0.19
Males	28 (51%)	23 (37%)	0.19
PPV‡			
23G*	2 (4%)	56 (90%)	<0.001
25G**	53 (96%)	6 (10%)	<0.001
Primary outcome	1 (1.8%)	0	0.95
Secondary outcome	0	0	n/a

PPV‡: pars plana vitrectomy; 23G*: 23-gauge; 25G**: 25-gauge

The control group had 55 patients with mean age of 66.2 ± 10.7 years old. There were 27 females and 28 males (49% and 51%, respectively). Fifty-three patients had 25G vitrectomy and two patients had 23G vitrectomy (96% and 4%, respectively). Primary outcome analysis of the control group identified one patient with a superior rhegmatogenous RD secondary to a SRRB one month after 25G PPV (1.82%), this was consistent with reported postoperative SRRBs rates in the literature.[1] Secondary outcomes analysis had no patients with pupillary dysfunction or neurotrophic keratopathy.

The prophylactic laser group had 62 patients with mean age of 64.7 ± 11.9 years old. There were 39 females and 23 males (63% and 37%, respectively). Fifty-six patients had 23G vitrectomy and six patients had 25G vitrectomy (90% and 10%, respectively). Primary outcome analysis of the laser group identified no patients with postoperative SRRBs or RDs. Secondary outcome analysis had no patients with postoperative pupillary dysfunction or neurotrophic keratopathy.

Statistical analysis detected balanced study groups when comparing sample size ($p = 0.58$), mean age ($p = 0.59$), and gender ($p = 0.19$). There was a statistically significant difference between groups when comparing surgical wound size ($p < 0.001$) with 96% of the control group having smaller surgical wounds (25G) and 90% of the laser group having larger surgical wounds (23G). This difference places the laser group at a disadvantage because smaller (25G) surgical wounds have a lower chance of SRRBs development compared to larger (23G) wounds.

DISCUSSION

This study compared the effect of prophylactic laser treatment posterior to sclerotomy wounds on SRRB development after 23G and 25G macular vitrectomies. There were no SRRBs, RDs, pupillary dysfunction, or neurotrophic keratopathy in the prophylactic laser group after one year. This is similar to reported data of localized laser treatment posterior to sclerotomy sites in 20G vitrectomy.[10] On the other hand, the control group had one patient who developed a superior RD secondary to a SRRB after 25G vitrectomy, which is within the reported incidence rate in the literature. No pupillary dysfunction or neurotrophic keratopathy developed in the control group.

Residual vitreous plays a major role in SRRBs development. Incarcerated vitreous in the surgical wound contracts and pulls on the retina causing postoperative SRRBs.[3] In prior literature, attempts to decrease vitreous incarceration by creating smaller self-sealing wounds have decreased the rate of postoperative SRRBs and RDs.[4] However, it did not completely prevent vitreous incarceration, which was similar across 23G, 25G, and 27G wounds. In this study, all patients had their surgical wounds evaluated for closure by the end of surgery. If a possible wound leak was present, a 7-0 Vicryl® suture was used to confirm wound closure.

Supporting neurosensory retina adhesion to the underlying retinal pigment epithelium (RPE) is another approach to decrease SRRBs development. This is achieved by creating a tightly adherent retinal scar using laser treatment or cryotherapy. Surgical 360-degree endolaser treatment has been shown to decrease postoperative SRRBs and retinal detachment after macular surgery.[6] However, 360-degree endolaser damages short and long posterior ciliary nerves, decreases corneal sensation, and can cause anisocoria and mid-dilated pupils.[8,9] Local laser treatment behind sclerotomy sites avoids damaging the horizontal long posterior ciliary nerves. In this study, none of the laser treatment group patients developed pupillary dysfunction. Corneal sensation was not assessed in this retrospective study, but the corneal surface was evaluated as part of the comprehensive clinical exam.

Epiretinal membrane (ERM) formation is a hypothesized side effect after 360-degree endolaser.[11] Blood-retina barrier damage and serum leakage into the vitreous cavity may attract RPE migration and ERM formation.[12] None of the laser group patients developed ERM within one year after surgery. This finding may be explained by the fact that localized laser treatment around sclerotomy sites causes less extensive retinal damage compared to 360-degree laser or cryotherapy. Another possible explanation is that the peeling of the internal limiting membrane during macular surgery removes the physiological scaffold for recurrent macular ERM formation.

Cryotherapy decreases postoperative SRRBs and RDs by creating a strong retinal scar.[7] However, 360-cryotherapy affects a larger surface area and causes more tissue damage compared to laser. This increases the risk of postoperative PVR and membrane formation. In addition, cryotherapy is more painful and can cause severe postoperative eye inflammation. Scleral buckling is another approach to support neurosensory retina attachment that avoids retinal scarring by scleral indentation.[5] While scleral buckling supports the retina periphery 360-degree when treating retinal detachments, it is too invasive to perform prophylactically with macular surgery and can cause undesirable side effects (e.g., increased postoperative pain, double vision, refractive error, and anterior segment ischemia). In the presented study, the laser group had zero SRRBs and RDs, like reported results after 20G macular vitrectomy,[10] and avoided the negative side effects associated with cryotherapy or scleral buckling.

Surgical experience is an important factor that frequently arises when studying surgical outcomes. The surgeon's experience has not been shown to affect the rate of intraoperative retinal tears or postoperative RDs.[13] Wilkinson et al.[14] did not find an increased incidence of RDs after PPV surgeries performed by vitreoretinal fellows when compared to attending surgeons. In the presented study, participating surgeons had five to six years of experience performing retinal surgery. It was hypothesized that the similarity in experience levels between the surgeons minimizes surgeon's experience bias between the study groups. Furthermore, the rate of SRRBs and RDs in the control group was 1.82%, which was in the lower range of the rates reported after 25G macular surgery. It is essential to highlight that this study focused on macular vitrectomy patients, and the results should not be applied to RD cases. Many of the techniques discussed earlier (e.g., 360-degree endolaser, cryotherapy, and scleral buckling) improve the success rate of RD repair and have an important role in today's retina procedures.

This study has several strengths. A key strength was the extended postoperative follow-up duration of one year. This duration exceeded the three to six months postoperative duration for SRRBs and RDs reported in prior literature.[15] It also surpassed the mean postoperative period for other complications like ERM formation, pupillary dysfunction, or decreased corneal sensation.[9] The one-year follow-up also provided input on delayed wound-related outcomes.

Age is another important factor that affects wound healing. When compared to older patients, young patients have greater healing ability and a higher risk for proliferative vitreoretinopathy.[16] The age balanced groups were a strength of this study because it reduced the age-related bias in wound healing and vitreous-retinal traction risk.

Another strength in the study was the larger number of 23G surgical wound patients in the laser group. Wound-related complications have been shown to increase with larger wound size (23G) compared to smaller wound size (25G).[1,17] Despite the increased wound-related complication risk in the laser group, none of the laser group patients developed postoperative SRRBs or RDs after one year. It was hypothesized that these results were because of the protective effect of localized laser treatment in stabilizing the retina posterior to sclerotomy wounds.

The retrospective nature of the study was one of its limitations. It did not allow for randomization of participants and resulted in an unbalanced distribution of 23G and 25G vitrectomies between groups ($p < 0.001$). Another study limitation was the difference in the number of phakic and pseudophakic/aphakic patients between groups since phakic patients are at increased risk of developing SRRB. The one patient who developed SRRB in the control group was phakic. However, there was no statistically significant difference in the proportion of phakic patients between the study groups; 27 patients in the control group (49%), and 23 in patients in the laser group (37%; $p = 0.26$).

The effect of localized laser treatment posterior to 27G sclerotomy wounds remains unknown. Although 27G vitrectomy wounds are made perpendicular to the sclera because of their smaller wound size, the rate of vitreous wound incarceration was found to be similar to larger gauge wounds.[4] Reports on postoperative outcomes after 27G vitrectomy have inconsistent results and complications.[4,18,19] Our institution rarely performed 27G vitrectomy, but it was hypothesized that the smaller gauge wounds limit the amount of vitreous incarcerated and later contracted. Further studies need to be conducted to understand the effect of localized laser treatment on SRRBs after 27G vitrectomy.

CONCLUSIONS

The present study was designed to determine the effect of prophylactic laser treatment posterior to sclerotomy sites in 23G and 25G macular surgeries. The prophylactic laser treatment group had a superior outcome compared to the control group with no postoperative SRRBs or RDs. However, this difference was minimal and not statistically significant. Larger prospective studies are needed to further an understanding of the role of retina laser treatment posterior to sclerotomy wounds.

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Keywords: retinal breaks, retinal detachment, ophthalmological surgical procedures, vitrectomy, treatment outcome

KANSAS JOURNAL of MEDICINE

In-Person Education During the Early COVID-19 Pandemic at Wichita Collegiate School

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ABSTRACT

Introduction. The COVID-19 pandemic forced most Kansas schools to adopt remote or hybrid learning in 2020-2021. Wichita Collegiate School proceeded with an in-person teaching model. The purpose of this study was to determine if in-person learning can be done safely during the COVID-19 pandemic prior to vaccine use.

Methods. Wichita Collegiate is a private school located in Sedgwick County, Kansas. The study population included 671 students (grades 1 - 12) and 130 staff. The procedures implemented during the school year (August 19, 2020 - May 21, 2021) included: mandatory face coverings, six feet physical distancing, and daily temperature checks. A registered nurse performed contact tracing and executed quarantine requirements per the U.S. Centers for Disease Control and Prevention guidelines.

Results. Over the study period, 487 students and staff were tested for COVID-19 and 18.5% (n = 90) were positive. Overall, students and staff rate of COVID-19 infection was lower than the expected rate when compared to the surrounding community of Sedgwick County. Thorough contract tracing of positive cases revealed that 2.2% (n = 2) individuals were likely exposed to COVID-19 at school.

Conclusions. This study suggested that transmission of COVID-19 was infrequent in a school setting with in-person attendance, even before widespread vaccine availability. By following public health guidelines and utilizing contact tracing, it was possible to limit the spread of COVID-19 during in-person learning. This has immediate implications for how schools safely returned to in-person learning in the post-vaccine era. ***Kans J Med 2022;15:202-204***

INTRODUCTION

Throughout the 2020-2021 school year, the COVID-19 pandemic challenged schools across Kansas to ensure the safety of students and staff, while providing the best possible education. With limited data to guide early decisions, most schools adopted remote or hybrid learning. Wichita Collegiate School (WCS) was one of the only schools in Kansas to proceed with a continuous in-person education model for all students throughout the entire school year. Collegiate, following U.S. Centers for Disease Control and Prevention (CDC) guidelines, implemented safety protocols such as: mandatory face coverings, daily temperature checks, and six feet physical distancing.[1]

It was hypothesized that implementing safety protocols based on CDC guidelines could protect the students and staff adequately during in-person education. In addition, cases of COVID-19 at WCS during the school year were predicted to not exceed the expected number of cases based on Sedgwick County rates during the same time frame. To determine the effectiveness of safety protocols and describe how in-person learning contributed to COVID-19 cases in the WCS community, data were collected to describe the frequency and transmission patterns of COVID-19 cases among the students and staff. Contact tracing provided useful data, more importantly, it curtailed the spread of the virus in the community.

The purpose of this study was to determine if in-person learning can be done safely during the COVID-19 pandemic in the pre-vaccine era.

METHODS

For this retrospective, single center study, COVID-19 data were collected from Wichita Collegiate School (WCS) students and staff during the in-person school year: August 19, 2020 - May 21, 2021. The holiday break when school was not in session (December 20, 2020 - January 6, 2021) was excluded.

WCS is a private Pre-K through 12th grade school located in Sedgwick County, Kansas. The school is organized by grade level and division. The study population included 671 students and 130 staff in grades 1 - 12, for a total of 801 people. Preschool and kindergarten students were excluded from our study because younger children were not required to wear face coverings, thus following a different set of safety protocols.

Sedgwick County is comprised of 523,824 residents according to the 2020 national census, making it the second-largest county in Kansas.[2] Sedgwick County contains 20 unified school districts. Moreover, WCS is located inside the Wichita metropolitan area, which is the most extensive metropolitan area in Kansas as it encompasses Sedgwick, Butler, Harvey, Kingman, and Sumner counties and has a population of over 600,000 people.

WCS implemented safety procedures in accordance with CDC recommendations. All students and staff were required to wear face coverings and maintain six feet physical distancing. Daily temperature checks were implemented upon arrival at school. Students and staff were instructed to contact the school registered nurse (RN) with any symptoms of COVID-19, possible exposures to COVID-19, or COVID-19 test results.[3]

The RN collected COVID-19 data, including classification of student or staff, date of illness presentation to the nurse, presence of symptoms or known exposure, source of exposure, and test results. Information was collected for the purposes of contract tracing. Data were kept in a Microsoft® Excel spreadsheet on a password protected computer. Data were collected prospectively, but analyzed at the conclusion of the school year. At that time, the database was de-identified by the nurse and provided to the research team for analysis. No protected health information was disclosed during the study.

Initially, all COVID-19 testing was conducted off campus. However, beginning November 2020, the RN provided on-site PCR testing at the request of the individual. Tests were sent to the Molecular Diagnostics Laboratory (MDL) at Wichita State University (WSU) for same day results. The RN also accepted test results from an outside lab or doctor's office.

The RN conducted thorough contract tracing of each reported positive case and executed quarantine protocol per CDC guidelines. Information on possible previous exposures for each positive case were collected and categorized as home, in school, school-related activities, community, or unknown.

This study described the number and distribution of positive cases within the WCS community, how cases presented, and the likely source of COVID-19 exposure discovered through contact tracing. Additionally, the rate of positive cases at WCS was compared to that of the surrounding community using data provided by the Sedgwick County Health Department.

Statistical analysis was done using SPSS (IBM® Statistical Analysis). Categorical variables were expressed as descriptive statistics, including frequencies, ranges, and percentages. A Chi-square was utilized to determine whether a statistical significance is present in observed relationships.

RESULTS

During the data collection period, a total 487 COVID-19 tests were undertaken by the study population. Ninety positive cases were identified for an overall positivity rate of 18.5%. Of note, 71 positive cases from 292 tests were identified during the first semester for a positivity rate of 24.3%. The second semester only accounted for 19 cases of 196 tests for a lower positivity rate of 9.7%. Of the 90 positive cases, 50 persons were tested because of possible exposure, while 40 were tested due to possible COVID-19 symptoms. Of the 90 positive cases, 17 (18.9%) were staff members and 73 (81.1%) were students. Staff were overrepresented compared to students, as they only comprised 16.2% of the study population.

Contact tracing found that only two (2.2%) positive COVID-19 cases traced back to in-person education. However, 17 (18.8%) positive cases were exposed during school-related activities, 29 (32.2%) inside their own home, and 11 (12.2%) were traced back to the community. The origins of 31 (34.4%) of the cases were unknown. Fortunately, no students or staff members were hospitalized or had serious health complications due to COVID-19 during the school year.

A Chi-square test of independence (χ^2) was calculated comparing rate of COVID-19 in WCS and Sedgwick County. A significant relationship was observed (χ^2 (1) =78.95; p = 0.016). Students and staff were less likely to test positive for COVID-19 when compared to the general population of Sedgwick County.[4] This might be explained by a different age group population, mostly children and teens at WCS. The rate of COVID-19 infections in children and teens was overall less than the rate in adults in the U.S. during the time frame of the study.

DISCUSSION

This study was a summary of real-life experience of in-school attendance during the early days of the COVID-19 pandemic. The most important finding was that our primary objective held true throughout the school year. The rate of COVID-19 transmission at WCS did not exceed the community rate of COVID-19 transmission in Sedgwick County over the same period. This was demonstrated further in Chicago during the same fall semester period corroborating that in-person education does not exceed community rates.[5]

Factors that made this possible were likely strict adherence to CDC guidance in regard to distancing, masking, testing, contact tracing, and quarantining.[6] A major investment was the allocation of a dedicated RN to apply and enforce those protocols. Without proper tracing the rate of transmission likely would have been higher and entire classrooms possibly would have had to quarantine rather than just close exposures. In addition, the free and readily available PCR test administered at school with a 24-hour turn around period made tracing more efficient. The creation of MDL at WSU with partial government funding was a turning point for the community regarding COVID-19 identification.

A challenge was the ever-changing nature of the national guidelines, but constant communication between the school board, the RN, and families helped with timely updates. Another salient factor was the willingness of the parents, school governance, and students to follow the guidelines, especially when inconvenient to them.

An area of concern was the number of cases traced back to school-related activities. The rate of COVID-19 was higher among students participating in sports compared to the general student body. Those groups were not able to mask and/or distance during sporting events. Therefore, their risks and exposures were different than the rest of the students. Again, showing that protocols in place had allowed in-person attendance and protected students to a certain degree while at school.[7]

It was important to remember that during the time of this study, a COVID-19 vaccine still was not widely available to the public. The Pfizer vaccine was made available to children ages 16 to 18 years of age in April 2021. The Pfizer and Moderna vaccines only had become available to adults (at least 18 years of age) in January and February of 2021. The decline in cases seen in the spring of 2020 was not yet the result of vaccination, but rather the overall enforcement of CDC guidance in the fall of 2020 in the community and at WCS. It was possible that the vaccines influenced rates in the latter part of the school year. It would be of value to analyze data again at the end of the 2022 school year, when that COVID-19 vaccines were widely available and approved for children 5 years and up. Of course, the rate of vaccination at school and in the community would need to be compared to understand any differences seen in rates of COVID-19 infection.

In the academic 2020-2021 school year, few schools adopted full-time, in-person learning. That decision had academic and psychological ramifications on students that possibly could have been avoided by adopting a model similar to the WCS experience.[8] In the academic 2021-2022 school year, most schools adopted a full-time in-school attendance due to the availability of vaccines and testing. However, sports teams and large classroom sizes still struggled with COVID-19 outbreaks. This highlighted the importance of keeping up with precautions to decrease exposures and encouraging vaccine acceptance.

CONCLUSIONS

In summary, it remains important to adhere to public health guidelines as more is learned about COVID-19 during this ongoing pandemic. Effective preventative measures when implemented properly and widely adopted can curb the trajectory of transmissible disease in any community. Early and open communication was key to success when multiple groups were involved, in this instance parents, students, teachers, and support staff. Trust and flexibility were needed to ensure a positive outcome. This study highlighted the safety of in-person learning in the pre-vaccine era and showcases WCS success in maintaining low COVID-19 cases at a time when very few establishments believed this was achievable.

In the WCS experience, the risk of COVID-19 infection early in the pandemic course was not increased by attending in-person school versus living in the Sedgwick County community, if CDC guidelines were followed.

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Keywords: COVID-19, pandemic, public health, return to school, education

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Cerebrospinal Fluid Leaks: A Case Series of Sinus Opacification on Computed Tomography (CT) Imaging

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ABSTRACT

Introduction. Cerebrospinal fluid (CSF) leaks occur when fluid seeps through a dural or skull base defect, typically in the nose or ear. CSF leaks commonly are identified and diagnosed by use of computed tomography (CT) and CT cisternogram. CT findings suggestive of a CSF leak include a skull-based bone defect along with opacification of the contiguous sinus. This study examined a series of CSF leaks on CT imaging to document imaging findings.

Methods. A single-institution retrospective review of cases of CSF leak diagnosed by CT maxillofacial or CT cisternogram from January 1, 2008 to March 12, 2018 was performed. Patient demographics, history, imaging findings, and treatment were recorded.

Results. Thirty-nine patients met the inclusion criteria for the study. The average age was 51, and a large majority were female (76.9%). Among the 25 patients in which it was reported, the mean size of skull base defect was 0.472 cm. Of the 39 total cases, 27 patients (69.2%) presented with sinus opacification on CT imaging.

Conclusions. Radiologists should be aware of the possibility of notable sinus opacification observable on CT when investigating a potential CSF leak. Opacification may vary in both location and size depending on the nature and location of a CSF leak. Further research is needed to draw a correlation between sinus opacification seen on CT scan and the diagnosed origin of a CSF leak. ***Kans J Med 2022;15:205-207***

INTRODUCTION

Cerebrospinal fluid (CSF) leaks occur when CSF seeps through a dural or skull base defect, typically in the nose or ear.[1] Trauma is the most common cause of CSF leaks, with prior studies reporting 80% of CSF leaks were secondary to trauma, with a smaller portion occurring non-traumatically or spontaneously.[1,2] Spontaneous CSF leaks increasingly have been diagnosed and linked with obesity.[3] Complications of CSF leaks can be severe and may result in meningitis, brain herniation, or coma, necessitating early detection.[1] Although some CSF leaks are managed conservatively, treatment typically requires endoscopic nasal surgery.

Imaging plays a pivotal role in the diagnosis and treatment of CSF leaks. While laboratory workup can confirm a CSF leak by the presence of beta 2 transferrin in the rhinorrhea, it is unable to locate the origin of the leak.[4] CSF leaks can be identified on several imaging modalities. Computed tomography (CT) is often the first study obtained due to its ability to characterize osseous defects.[5] Fine detail CT scans, with 1-2 mm sections through the skull base, can identify the location of the CSF leak and show small bony irregularities and fractures.[4] CT scans also have demonstrated accurate correlation with intraoperative endoscopic findings.[6] While high-resolution CT is typically the initial screening study, CT cisternogram is also useful in diagnosing CSF leaks if there are multiple skull base defects or if the initial CT scan is negative.[4,5,7,8]

The goal of imaging CSF leaks is to confirm the diagnosis, determine the cause, and localize and characterize the defect.[5] CT findings suggestive of a CSF leak include a skull-based bone defect along with opacification of the contiguous sinus. The most common location for CSF leaks is the anterior cranial fossa following a defect in the cribriform plate, although one also may arise from the ethmoid, sphenoid, or frontal sinuses. Size and imaging characteristics of the defect, such as adjacent soft tissue or mucosal thickening, are also important for adequate surgical planning.[1,4,5]

Although prior research has documented that CT findings of CSF leaks include opacification of a contiguous sinus,[5] an association between the specific type of sinus opacification and CSF leak has not been well studied. Knowing if there is a pattern between sinus opacification and CSF leaks could guide radiologist search patterns and improve accuracy of CSF leak diagnoses, particularly if they were incidental findings, which may improve timeliness of CSF leak diagnosis and influence treatment strategy. Doing so could enable patients to receive appropriate care and result in fewer complications secondary to CSF leaks. The purpose of this study was to describe imaging findings of patients with CSF leaks.

METHODS

Institutional review board approval was obtained, and patient medical records were reviewed in compliance with Health Insurance Portability and Accountability Act guidelines. A retrospective review of all patients diagnosed with a CSF leak by CT maxillofacial or CT cisternogram from January 1, 2008 to March 12, 2018 was conducted. Imaging findings and characteristics were recorded along with clinicopathologic features. Patient demographics and clinical information, including date of birth, gender, race, ethnicity, body mass index (BMI), history of intracranial hypertension, and history of skull base surgery, were obtained from the electronic medical record. Imaging and results were obtained from the Picture Archiving and Communications Systems (PACS).

RESULTS

Images from 39 patients with CSF leaks were examined. The average age was 51 years, and a large majority were female (76.9%), White (69.2%), and non-Hispanic/Latino (89.7%). The mean body mass index among patients was 36.45. Most had no history of intracranial hypertension (84.6%) and had no history of skull base surgery (79.5%, Table 1).

In 39 patients with CSF leak, 20 patients had an identifiable cause of CSF leak: seven were traumatic (18.0%), four (10.3%) were non-traumatic, and nine (23.1%) were spontaneous. The cause was unknown in

the remaining 19 (48.7%) of them. Of the 39, CSF leaks were located in the cribriform plate (30.8%), ethmoid sinus (35.9%), sphenoid sinus (33.3%), and frontal sinus (10.3%). Among the 25 patients in which it was reported, the mean size of skull base defect was 0.472 cm. A total of 30.7% of the patients were examined by CT cisternogram and 87.2% were examined by CT maxillofacial. Thirty of the 39 patients presented with elevated levels of Beta 2 transferrin; the nine remaining patients did not have this information reported.

Patients in this study had their CSF leak treated or managed in a variety of ways. Twenty-nine patients (74.4%) underwent a lumbar drain, and 31 (79.5%) underwent endoscopic nasal surgery. Five patients (12.8%) underwent open craniotomy, and two (5.1%) had their leak managed conservatively (Table 2).

Of the 39 total cases, 27 patients (69.2%) presented with sinus opacification on CT imaging. Sinus opacification was noted in the frontal (18.5%), ethmoid (7.4%), maxillary (40.7%), and sphenoid (66.7%) sinuses. Nine (33.4%) of these 27 patients had bilateral sinus opacification, and eleven (40.7%) had solitary sinus opacification. Nine patients (33.4%) had full sinus opacification compared to the remaining eighteen (66.7%) patients with partial sinus opacification (Table 3).

Table 1. Patient characteristics.

	Case Group (N = 39)
Age, mean (SD)	51.9 (15.1)
Sex, n (%)	
Male	9 (23.1%)
Female	30 (76.9%)
Race, n (%)	
Asian/Pacific Islander	0
Black	7 (18.0%)
White	27 (69.2%)
Other	5 (12.8%)
Ethnicity, n (%)	
Non-Hispanic/Latino	35 (89.7%)
Hispanic/Latino	4 (10.3%)
BMI, mean (SD)	36.45 (11.23)
History of intracranial hypertension, n (%)	
Yes	6 (15.4%)
No	33 (84.6%)
History of skull base surgery, n (%)	
Yes	8 (20.5%)
No	31 (79.5%)

DISCUSSION

There were several limitations to our study. While sinus opacification and its qualities were observable on CT for a majority of the patients in the study, there was no means of drawing a correlation between these observations and the location of the CSF leak. Without a control group, it was not possible to establish a definitive link between sinus opacification and the origin of a CSF leak. Nineteen of the 39 patients had an unknown or unidentified type of CSF leak, which barred our ability to observe for links between type of CSF leak and sinus opacification. Report of beta 2 transferrin levels to confirm CSF leak was missing for 9 of 39 patients.

Table 2. CSF leak characteristics.

	Case Group (N = 39)
Type of CSF leak, n (%)	
Traumatic	7 (18.0%)
Non-traumatic	4 (10.3%)
Spontaneous	9 (23.1%)
Unknown	19 (48.7%)
Location of CSF leak, n (%)	
Anterior skull base	0
Cribriform plate	12 (30.8%)
Ethmoid sinus	14 (35.9%)
Sphenoid sinus	13 (33.3%)
Frontal sinus	4 (10.3%)
Mean size of skull base defect, mean (SD)*	0.472 cm (0.285 cm)
Diagnosis method of CSF leak, n (%)	
CT cisternogram	12 (30.8%)
CT maxillofacial	34 (87.2%)
CSF leak management, n (%)	
Conservative management	2 (5.1%)
Lumbar drain	29 (74.4%)
Open craniotomy	5 (12.8%)
Endoscopic nasal	31 (79.5%)
Procedure Cancelled	1 (2.6%)
Elevated Beta 2 transferrin, n (%)	
Positive	30 (76.9%)
Negative	0
Not reported	9 (23.1%)

*Only 25 patients reported their size of skull base defect.

Table 3. Sinus opacification characteristics.

	Patients with Sinus Opacification (N = 27)
Type of sinus opacification, n (%)	
Frontal	5 (18.5%)
Ethmoid	2 (7.4%)
Maxillary	11 (40.7%)
Sphenoid	18 (66.7%)
Bilateral sinus opacification, n (%)	
Yes	9 (33.3%)
No	18 (66.7%)
Solitary sinus opacification, n (%)	
Yes	11 (40.7%)
No	16 (59.3%)
Size of sinus opacification, n (%)	
Full	9 (33.3%)
Partial	18 (66.7%)

The patients included in this study had an average BMI of 36.45, which would be categorized as obese. A prior study by Quatre et al.[3] discussed an association between body weight and incidence of spontaneous cerebrospinal fluid leak. Twenty-three percent of the patients in this study had a CSF leak identified as spontaneous. As obesity continues to rise as a leading health issue, physicians must remain aware of the need to identify and diagnose a spontaneous CSF leak in obese patients.

In conclusion, among the 39 cases of CSF leak in this study, nearly 70% presented with some form of sinus opacification on CT imaging. Sinus opacification can be observed in one or multiple sinuses in the presence of a CSF leak and may be bilateral or solitary as well as partial or full. Radiologists and physicians should be aware of this potential finding when evaluating a patient for a possible cerebrospinal fluid leak. As previously mentioned, timely diagnosis and treatment of CSF leak is essential to preventing further complications. More research is needed

to establish a definitive correlation between sinus opacification on CT scan and the location of a cerebrospinal fluid leak. An established association between the two will further aid physicians in making a more accurate and faster diagnosis for these patients.

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Keywords: cerebrospinal fluid hypovolemia, skull base, nasal sinuses, computed tomography, x-ray

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Rodeo Trauma: Outcome Data from 10 Years of Injuries

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ABSTRACT

Introduction. There are few data addressing rodeo injury outcomes, though injury incidence has been well described. The purpose of this study was to describe rodeo-related injury patterns and outcomes.

Methods. A 10-year retrospective case series was performed of patients injured in rodeo events and who were treated at an ACS-verified level I trauma center. Data regarding demographics, injury characteristics, and outcomes were summarized.

Results. Seventy patients were identified. Half were injured by direct contact with rodeo stock and 34 by falls. Head injuries were most common, occurring in 38 (54.3%). Twenty injuries (28.6%) required surgery. Sixty-nine patients (98.6%) were discharged to home. There was one death.

Conclusions. Head injuries were the most common injury among this cohort. Apart from one fatality, immediate outcomes after injury were good, with most patients dismissed home. Improved data collection at the time of admission may help to evaluate the success of current safety equipment use. ***Kans J Med 2022;15:208-211***

INTRODUCTION

The sport of rodeo has evolved from the specialized skill set that vaqueros and cowboys developed while working cattle in the late 1800s. Many rodeos are sanctioned by organizations such as the Professional Rodeo Cowboys Association and National Intercollegiate Rodeo Association (NIRA). The NIRA has guidelines related to the use of protective equipment.[1] Professional events include timed calf roping, team roping, and barrel racing. Rough stock events, which typically are associated with more injuries, include bull riding, steer wrestling, saddle bronc riding, and bareback bronc riding.

Given the dangerous nature of rodeo events and the proximity of the athletes to the animals with which they interact, it is not surprising that competitors often are injured severely from the tremendous force exerted by the massive livestock. Serious head injuries have been shown to occur in rodeo athletes at a rate of up to 15 per 1,000 rides.[2] Other athletes, such as professional football players, suffer serious head injuries at a rate of 5.8 per 100,000 players. In addition, a study by Savage, et al.[3] demonstrated that the average ground reaction force produced by the hind hooves of a large bull is 106.3 kN. In comparison, the force produced by an Olympic boxer delivering a straight punch is 3.4 kN.[4]

Independent of the rodeo event type (contact or non-contact), the potential for injury requiring medical intervention is high for rodeo athletes. Meyers and Laurent[5] found bull riding was responsible for the greatest proportion of rodeo injuries, accounting for 28 - 50% of all rodeo-related injuries. Subsequent injury rates included: saddle bronc and bareback riding events (20 - 23%), calf roping (3 - 12%), steer wrestling (8%), team roping (1 - 4%), and barrel racing (0 - 3%).

Rodeo injuries presenting as traumas tended to include the most severe. However, decisions by injured rodeo athletes to seek medical treatment often were influenced adversely by stoicism, perceptions of peer pressure, and a tradition of machismo or the desire to continue participating.[5] To improve outcomes among this reticent group of patients, injuries often were triaged at the rodeo, allowing many to be managed on an outpatient or non-emergent basis. The availability of arena-side medical attention has improved health care access at the professional level where incidence rates of 1.47 to 1.66 per 100 competitive exposures have been demonstrated.[6,7] When looking only at the bull riding event, Butterwick et al.[6] found an injury incidence of 3.22 injuries per 100 competitive exposures. Injury rates per 100 competitor exposures for other events included: 2.45 for bareback riding, 1.75 for saddle bronc riding, 0.92 for steer wrestling, 0.18 for calf roping, and 0.15 for ladies' barrel racing.

Stigma regarding style and tradition may affect the usage rates of protective gear designed to prevent or minimize the severity of injury including helmets and vests.[5] Research to improve preventative equipment design has been focused on advancements in function and reliability with a focus on maximizing the biomechanical needs of these athletes in a manner which does not jeopardize the rodeo tradition.

Despite the availability of data related to rodeo injury, there was a paucity of literature which addressed injury outcomes. The purpose of the presented study was to conduct a 10-year retrospective review of rodeo-related injuries and outcomes of patients admitted to a Level I trauma center.

METHODS

A retrospective case series was conducted of all patients who sustained injuries from participation in rodeo-related events. Patients were treated at an American College of Surgeon-verified level I trauma center over a 10-year period between January 1, 2000 and December 31, 2009. Potentially eligible patients were identified through query of the trauma registry and a review of the medical records. Data collected included: patient demographics (e.g., age, gender), trauma activation level, mechanism of injury (i.e., competitor came into contact with rodeo stock or arena infrastructure, competitor fell from animal), type of rodeo event if available, type of protective equipment worn (usage included in the history and physical), injury type, Injury Severity Score (ISS), need for operative or procedural intervention, elapsed time from injury to presentation, radiological results, level of care required (i.e., intensive care unit or nursing unit), length of stay, complications, use of alcohol or drugs, disposition (i.e., home, rehabilitation, skilled nursing facility), and mortality.

Data were collected, organized, and summarized using SPSS release 19.0 (IBM® Corp, Somers, New York). This study was approved for

implementation by the Institutional Review Board of Via Christi Hospitals Wichita, Inc, Wichita, KS.

RESULTS

Seventy patients injured while participating in rodeo events were evaluated and treated at the institution as a trauma team activation. Patient demographics, injury mechanism, injury severity, and trauma activation data are shown in Table 1. The majority of these patients were male (77.1%) with an average age of 29.8 years and mean ISS of 8.0. One-half were injured by direct contact with rodeo stock (i.e., collision with an animal, being stepped on, gored). Nearly one-half (48.6%) were injured by falls from animals. Most were evaluated as level II trauma activations (84.3%).

Table 1. Demographics, mechanism of injury, injury severity, and hospital stay information for patients injured while participating in rodeo events.

Parameter	Number (%)
Number of patients	70 (100%)
Age (years)*	29.8 ± 15.8 (5 - 75)
Male	54 (77.1%)
Mechanism of injury	
Contact with rodeo stock (i.e., collision, rolled on, gored)	35 (50.0%)
Falls from animals	34 (48.6%)
Struck by gate	1 (1.4%)
Admission level	
Level I	5 (7.1%)
Level II	59 (84.3%)
Consult, or non-trauma service	6 (8.6%)
Injury Severity Score (ISS)**	7.0 (4 - 10)

*Mean ± SD (range); **Median (IQR).

Classification of injuries by location is presented in Table 2. Head injuries were most common, occurring in 38 patients (54.3%), 10 (26.3%) of whom sustained intracranial hemorrhage. Thoracic injuries were the next most common (n = 11, 15.7%), followed by extremity fractures (22.9%). Upper and lower extremity fractures occurred in seven (10.0%) and nine patients (12.9%), respectively. Twenty injuries (28.6%) required surgical intervention and included four for head, two for thoracolumbar spine, one for cervical spine, one for abdominal, three for upper extremity, and nine for lower extremity. There were 11 non-surgical thoracic injuries (eight patients with rib fractures, six with pneumothorax (five treated with thoracostomy tube), two with clavicular fractures, and two with pulmonary contusions).

There were three pelvic fractures that were non-surgical, and three intraabdominal injuries. A splenic laceration and a liver laceration were managed conservatively, while a pancreatic injury required distal pancreatectomy. The patient with the pancreatic injury was managed initially at an outside facility where a computed tomography (CT) scan done at the time of admission failed to demonstrate the pancreatic injury. A repeat CT scan done 72 hours after injury demonstrated pancreatic transection and prompted transfer to the trauma center. Distal pancreatectomy was performed with temporary abdominal closure. He was closed the following day following a second-look laparotomy. The patient was doing well at clinical follow-up.

Table 2. Injury characteristics and patterns for patients injured while participating in rodeo events.

Body Region	Number of Patients with Injuries (%)	Number of Patients Requiring Surgery (%)
Head	38 (54.3%)	4 (5.7%)
Spine	7 (10.0%)	3 (4.3%)
Thoracic	11 (15.7%)	0 (0.0%)
Abdominal	3 (4.3%)	1 (1.4%)
Pelvic	3 (4.3%)	0 (0.0%)
Extremities (upper)	7 (10.0%)	3 (4.3%)
Extremities (lower)	9 (12.9%)	9 (12.9)

Data regarding the use of protective equipment were lacking in all but nine patients. Of these, seven wore protective equipment. Two wore a helmet, two a helmet with mask, one a helmet and mouthguard, one a helmet and a vest, and one wore a vest only. No information was available for the other 61 patients.

Abuse of alcohol or drugs did not appear to play a large role in these injuries. A blood alcohol level was performed on 11 of the 70 patients (15.7%). Six of the 11 tested positive for alcohol, but only three tested above the legal driving limit for the state of Kansas (80 mg/dL). The mean blood alcohol level for these 11 patients was 60 ± 90.4 mg/dL (range = 0 to 276 mg/dL). Ten patients (14.3%) underwent drug toxicology screening. Five tested negative. Two tested positive for opiates but already had been given opiates by health care personnel prior to their test. One tested positive for opiates, benzodiazepines, and barbiturates, though this patient had been administered opiates and benzodiazepines by first responders. Two tested positive for benzodiazepines with no record of administration by health care personnel.

Data regarding patient hospitalization and disposition are detailed in Table 3. Nearly one-quarter of patients (22.9%) required admission to the intensive care unit with an average length of stay of 1.9 days. Three patients required mechanical ventilation. The mean hospital length of stay was 2.0 days, but the majority (n = 40, 57.1%) had a hospital length of stay of one day. All but one patient sustained non-fatal injuries. Each was discharged to home, with none requiring inpatient rehabilitation or long-term care. There was one death (1.4%); the patient who died was thrown from a horse and the horse rolled over his torso and head, crushing his skull. There was no documentation of protective equipment use. He suffered a severe brain injury as well as numerous facial fractures. The patient succumbed to his injuries approximately 12 hours after admission.

Table 3. Hospitalization and discharge data for patients injured while participating in rodeo events.

Parameter	Number (%)
Number of patients	70 (100%)
Intensive care unit admission	16 (22.9%)
Intensive care unit length of stay (d)	1.9 ± 1.1 (1 - 4)*
Required mechanical ventilation	3 (4.3%)
Hospital length of stay (d)	2.0 ± 1.7 (1 - 11)*
Disposition	
Home	69 (98.6%)
Death	1 (1.4%)

*Mean ± SD (range)

DISCUSSION

This study examined injury patterns and outcomes of rodeo participants treated at a level I trauma center and represented a cross-section of the severely injured patients initially evaluated by arena-side providers then transferred to the medical center for definitive care. Injury patterns have been described by several investigators who collected information while providing arena-side medical care for rodeo participants.[5,6,8-10] Contusions, strains, and concussions were the most common injuries described previously (42%, 16%, and 11%, respectively); for roughstock events, injury to exposure potential has been demonstrated to be as high as 6:1.[10] Additionally, craniofacial trauma for bull riding injuries ranging from low grade concussions to head injuries and neck injuries represented 0.087 per 100 of injuries, while concussions represented 0.34 per 100 injuries.[11] These studies afforded an excellent understanding of the breadth and severity of the injuries sustained during rodeos, but outcome data regarding these injuries were not available.

Head injuries were the most common injury in this study, where over half of the patients sustained a traumatic brain injury. Incidence of head injury, which included both concussion, as well as traumatic brain injury, was higher than previous reports with incidence of cranial trauma of 11 - 14%.[5] The higher head injury reported in the current study may be a result of only receiving the more severely injured riders being transported to our level I trauma center. Other specific injuries typical among this population, such as digit amputation, especially thumb amputations, were not prevalent in our population.[12] In addition, although tendon and ligamentous injuries occurred frequently, the current study demonstrated a single patient with ligamentous knee injury that required surgery. Though more severely injured, our patients achieved excellent outcomes, with none requiring inpatient rehabilitation, and included only one fatality. Aside from the lack of contusions and sprains seen in other studies, our distribution of injuries seemed consistent with previous studies of rodeo-related injuries.

Sanctioned rodeo events often require use of protective equipment for athletes,[1,2] however, claims related to efficacy and lower injury incidence rates are largely unsupported in literature and remain controversial. Information regarding the use of safety equipment or training among our population was missing for most of the patients. Efforts to reduce injury by wearing protective vests have been adopted by rodeo sanctioning organizations, though few data are available to prove they significantly reduce the incidence of catastrophic thoracic injury.[13] Utilization of protective thoracic vests over the past 20 years was believed to have reduced the severity of compression thoracic injury by dispersing and absorbing the impact of a traumatic blow.[14] This belief was based on anecdotal evidence, and did little to dispel the controversy surrounding whether vests provide adequate protection, since deaths still were reported when vests are used.[13] There are no known manufacturing safety standards for vests or design improvements.

Protective helmets, on the other hand, have been shown to reduce the incidence of head injuries, lowering incidence of head injury from 1.54% per ride (11 head injuries per 713 rides) to 0.80% per ride (28 head injuries per 3,518 rides).[15] Moreover, concussions and loss of consciousness occurred less frequently in those who wore helmets compared to those who did not (44% vs. 61% and 39% vs. 59%, respectively).[16] The current study demonstrated 30 of 70 patients (42.9%) sustained a head injury over a 10 year time period. It is unknown how many of these patients were wearing protective head gear at the time of their injury. Although rodeo athletes have been slower to adopt the use of helmets, encouragingly their use has increased in recent years.[16] Additionally, neck rolls, various orthotics, face masks, and conditioning programs have been suggested as potential methods to reduce injury.

Limitations. This study suffered for all the limitations inherent to any retrospective review. As all three types of sanctioned and non-sanctioned rodeo competitions (rodeo, ranch rodeo, and charreada) were common in Kansas, one aim of this study was to compare injury patterns between the three. However, this retrospective review failed to be able to identify the types of rodeos in which injured athletes had participated, therefore did not yield the capability to compare the three types of rodeo competitions. Additionally, information on use of protective gear was very limited. Another limitation was not having the data to capture an injury rate in relation to competitive exposures. This study also was limited to those who visited one specific hospital. Because of various reasons, such as patients going to a different hospital and the feeling of machismo, some injuries likely have been missed, leaving this study with a less than full picture of the scope of injuries that occur at the rodeo.

CONCLUSIONS

For athletes competing in rodeos, head injuries were the most common injury, followed by thoracic, then extremity injuries, a pattern which may be influenced by current recommendations regarding protective equipment use. Current standards for protective head and neck gear use seemed reasonable considering these data; however, information regarding protective gear was limited. With limited numbers, prospective studies with a focus toward safety equipment use are recommended to determine the effectiveness of this equipment if and when their use becomes more prevalent.

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Keywords: sports, injuries, retrospective studies, trauma centers, animals

KANSAS JOURNAL of MEDICINE

The Utility of Frequent Laboratory Monitoring for Patients on Tumor Necrosis Factor-Alpha Inhibitors in Dermatology

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ABSTRACT

Introduction. Tumor necrosis factor-alpha inhibitors (TNF-ai) are becoming increasingly common to use among patients with skin disease. To safely take these medications, it is recommended to monitor laboratory values routinely; however, the utility of this practice and the risk-benefit of frequent laboratory monitoring has not been explored fully in patients with skin disease. The purpose of this study was to evaluate the necessity of routine laboratory monitoring in patients taking a TNF-ai with a dermatological disease.

Methods. Retrospective chart review evaluated laboratory abnormalities (complete blood counts and liver function tests) in adult patients who took a TNF-ai for a dermatologic disease at The University of Kansas Hospital.

Results. There were 27 patients included for a total of 45 entries. The most common skin disease was hidradenitis suppurativa (23/45) and infliximab (22/45) was most the commonly used medication. Of the 45 entries, there were only seven patients that developed abnormal monitoring laboratory values related to initiation of TNF-ai. These abnormalities were transient and most frequently occurred after 12 months, with 2 of the 45 resulting in no discontinuation or dose reduction of TNF-ai. One patient discontinued medication due to anemia that did not improve after medication withdrawal.

Conclusions. Laboratory abnormalities due to TNF-ai were infrequent and when they did occur were transient and mild. The study was limited by the small sample size of patients, and larger prospective studies are needed to evaluate these findings fully. However, dermatologists may be able to employ less frequent laboratory monitoring safely for patients on TNF-ai. ***Kans J Med 2022;15:212-214***

INTRODUCTION

Tumor-necrosis-factor alpha inhibitors (TNF-ai) have been proven beneficial for dermatologic diseases such as psoriasis and hidradenitis suppurativa, among others.[1] It was recommended to monitor for laboratory abnormalities from baseline to every three months, although no published guidelines exist for the vast majority of skin diseases, except for psoriasis.[2,3]

Excessive monitoring comes at an inconvenience to patients and increases health care costs to the patient in the form of burden (i.e., travel, time, expenses, blood draws) or prematurely stopping a treatment regimen without evidence that continuing will result in complications.[4] However, it is important to ensure patient safety by appropriately screening patients for potentially dangerous abnormalities. The purpose of this retrospective study was to evaluate when and how severe adverse laboratory events were experienced to determine if less frequent laboratory monitoring can be employed in adults taking TNF-ai for a variety of skin diseases.

METHODS

An IRB approved retrospective review was conducted to assess our patient experiences. To be included in the study, patients (1) received dermatology care at The University of Kansas Health System (TUKHS), (2) were prescribed a TNF-ai for a skin condition, (3) were compliant with laboratory monitoring and the medication, and (4) were ages 18 or older. Patients consecutively treated with adalimumab, etanercept, certolizumab, golimumab, and infliximab could contribute data to all biologics. Laboratory values of interest included a complete blood count, liver function tests, and inflammatory markers. Quantitative data were reported as counts and percentages.

RESULTS

Twenty-seven participants included in the study contributed data for 45 entries (Table 1). The majority of patients took infliximab (n = 22), followed by adalimumab (n = 17), etanercept (n = 4), and golimumab (n = 2). While 19 patients had baseline abnormalities, this did not prevent the initiation of medication. Only seven patients developed abnormal laboratory values after initiation of TNF-ai, with the majority occurring after 12 months and returned to baseline by the following laboratory draw (n = 6; Table 1). These abnormalities were presumed related to initiation of TNF-ai. However, given the abnormalities were transient, there was no discontinuation or reduction of dose. Only one patient with baseline laboratory abnormalities had to discontinue infliximab due to severe anemia that did not improve despite medication withdrawal.

DISCUSSION

Our study evaluated the utility of routine laboratory monitoring for patients with skin disease taking a TNF-ai. Adverse laboratory events that developed while taking the TNF-ai were rare and, when they did occur, they were transient and resolved by the following laboratory draw. A prospective trial evaluating psoriatic patients on etanercept and adalimumab concluded routine laboratory monitoring for those two TNF-ai may be unnecessary, as the abnormalities noted were either transient, present at baseline, or unrelated to the medication and did not result in a reduction of discontinuation of the drug, similar to our findings.[5] However, our study evaluated two additional TNF-ai and expanded over a wider range of skin diseases that have not been evaluated previously. A review reported adverse events of TNF-ai for patients diagnosed with either rheumatoid arthritis or Crohn's disease and concluded that laboratory adverse events, such as hepatotoxicity or cytopenia, are exceedingly rare, suggesting, similar to our current study, that less frequent monitoring may be appropriate.[6]

Our study was limited by the number of patients that met inclusion criteria. Larger, prospective studies are needed to appreciate more fully the utility of routine laboratory monitoring in adult patients taking a TNF-ai for a skin condition. Nonetheless, based on our findings and the established data, dermatologists safely may be able to evaluate laboratory monitoring less frequently.

Table 1. Demographics and timing of laboratory abnormalities per medication.

	Infliximab	Adalimumab	Etanercept	Golimumab
Number of patients	22	17	4	2
Age in years, median (range)	39.5 (20-78)	33 (19-73)	51.5 (29-73)	55.5 (43-68)
Male: Female	6: 16	6: 11	1: 3	1: 1
Diagnosis				
Hidradenitis suppurativa	11	12	0	0
Pyoderma gangrenosum	6	1	1	0
Psoriasis/psoriatic arthritis	5	4	3	2
Exposure to drug in months, median (range)	6.1 (3.6-57.8)*	19.3 (3.3-89.7)	5.2 (4.5-83.0)	24.1 (11.4-36.7)
Baseline abnormality	11	4	2	2
Resolved	5	1	1	2
Continued, duration in months	5	3	1	0
Duration in months, (range)	7.5 (3-48)	6 (6-18)	3	
Discontinued drug due to abnormality	1[β]	0	0	0
Monitoring abnormality	1	5	0	1**
Resolved	1	5	0	1**
Continued in months, duration	0	0	0	0
Discontinued drug due to abnormality	0	0	0	0
Timing of abnormality				
Baseline	11/12	4/9	2/2	2/2
After baseline and < 6 months	1/12	0	0	0
≥ 6 months and < 12 months	0	0	0	0
≥ 12 months and < 18 months	0	1/9	0	1**
≥ 18 months	0	4/9[α]	0	1**
Discontinued, n	7	15	3	2
No benefit	3	13	1	2
Allergy	2	1	0	0
Laboratory abnormality	1	0	0	0
Infection	0	1	1	0
Pregnant	1	0	0	0
Not stated	0	0	1	0

*One patient discontinued at day 1 of infusion due to drug allergy.
**This patient also had baseline abnormality that resolved. Patient had transient leukocytosis at 12, 24, and 36 months that all resolved at following laboratory draws.
[α]Transient laboratory abnormalities at 18, 27, and 51 months.
[β]Patient had chronic anemia that did not improve despite discontinuing infliximab.
Note: *BL*: baseline; *Resolved*, abnormality was not present by subsequent laboratory draw. Resolved abnormalities were not present at the following 3-month laboratory draw.

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Keywords: tumor necrosis factor-alpha, dermatology, adverse drug events, clinical laboratory techniques, patient monitoring

KANSAS JOURNAL of MEDICINE

Virtual Adaptation of Resident I-PASS Training Session During COVID-19

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ABSTRACT

Introduction. Effective communication during the patient handoff process is critical for ensuring patient safety. At our academic medical center, first-year interns complete hand-off training before starting clinical rotations. The purpose of this study was to evaluate a virtual handoff training for residents as an alternative to in-person sessions due to limitations imposed by COVID-19.

Methods. Fifty residents were administered pre/post surveys to gauge the helpfulness of the training for clinical practice, familiarity and confidence in providing a hand-off, and whether they would recommend the virtual format for incoming interns. Additionally, faculty rated the virtual form of the hand-off activity, made comparisons to in-person sessions, and assessed the helpfulness of the session for residents in clinical practice.

Results. Forty-four residents (88%) and 11 faculty (85%) completed surveys. After the training session, residents who received instruction and feedback reported significant improvements in familiarity with the hand-off tool and confidence in their hand-off abilities (both $p < 0.001$). Both residents and faculty were satisfied with the virtual format of hand-off training. Most faculty felt the virtual platform was comparable to in-person sessions and would recommend ongoing use of the virtual platform when in-person sessions were not possible.

Conclusions. Teaching hospitals mandate resident training to include strategies for a uniform hand-off method to avoid medical errors. Adaptation to a virtual platform can be a successful instruction strategy, allowing for didactic and interactive sessions with direct faculty observation and feedback. ***Kans J Med 2022;15:215-217***

INTRODUCTION

Communication failures are the leading cause of patient medical errors in hospitals.[1,2] Patient hand-offs, the transfer of patient-specific clinical information from one physician to another, are especially vulnerable to miscommunications.[3] Formalized training to optimize the hand-off process can improve communication and patient safety, thus the Accreditation Council for Graduate Medical Education has identified improving hand-offs as a priority to improve patient safety, and requires residency programs to provide formal instruction and monitor the quality of handoffs.[4,5]

At the University of Kansas Medical Center, the Internal Medicine's resident hand-off training program is run by core resident faculty. First-year interns complete hand-off training before they begin clinical rotations. Using a standardized hand-off bundle, I-PASS (a mnemonic for illness severity, patient summary, action list, situational awareness with contingency planning, and synthesis by the receiver),[6] the training session is designed to familiarize incoming residents with elements of team structure, use of the electronic health record, and to provide a uniform method for patient hand-off.[7] I-PASS is a comprehensive hand-off program designed to train clinicians to exchange and synthesize patient information concisely.[8] However, as social distancing and limitations on in-person gatherings were initiated during COVID-19, adaptation of the I-PASS training session was required.

While some of the I-PASS training content could be delivered through recorded lectures, it did not permit residents to participate in an active process of delivering and receiving a hand-off with faculty feedback. Therefore, the existing in-person I-PASS session was restructured for use on the Zoom platform. This virtual platform allowed for delivery of didactic material with direct faculty observation and feedback through Zoom's breakout room feature. Formalized training is important in improving patient safety and reducing medical errors, but there are a lack of data about hand-off training using a virtual format.

The aims of this study were to characterize the adapted workshop and to assess the perspectives of residents and faculty who participated in the training session.

METHODS

Institutional Review Board exemption was obtained for educational purposes.

Setting and Participants. This study was conducted at the University of Kansas Medical Center, which is a full-service 623-bed tertiary care center and medical training facility with over 600,000 patient visits annually. For this study, 50 preliminary (Anesthesia, Dermatology, Ophthalmology, Radiology, Neurology, and Physical Medicine and Rehabilitation) and categorical (Internal Medicine or Internal Medicine/Psychiatry) residents participated in a 60-minute interactive workshop held in 2020 through the Zoom platform.

Intervention. The instructional strategy for the virtual session was guided by Bloom's mastery learning model in which specific principles were integrated into the educational session.[9] These principles included communicating learning expectations clearly at the onset of the education session, outlining specific learning objectives, giving prompt feedback during direct observations, and encouraging interaction between faculty and residents.[10] Before the virtual session, residents viewed a video presentation in which teaching faculty examined the role of hand-offs in enhancing patient safety, described elements of both satisfactory and unsatisfactory hand-offs, and discussed individual components of the I-PASS tool. At the beginning of the virtual session, faculty shared learning expectations and addressed communication skills necessary to perform effective hand-offs.

At the start of the Zoom session, all residents and participating teaching faculty joined the main room for a review of course objectives and a synopsis of the video content previewed by residents before the workshop. Next, faculty members provided I-PASS modeling in the context of a clinical case. After modeling, residents were asked to evaluate the quality of the hand-off.

For resident practice and observation, Zoom breakout rooms were utilized. Each faculty member was assigned a breakout room for a

twenty-minute interval. Residents were paired and then joined a faculty member in the breakout room. Faculty provided case scenarios and residents were asked to indicate key elements of the I-PASS hand-off. Following practice, each resident handed off patients to one another using provided case scenarios, and each was provided feedback from his/her peer and the faculty member on one another's hand-off performance. Once all residents had completed their partnered activity, they re-entered the Zoom main room where additional faculty were available for questions. At the conclusion of the session, post-workshop surveys were sent to both learners and teaching faculty to evaluate the session.

Outcomes Measured

Resident Survey. The online survey consisted of 10 items with yes/no or Likert-format responses. Items included post-graduate training status (preliminary, categorical), hand-off experience as a medical student (both written and verbal), I-PASS tool familiarity, importance of hand-offs to patient care, confidence in providing a hand-off, and helpfulness of hand-off training for clinical practice. The post survey mirrored the pre-workshop survey with the addition of an overall rating of the virtual hand-off session and level of agreement to recommend the I-PASS session for incoming interns. All survey responses were anonymous.

Faculty Survey. After the session, faculty completed a 10-item survey, which included location of residency completion, familiarity with I-PASS hand-offs, hand-off experience, Likert-scale ratings of the session, Zoom platform use and its comparison to in-person sessions, helpfulness of hand-off training in clinical practice, likelihood of recommending the virtual format for interns and preference for format type for future trainings. Respondent names or other unique identifiers were not required for survey completion.

Analysis of Outcomes. Descriptive statistics were calculated for resident characteristics and responses to survey questions (i.e., frequencies and percentages for categorical variables and means and standard deviations for continuous variables). Paired-samples t-test was performed to examine the pre-post changes in (a) helpfulness of hand-off training for clinical practice and patient care, (b) familiarity with the hand-off tool, and (c) confidence in providing a hand-off. Statistical significance was determined at the 0.05 alpha level and effect size (e.g., Cohen's d) was calculated for each comparison. REDCap®,[11] a secure, web-based application designed to support data capture for research, was used to collect and manage study data. All analyses were conducted using IBM SPSS statistical software version 24 (IBM SPSS Statistics, Armonk, NY).

RESULTS

Forty-four residents (88%) completed both pre- and post-workshop surveys. Six residents did not complete post-workshop surveys and their data were excluded from analyses. Prior to the workshop, almost two-thirds of residents (65%) indicated not receiving hand-off training for patient care during medical school. Further, most residents (59%) reported not having provided a verbal patient hand-off, although most had experience with providing a written hand-off as medical students.

To understand the level of experience with a standardized system of verbal hand-offs and written sign-outs, residents were asked to indicate how often they have used the I-PASS hand-off method. Although 98% of residents indicated hand-offs for patient care are extremely or very important and all residents strongly or somewhat agreed that hand-off training is helpful to clinical practice, most residents (82%) indicated they had never or rarely used a hand-off practice to standardize inpatient transitions in care.

After training, self-perceived confidence for providing a hand-off significantly increased ($p < 0.001$, $d = 1.10$ [large]), with 70% of residents indicating their confidence level was good to excellent. Additionally, residents' familiarity with the I-PASS hand-off tool significantly increased ($p < 0.0001$, $d = 1.15$ [large]). When asked if they would recommend the virtual workshop for incoming interns, most residents (95%) indicated they would do so. All residents completed the training activity without need for remediation.

Eleven of 13 teaching faculty completed a post-workshop survey. Of those, 8 (73%) completed their residency at the academic medical center where this study took place. Faculty were asked to indicate their familiarity with I-PASS for hand-offs before the session. All faculty were familiar with I-PASS hand-offs before the workshop took place, with most (82%) indicating they were very to extremely familiar with the process. Ten of 11 faculty indicated they had participated in hand-off training previously. Overall, all faculty rated the virtual training as satisfactory to excellent and believed it would be helpful for residents in clinical practice. Most faculty felt the virtual platform was comparable to in-person sessions with about one-fourth (27%) indicating the Zoom platform was somewhat or significantly better for the conduct of direct observation and feedback. Technical challenges were minimal. All faculty recommended ongoing use of the virtual platform when in-person sessions were not feasible.

DISCUSSION

Patient hand-off training often includes both interactive and observational components that are challenging to perform due to in-person restrictions during COVID-19. Direct observation of hand-off skills is essential to assess trainees and to provide them with supportive feedback.[12] Importantly, the virtual platform used in this study permitted faculty to provide direct observation and feedback for residents using the breakout room feature. Following training, residents were significantly more familiar with the hand-off tool and expressed increased confidence in their abilities to provide a hand-off. Several research studies also have shown that feedback following direct observation leads to improvements in trainee comfort and their ability to perform essential clinical skills.[13-16]

Transitions in patient care and hand-offs between health care providers are a potential source of preventable errors. Providing formal patient hand-off instruction is necessary to help residents develop the necessary communication skills to avoid clinical errors. Researchers have reported that trainees who received instruction and feedback had significantly higher confidence in their hand-off abilities,[17-19] leading to a decrease in medical errors and preventable adverse events.[7,20]

Study limitations include a relatively small sample size representing a single institution that may limit generalizability. Ongoing use of I-PASS was not assessed, which would have enhanced the study by addressing sustainability of hand-off elements learned during the virtual training session and identifying any needs for corrective action. Although interventions to improve communication between healthcare providers have been associated with improved patient safety,[21,22] it was beyond the scope of this study to track change in rate of medical errors.

Virtual hand-off training and its effects on the communication process and patient safety warrants further study.

CONCLUSIONS

Teaching hospitals mandate resident training to include strategies for a uniform hand-off method to avoid communication failures and preventable medical errors.[23] Residents are expected to conduct effective hand-offs, but without feedback and instruction, they do not always possess the necessary hand-off communication skills.[24] To meet this requirement during the COVID-19 pandemic, a virtual format for hand-off training can be used as one successful instructional strategy to standardize patient hand-off methods, allowing for didactic and interactive sessions with direct faculty observation and feedback.

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Keywords: internship and residency, patient hand-off, COVID-19, online education

KANSAS JOURNAL of MEDICINE

An Unusual Presentation of Systemic Lupus Erythematosus

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INTRODUCTION

Systemic lupus erythematosus (SLE) is a connective tissue disorder characterized by the production of autoantibodies that can affect multiple organs in the body.[1] Cardiac involvement is one of the most affected organs in the SLE.[2] It can affect any part of the heart, including the pericardium, myocardium, heart valves, cardiac conduction system, and coronary arteries, leading to significant cardiac morbidity and mortality. Elderly patients are more likely to have cardiac involvement.[3]

Only a few cases of cardiac involvement as the initial manifestation of SLE have been reported in the literature. Pericardial effusion and cardiac tamponade are the rare initial manifestations of the SLE.[4] Complete pericardial drainage by pericardiocentesis along with steroids and anti-inflammatory drug treatment is the mainstay of therapy in lupus-induced pericardial effusions.[5] Refractory cases also may need surgery.

In this case report, a young female was described who presented to the hospital with non-specific symptoms, found to have pericardial effusion, and diagnosed with SLE.

CASE REPORT

A 23-year-old patient with no significant past medical history came in for generalized malaise, nausea, vomiting, and diarrhea. She started feeling unwell two months prior when she took over-the-counter medications for symptom relief, but they did not help. She went to a local hospital, had a chest x-ray, and was told that it looked normal. She was recommended to continue symptomatic treatment for a possible viral upper respiratory infection. Over the next three weeks, she experienced body aches, decreased appetite, intermittent nausea, and vomiting. She was sent back to the hospital where a chest x-ray showed a left-sided pleural effusion, confirmed on the chest CT scan. She had a thoracentesis with a total of 650 mL fluid removed.

She was diagnosed with an uncomplicated parapneumonic effusion, given empiric antibiotics, and was discharged home to complete her course of antibiotics orally. After two weeks, she was seen by her primary care physician and given a short five-day course of prednisone without much improvement. Her symptoms worsened over the next two weeks, and she was seen in the emergency room. Her symptoms this time included fever, chills, fatigue, malaise, dyspnea on exertion, non-productive cough, nausea, vomiting, and diarrhea.

The physical examination showed an arterial blood pressure of 119/77 mmHg, a respiratory rate of 32/min, a pulse rate of 134, and a body temperature of 101.2°F with distant cardiac sounds and left-sided decreased breath sounds. An electrocardiogram showed sinus tachycardia. Chest x-ray showed cardiomegaly without pulmonary edema and left pleural effusion with basilar airspace opacity. She was diagnosed with sepsis from left lower lobe pneumonia; cultures were taken, intravenous fluids were given, and empiric antibiotics were started.

Over the next two days, the patient made minimal improvement clinically. A repeat chest x-ray showed a moderate left-sided pleural effusion and cardiomegaly (Figure 1). Thoracentesis was ordered, but ultrasound showed there was not enough pleural fluid to be drained. There was a concern for immunodeficiency with repeated infections and pneumonia. Blood and sputum cultures were negative.

Laboratory tests, including troponins, were within the normal range, except for moderate anemia with hemoglobin of 10.6 g/dl. A 2-D transthoracic echocardiogram showed a moderate to large pericardial effusion (Figure 2). The echocardiogram did not show any findings of cardiac tamponade, such as respiratory mitral/tricuspid inflow variation, or right atrial or ventricular diastolic collapse.

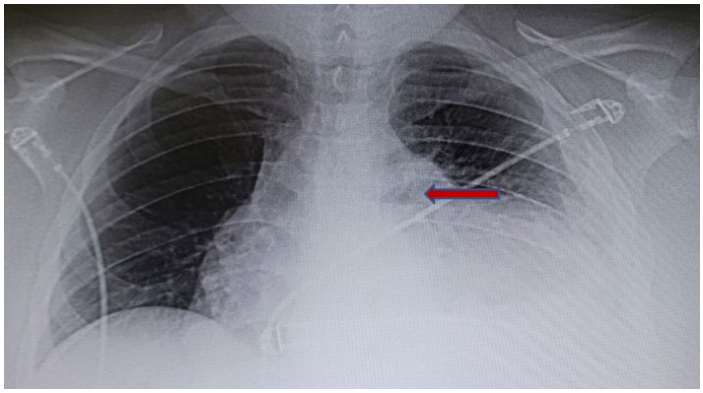

Figure 1. Chest x-ray showed cardiomegaly due to pericardial effusion.

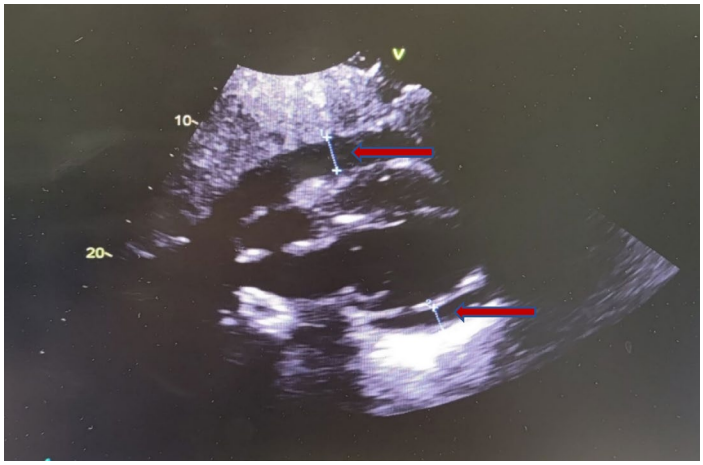

Figure 2. 2-D transthoracic echocardiogram showed pericardial effusion (arrows).

The cardiology service was consulted, and the patient underwent pericardiocentesis. Analysis of fluid revealed a white blood cell count of 314/mm^3 (neutrophils 24%, lymphocytes 19%, monocytes 57%), total protein 4.2 g/dl, albumin of 1.7 g/dl (serum Alb 2.5), glucose of 46 (serum glucose 78). Further questioning revealed that she had pain in her metacarpophalangeal and interphalangeal joints. Blood analysis for the autoimmune panel was positive for anti-dsDNA antibodies (Table 1).

Table 1. Pertinent serum autoimmune panel.

Smith IgG Ab	> 8 U/ml
dsDNA Ab	> 300 IU/ml
Chromatin Ab	> 8 U/ml
Anti U1-RNP Ab	> 8 U/ml
RF	< 1 IU/ml

Abbreviations: Smith IgG Ab = Anti- Smith antibodies, dsDNA Ab = Anti deoxyribonucleic acid antibodies, Chromatin Ab = Anti chromatin antibodies, U1-RNP Ab = Anti ribonucleoprotein antibodies, RF = Rheumatoid factor.

The patient had a pericardial drain placed after pericardiocentesis, which was removed the next day. She met the criteria for SLE and lupus-induced pericardial effusion. She was discharged and referred to a rheumatology clinic, where she was started on immunosuppressive therapy.

DISCUSSION

SLE can cause many cardiac manifestations, such as myocarditis, pericarditis, endocarditis, and cardiac conduction system abnormalities.[6] The acute or chronic inflammatory changes of SLE can involve pericardium causing granular deposition of immunoglobin and c3 immune complexes detected by direct immunofluorescence. The detection of these immune complexes ropes the mechanism of pericardial involvement in SLE, especially in pericarditis. Echo cardiac studies have reported the prevalence of pericardial abnormalities among SLE patients ranging from 10 - 55%. Pericarditis is considered the most common symptomatic clinical manifestation of SLE and is estimated to occur in 25% of cases at some point in the disease course. Pericardial effusions are more common to occur in SLE patients. More than 40% of SLE cases can have asymptomatic pericardial effusion detected by echocardiography during the disease course.[5,6]

When present, pericardial effusions in SLE are usually small and do not cause severe hemodynamic complications.[7] Signs and symptoms of pericardial effusions more likely can be pericardial pain and active lupus symptoms elsewhere in the body. Echocardiography is the standard method to detect small pericardial effusions in SLE patients. SLE-related pericardial effusion differential diagnosis includes viral, bacterial, tuberculosis, post-myocardial infarction, traumatic, uremic, neoplastic, and idiopathic.[7,8]

Cardiac manifestations usually occur in the later stage of the disease course in older patients.[1,8] Pericardial effusion in this young patient as an initial manifestation was another striking finding. Topaloglu et al.[9] reported a case of cardiac tamponade due to large pericardial effusion in a young male patient leading to the surgical treatment. Weich et al.[10] described large pericardial effusions diagnosed by echocardiography in a case series of eight patients, but none of them had pericardial effusions as the presenting manifestation of SLE.

CONCLUSIONS

In essence, this case report highlighted pericardial effusion as an unusual initial manifestation of SLE even in the absence of typical symptoms. It should be part of differential diagnosis, especially in young patients presenting with non-specific repeated infections. Undetected pericardial effusion can lead to the pericardial tamponade, thus increasing significant mortality risk.

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Keywords: systemic lupus erythematosus, heart, pericardial effusion, case report

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Thiazide-Induced Pancreatitis

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INTRODUCTION

Acute pancreatitis (AP) is an acute inflammatory disease of the pancreas and is associated with a wide spectrum of clinical manifestations, ranging from mild disease to more severe forms, even requiring intensive care unit hospitalization.[1] The reported annual incidence of acute pancreatitis in the United States ranges from 4.9 to 35 per 100,000 population.[2] Pancreatitis due to medications is rare (< 5%).[3] Published reports have identified about 50 drugs that definitely or possibly may be held responsible for inducing acute pancreatitis.[4] Also, the global prevalence of hypertension is high, and among nonpregnant adults in the United States, treatment of hypertension is the most common reason for office visits and the use of chronic prescription medications.[5]

Drug-induced pancreatitis remains a challenge for physicians. It needs further consideration when a patient has a clinical presentation suggestive of acute pancreatitis without a significant cause. This report involved a case of hydrochlorothiazide-induced pancreatitis in a patient who recently had started this medication for blood pressure control. We aimed to determine the association of thiazide drugs with the incidence of pancreatitis and add to the literature this rare case.

CASE REPORT

A 48-year-old white man was referred to a cardiology practice for management of uncontrolled hypertension. He reported a history of hypertension for more than 20 years that was never well controlled. In addition, he was mildly obese and was compliant with continuous positive airway pressure ventilation for his obstructive sleep apnea. He was asymptomatic and denied any headache, chest pain, shortness of breath, orthopnea, leg swelling, or paroxysmal nocturnal dyspnea. With regards to family history, his father had early-onset hypertension and died of a massive myocardial infarction at age 47. On initial encounter, blood pressure markedly was elevated at 170/100 mmHg. Physical examination was unremarkable.

The patient reported that he had been on amlodipine, but this was stopped due to a side effect of bilateral leg swelling. He was continued on metoprolol succinate 200 mg day and newly started on losartan-hydrochlorothiazide 100-25 mg tablets once per day.

Secondary hypertension work-up was unremarkable. A 2-D echocardiogram for the evaluation of cardiac function revealed normal left ventricular (LV) systolic function, estimated ejection fraction 55 to 60%, mild concentric LV hypertrophy, and no significant valvular disease. The patient was counseled on weight loss, exercise, and following a "Dietary Approaches to Stop Hypertension (DASH)" diet.

Four weeks later, the patient presented to the emergency department with severe abdominal pain. The pain was in the mid-epigastric abdominal area, qualified as "burning and tearing" in nature, briefly relieved with positional changes, and mildly relieved with pain medications. The patient denied nausea, vomiting, chest pain, or shortness of breath.

The patient was hemodynamically stable and afebrile. Physical examination was remarkable for mild epigastric tenderness. Labs showed leukocytosis of 12,000 cells/mm^3, an elevated lipase level of 134 units per liter, and a mild transaminitis (AST was 42 U/L, ALT was 69 U/L). Triglycerides were elevated slightly at 177 mg/dL.

Abdominal computed tomography showed acute interstitial pancreatitis (Figure 1). Gallbladder imaging was unremarkable, and the patient did not have any history of excessive alcohol use. He was admitted, treated with IV fluids and analgesics, and provided supportive care. Thiazide-induced pancreatitis was suspected and thus losartan-hydrochlorothiazide was stopped resulting in improvement of symptoms and no recurrent episodes. Repeat amylase level was normal, as well as liver function enzymes. The patient was started on spironolactone 50 mg and losartan 100 mg once per day with improved blood pressure control.

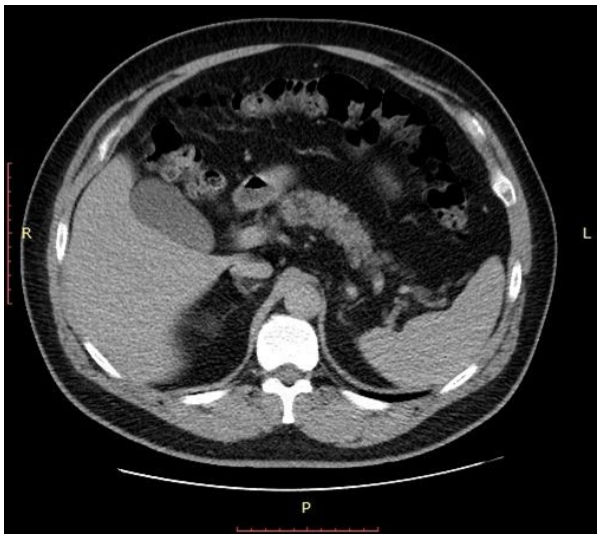

Figure 1. Computed tomography of the abdomen and pelvis with contrast showing acute interstitial pancreatitis involving the uncinate process of the pancreas.

DISCUSSION

Hypertension is a major and modifiable risk factor for cardiovascular disease and stroke.[6] The staging system of hypertension diagnosis is very crucial as it guides the appropriate management. Normal blood pressure is defined as less than 120/80 mmHg; elevated blood pressure 120-129 or less than 80 mmHg; hypertension stage 1 is 130-139 or 80-89 mmHg; and hypertension stage 2 is greater than 140/90 mmHg.[7] However, once an individual with hypertension qualifies for pharmacological treatment, including patients with masked hypertension, prescription of drug therapy is recommended to come from one of four drug classes (usual first-line therapy), thiazide diuretics, calcium antagonists, angiotensin-converting enzyme (ACE) inhibitors, or angiotensin receptor blockers (ARBs), unless there is a comorbidity consideration favoring the use of a different drug class. Our patient was diagnosed with stage 2 hypertension and prescribed a thiazide diuretic.

Pancreatitis is acute inflammation of the pancreas.[8] Its severity

ranges from a benign course to life-threatening with increased mortality, one requiring hospitalization. The major causes of acute pancreatitis are gallstones (30 - 60%) and heavy alcohol use (15 - 30%) in addition to other common causes, such as hypertriglyceridemia, hyperparathyroidism, endoscopic retrograde cholangiopancreatography, trauma, pancreatic tumors, surgery, infections, and medications. Agents reported to have a definite association with pancreatitis are asparaginase, azathioprine, didanosine, estrogens, furosemide, mercaptopurine, pentamidine, sulfonamides, sulindac, tetracyclines, thiazides, and valproic acid.[9] In our case, all other causes of pancreatitis were excluded, and drug-induced pancreatitis was suspected.

Thiazide-induced pancreatitis was first described in 1959 by Johnston et al.[10] in four patients who developed pancreatitis while receiving chlorothiazide. The possible mechanisms for drug-induced pancreatitis include pancreatic duct constriction, cytotoxic and metabolic effects, hypersensitivity reactions, drug-induced hypercalcemia, and drug-induced hypertriglyceridemia.[11]

Accurate diagnosis of acute pancreatitis requires at least two of the following three diagnostic features: abdominal pain consistent with acute pancreatitis, serum lipase or amylase levels that are at least three times the upper limit of the normal range, and findings of acute pancreatitis on cross-sectional imaging (computed tomography or magnetic resonance imaging).[12] Definite proof that a drug causes pancreatitis requires that pancreatitis develops during treatment with the drug, that other likely causes of pancreatitis are not present, that pancreatitis resolves upon discontinuing the drug, and that pancreatitis usually recurs upon re-administration of the drug.[13]

Early aggressive intravenous hydration remains the gold standard of management of acute pancreatitis. Early aggressive intravenous fluid resuscitation provides micro- and macro- circulatory support to prevent serious complications such as pancreatic necrosis.[14] The cause of acute pancreatitis must be assessed and treated. For drug-induced pancreatitis etiology, practitioners should eliminate the suspected drug to prevent future episodes.

CONCLUSIONS

A prompt diagnosis of drug-induced pancreatitis may lead to early withdrawal of the offending drug, thus, improving outcomes and reducing hospital stay. In the end, practitioners need to identify common as well as uncommon potential triggers for pancreatitis, including medications such as thiazide diuretics. Our case was challenging in terms of the suspected thiazide drug, which was the etiology of acute pancreatitis. The fact that most of his clinical symptoms and labs have normalized after stopping this medication has shown evidence that the pancreatitis was related to the drug.

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Kansas Needs Psychiatric Subspecialists

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Shortage of Psychiatrists in Kansas and Efforts to Address Shortage

In the era of physician shortage, it comes as little surprise that the need for psychiatrists is similarly high. The surge in mental health needs in the wake of the COVID-19 pandemic has been described as the "second wave" of the pandemic.[1] The reserve of psychiatrists is low and aging, with six of ten psychiatrists above the age of 55, and there is reasonable concern that retiring psychiatrists may outpace residency graduates.[2] In the state of Kansas, the ratio of psychiatrists to Kansas residents is 17/10,000 compared to the national average of 19.9/10,000.[3]

In 1992, the State of Kansas recognized the impending physician shortage and how it disproportionately impacts rural areas and instituted the Kansas Medical Student Loan (KMSL) program.[4] In 2017, psychiatry was added to the KMSL program and received funding in 2018 for six positions at any given time.[5] Since its inception, ten medical students have signed with the KMSL-Psychiatry program for future psychiatric practice in Kansas.[6] The Kansas Bridging Plan (KBP) is a similar program that was instituted in 1991, though only residents are eligible. Psychiatry was added to KBP in 2018 and eight psychiatry residents have participated in KBP.[7]

There is good news on the horizon for psychiatry, as applications to psychiatry residency programs and competitiveness of applicants have been increasing.[8] However, a similar increase has not carried over to psychiatry fellowship programs, all of which have experienced a decline in fellows.[9] The American Board of Medical Specialties maintains a record of all board-certified physicians in the U.S.; data for psychiatry and psychiatry sub-specialties in Kansas can be seen in Table 1. Though there have been efforts to address the shortage of physicians, including psychiatrists, in Kansas, the supply of subspecialist psychiatrists is also at a dire level and will require similar efforts to address.

Kansas Suffers from a Lack of Subspecialty Psychiatrists and Fellowship Training Programs

Addiction Psychiatry. Over 20 million people in the U.S. met criteria for substance use disorders and were in need of treatment in the past year, with 20% of the population using an illicit drug.[10] Substance use disorders occur more frequently in patients with mental illness, with 9 million and 3 million use disorders in acute and chronic mental illness, respectively. Substance use has increased in the COVID-19 era due to a variety of factors.[11] Not only has substance use been increasing steadily, worsened by the COVID-19 pandemic, but mortality due to substance use also has increased in the past decade.[12] A nationwide shortage of addiction specialty physicians has been identified, with the shortage especially impacting rural counties.[13] Kansas has nine board-certified addiction psychiatrists, which all practice within the Kansas City metropolitan area, and there is an addictions fellowship training program at University of Kansas Medical Center (KUMC) in Kansas City.[14,15]

Table 1. Board-certified general and subspecialty psychiatrists and available training programs in Kansas.

Psychiatrists in Kansas			
Specialty	**# of Psychiatrists**	**Graduating Psychiatrists per Year**	**Training Programs in Kansas**
General Psychiatry	339	12	2: KU* (Kansas City and Wichita)
Addiction Psychiatry	9	2	KU-Kansas City
Child/Adolescent Psychiatry	55	3 - 4	KU-Kansas City (KU-Wichita in planning)
Consult/Liaison Psychiatry	1	0	None
Forensic Psychiatry	4	0	None
Geriatric Psychiatry	13	0	None

*University of Kansas

Geriatric Psychiatry. The U.S. geriatric population will nearly double to 72 million people by 2030, exacerbating a geriatric mental health crisis that affects approximately one-fifth of the geriatric population.[16] The ratio of geriatric psychiatrists to geriatric patients with mental and/or substance use disorders is less than 1/6,000, which has been declared a crisis.[17] The geriatric population (age 65+) represents 15% of the population in Kansas, with growth of this demographic predicted to increase at four times the rate of younger demographics over the next two decades.[18] Existing psychiatric illness, as well as developing mood, substance, and cognitive disorders during later years of life, add to the burden, which contributes to less favorable outcomes and costs.[17] Sixty percent of geriatric psychiatry fellowships are unfilled, which is the lowest of all psychiatric subspecialties.[19] There are 13 board-certified geriatric psychiatrists in Kansas practicing in the Kansas City and Wichita metropolitan areas, Topeka, and Great Bend; there are no fellowship training programs in the state.[14]

Child/Adolescent Psychiatry (CAP). In October 2021, a national state of emergency in children's mental health was declared due to rising rates of mental health concerns and suicide over the past decade, which were exacerbated (increased 25 - 50%) by the many stressors of the COVID-19 pandemic.[20] Nearly 10% of children require psychiatric care and only 45% of those receive necessary treatment.[21] Rising suicide rates, which occur at a higher rate in rural areas, especially are concerning for Kansas.[22] In the 2020 National Residency Match Program, the fill rate for CAP programs was the highest among psychiatric subspecialties at 83%.[23] Current estimates indicated the U.S. has approximately half of necessary child psychiatrists to meet patient needs.[24] The American Academy of Child and Adolescent Psychiatry rated Kansas as having a severe shortage with only 9 CAP/100,000 patients.[25] Fifty-five CAP are board-certified in the state, practicing in the Kansas City and Wichita metropolitan areas, Topeka, Lawrence,

and Manhattan; there is a fellowship training program at KUMC in Kansas City and a program at KUMC in Wichita in the planning stages.[14,15]

Consult/Liaison Psychiatry (CLP). One-quarter to one-third of hospital inpatients have comorbid psychiatric illness, which adds to overall comorbidity and negatively impacts their stay and treatment. This can be improved by involvement of consult-liaison psychiatry (CLP), previously called psychosomatic medicine,[26] to reduce length of stay and cost.[27,28] Though many barriers to CLP involvement have been examined,[27] access in Kansas is likely to be a limiting factor. During the COVID-19 pandemic, CLP has been assisting in treating neuropsychiatric symptoms of COVID as well as an increase of hospital psychiatric symptoms and admissions.[29] Similarly during the pandemic, CLP has served as palliative care team members and directors,[30] which raises the possibility of CLP's continued involvement in oncology and palliative care. Fill rate for CLP programs in 2020 was 68%.[23] There is one board-certified consult/liaison psychiatrist in Kansas, who practices in Wichita, with no local fellowship training programs.[14,15] Though not CLP, dual-boarded Internal Medicine/Psychiatry physicians are well-suited to practice CLP and two complete training at the University of Kansas Medical School yearly.

Forensic Psychiatry. Mental illness affects over 50% of those in jails and prisons.[31] These patients at the intersection of psychiatry and the law are treated and evaluated by forensic psychiatrists. In Kansas, there are two hospitals operated by the state for mental illness, in Osawatomie and Larned. Only Larned has a formal forensic unit, the State Security Program.[32] Fifty-eight percent of forensic psychiatry fellowships are filled, though this process is complicated by an unregulated application system, unlike the match for medical residencies and other psychiatric fellowships aside from geriatrics.[33] There are four forensic psychiatrists boarded in the state practicing in Kansas City and Wichita metropolitan areas and Lawrence, with no local fellowship training programs.[14,15]

The need for psychiatric care has continued to rise over the past decade, with a "second wave" due to the COVID-19 pandemic. This escalation of need is superimposed on an existing shortage of general and subspecialty psychiatrists without a corresponding increase of these physicians to provide that care, cutting off patients in need from physicians with appropriate expertise and training. Kansas experiences a shortage in each of the subspecialties in psychiatry, with local fellowship training programs existing only for CAP and addiction psychiatry. Additional fellowships that would be beneficial to Kansans, but have not been formally approved by the Accreditation Council for Graduate Medical Education (ACGME), are emergency psychiatry and reproductive psychiatry.[34-37]

Emergency Psychiatry. Over 143 million emergency department (ED) visits occurred across the U.S. in 2018 and, in Kansas, roughly 18% (187,000) of ED visits were for mental health and substance use disorders.[38] Emergency department visits for psychiatric reasons (including suicide attempts, overdose, intimate partner violence, child abuse and neglect) increased during the COVID-19 pandemic.[39] Dedicated psychiatric emergency services with emergency psychiatrists (i.e., the Alameda Model) lead to improved outcomes, decreasing psychiatric patient boarding time, admissions, and cost, as well as increasing safety outcomes.[40,41] There are only four emergency psychiatry fellowships in the U.S., none of which are in Kansas.

Reproductive Psychiatry. Women of child-bearing age experience a similar burden of psychiatric illness and have increased risk of psychiatric illness at transitions in the reproductive cycle.[42] Approximately 13% of pregnancies involve exposure to antidepressants, not counting the many other categories of psychotropic medications. The American College of Obstetricians and Gynecologists and the U.S. Preventive Services Task Force recommended specialized screening and treatment during the peripartum period.[37] In light of this, fellowship programs are attempting to address this practice gap, as just over half of psychiatry residencies include reproductive psychiatry topics in their program.[43,44] With over a third of residencies having no reproductive psychiatry training and nearly three quarters of programs devoting less than five hours of instruction on the topic, there appears to be few opportunities to bring this knowledge to the state without a fellowship program.[43] Since 2002, 15 fellowships have been established in the U.S. to address this need, none of which are in Kansas.[45]

What are Subspecialists and How to Address this Shortage to Benefit Kansans

Concentration into specialties and further into subspecialties has been required as depth and extent of medical knowledge increases. There are nearly 12,000 ACGME-approved fellowship positions offered across the nation each year, indicating that nearly one-third of residents pursue further training in a fellowship. As illustrated above, however, the number of psychiatrists pursuing subspecialty training is lower than what is found in many other specialties.[23,46]

Why is it important to have subspecialty psychiatrists in the state? Subspecialists bring the highest standards of care necessary for complex cases and better expertise to treat patients. In addition, the presence of fellowship-trained physicians enriches the educational environment of residents and medical students through didactic or clinical educational efforts. For example, CAP is trained to distinguish developmentally normal fantasy from possible psychosis; geriatric and CLP work effectively with patients who have co-occurring medical conditions. Each one of the psychiatric subspecialties leverages their knowledge of their subject area to deliver the highest-efficacy and evidence-based treatment for the benefit of patients.

The elusive question remains: how to entice more psychiatry residents to pursue subspecialty training after residency? Escalating costs of debt carried through medical school and residency ($207,000 average) create a barrier to extending training, especially when need for psychiatrists is high.[2,47] A survey found residents weighed the following factors from most to least important when considering pursuing a fellowship: lifestyle, finances, academic opportunities, prestige, and research.[48] Child/adolescent psychiatry is the fellowship chosen most frequently, whereas geriatrics is least frequent. A survey of fellowship program directors revealed the burden and cost of relocating for the short period of time for fellowship training, as well as the cumbersome

application process due to programs not universally using the National Residency Match process, are significant barriers.[49]

Review of the literature on this topic showed there are many ideas potentially to increase the number of psychiatry residents that enter into fellowships. Psychiatry residency is a four-year training program. It has been suggested by some that ACGME milestones for general psychiatry can be met by the end of the third year of residency training.[9] Some CAP programs offer "fast track" positions in this model of leaving residency after three years to begin fellowship, which may contribute to CAP's popularity. CAP is the only two-year fellowship in psychiatry, while all other fellowships are one year. Financial incentives (i.e., loan forgiveness) tied to fellowship training may increase the likelihood of entering fellowship training.[50] To increase clinical expertise in subspecialty shortage areas without fellowship training, subspecialty fourth year tracks in general psychiatry residency programs could be created to increase expertise in a chosen subspecialty of interest.[51,52] This might be appealing for those residents who do not want to leave the geographic area they are in to attend a fellowship. Though there are many stakeholders that have interest in addressing the psychiatry subspecialty shortage on a national level, some changes can be made independently on a local level.

The State of Kansas has utilized the KMSL program to address critical shortages for decades and this provides a successful and preexisting model to address the shortage of general and subspecialist psychiatrists through loan repayment.[4] Additionally, the KBP also incentivizes the practice of general and child psychiatry, specifically in rural counties. However, both the KMSL and KBP programs only incentivize general psychiatry and CAP, which may be a barrier to growing subspecialty knowledge across the state. Psychiatry positions for KMSL and KBP are not being filled at similar rates compared to primary care. This raises two questions: 1) would these funds be better suited to increase general psychiatry residency positions in Kansas, and 2) is participation in these programs reduced by the inability to subspecialize? The critical shortage of subspecialty psychiatrists in Kansas should be of similar importance as the original target of these incentive finance programs, which both of these changes would address. Most critically, Kansas has no current way of supplementing these numbers through current incentive programs. To provide Kansas with subspecialty expertise in psychiatry, we must reexamine and address the current incentive programs to include verbiage to recruit and retain psychiatrists who pursue subspecialty training.

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Hypertension and Cardiovascular Diseases among Electronic and Combustible Cigarette Users

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ABSTRACT

Introduction. Combustible cigarette use is associated with an increased risk of several cardiovascular diseases; however, less is known about associations between these cardiovascular conditions and electronic cigarette use.

Methods. This study investigated relationships between electronic and/or combustible cigarette use and diagnoses of cardiovascular diseases using the National Health Interview Survey from 2014, 2016, 2017, and 2018.

Results. Compared to non-users, dual users of electronic and combustible cigarettes had increased likelihood of having prior diagnoses of hypertension (OR 1.660, 95% CI = 1.519-1.814), stroke (OR 2.396, 95% CI = 2.011-2.855), diabetes mellitus (OR 1.219, 95% CI = 1.108-1.341), coronary artery disease (OR 2.211, 95% CI = 1.837-2.660), and myocardial infarction (OR 3.839, 95% CI = 3.232-4.560). Exclusive use of electronic cigarettes was associated with an increased likelihood of having hypertension compared to non-users (OR 1.244, 95% CI = 1.048-1.477).

Conclusions. There were no differences in diagnoses of stroke, diabetes mellitus, coronary artery disease, or myocardial infarction among exclusive electronic cigarette users compared to non-users; however, these associations could change as young electronic cigarette users with hypertension age, indicating the need for continued research.

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INTRODUCTION

Cardiovascular diseases (CVDs), including myocardial infarction (MI) and stroke, accounted for more than 600,000 deaths among U.S. adults in 2017.[1] Many factors contribute to one's risk for developing CVDs, including tobacco use, hypertension, hyperlipidemia, diabetes mellitus (DM), and body mass index (BMI).[2-7] Controlling these modifiable risk factors decreases the development of CVDs and subsequent mortality. Although it has long been established that combustible cigarette use increases the risk of CVDs and some cardiovascular risk factors, such as hypertension,[2-4] the advent of electronic cigarettes (e-cigarettes) has brought new concerns to preventing and managing CVDs.

E-cigarettes, first introduced in 2006,[5] had an estimated 8.1 million U.S. adult users in 2018.[6] E-cigarettes offer an alternative to traditional combustible tobacco for nicotine delivery.[7] However, preliminary data indicated that e-cigarettes increased one's risk for the development of CVDs. For example, when compared to non-users, dual users of combustible and e-cigarettes have been associated with higher odds of MI, stroke, and coronary artery disease (CAD) than combustible cigarette users.[8,9] However, much is still unknown about e-cigarette use and cardiovascular risk, especially as the age of e-cigarette users has changed. Therefore, the purpose of this study was to investigate relationships between e-cigarette use, combustible cigarette use, and dual use of combustible and e-cigarettes and diagnoses of hypertension, stroke, CAD, DM, or MI.

METHODS

Study Population. Participants 18 years or older were included in this study if they completed the National Health Interview Survey (NHIS) tobacco use questionnaire in 2014, 2016, 2017, or 2018. Participants were categorized by their combustible and/or e-cigarette use based on their responses to the NHIS questions. Participants who did not complete all questions in a relevant section of the survey were excluded.

Measures. This study was conducted using the NHIS data from the years 2014, 2016, 2017, and 2018. These years were chosen due to similar coding of the e-cigarette use in the NHIS data. Administered in all 50 states by the U.S. Centers for Disease Control and Prevention as a household interview survey, the goal of the NHIS is to monitor a variety of diseases and health related concerns in the U.S., including tobacco use.[10] Because the NHIS is a de-identified database, IRB approval was not needed.

Participants were stratified into one of six groups based on their self-reported current or former use of combustible and e-cigarettes. The groups included: 1) current e-cigarette users, 2) current combustible cigarette users, 3) former combustible cigarette users currently using e-cigarettes, 4) former combustible cigarette users not currently using e-cigarettes, 5) current users of both combustible and e-cigarettes (referred to as dual users), and 6) never users of combustible or e-cigarettes (referred to as non-users). Those who reported using e-cigarettes every day or some days were identified as current e-cigarette users. Those who reported they had never used an e-cigarette, even one time, were considered non-users of e-cigarettes. Those who reported they had smoked at least 100 cigarettes in their entire lives were identified as combustible cigarette users; those who reported they had not smoked at least 100 cigarettes in their entire lives were considered non-users of combustible cigarettes.

Combustible cigarette users were stratified into current and former users; those who reported using combustible cigarettes every day or some days were considered current users of combustible cigarettes, and those who reported not at all were considered former users of combustible cigarettes. Former combustible cigarette users were stratified further into current and non-e-cigarette users based on their answers to the e-cigarette user questions. Participants who were non-users of combustible and e-cigarettes served as the comparison group for analyses.

Participants were evaluated for the presence or absence of a variety of CVDs based on their survey responses. Participants were considered

to have been diagnosed with hypertension, stroke, DM, CAD, or MI if they reported they had ever been told by a doctor or other health professional that they had hypertension (also called high blood pressure), stroke, diabetes or sugar diabetes (other than during pregnancy), CAD, or MI, respectively. Potential confounding variables included: sex, BMI, and age[11-14] and these were controlled for in each analysis.

Statistical Analysis. Data were analyzed using SAS version 9.4 (SAS Inst. Inc. Cary, NC). Since NHIS data are obtained through a complex, multistage sample design that involves stratification, clustering, and oversampling of specific population subgroups, survey procedures in SAS were used to handle problems such as oversampling, weighting, stratification, or clustering for the data from population-based representative surveys. Rao-Scott chi-square goodness-of-fit tests with Taylor series method to calculate the variance was used for the design-adjusted tests of independence, or no association, between the nominal and/or categorical variables. Generalized multiple linear logistic models applied to test the association between the outcome variables and smoking status (e-cigarette use and combustible cigarette use) after adjusting for confounding variables such as sex, BMI, and age. The maximum likelihood parameter estimates implemented for the multiple logistic regression with SURVEYLOGISTIC in SAS to incorporate complex survey sample designs, including designs with stratification, clustering, and unequal weighting. This procedure utilizes Taylor series linearization methods for NHIS variance estimation to avoid increasing the Type I error. Data were reported as frequencies, means, standard deviations, and other summary statistics. All statistical tests at $p \leq 0.05$ were considered significant.

RESULTS

A total of 121,884 people completed the NHIS survey in 2014, 2016, 2017, and 2018. Of the 84,553 respondents meeting the inclusion and exclusion criteria for this study, 3.1% (n = 2,619) were current e-cigarette users, 7.6% (n = 6,459) were current combustible cigarette users, 3.7% (n = 3,169) were former combustible cigarette users currently using e-cigarettes, 21.0% (n = 17,788) were former combustible cigarette users not currently using e-cigarettes, 7.8% (n = 6,581) were dual users, and 56.7% (n = 47,937) were non-users.

Dual users were 1.660 times more likely (95% CI = 1.519-1.814) than non-users to have been diagnosed with hypertension. Compared to non-users, combustible cigarette users were 1.384 (95% CI = 1.277-1.499) times more likely, and e-cigarette users were 1.244 (95% CI = 1.048-1.477) times more likely to have been diagnosed with hypertension. Former combustible cigarette users currently using e-cigarettes were 1.308 (95% CI = 1.162-1.472) times more likely, and former combustible cigarette users not using e-cigarettes were 1.139 (95% CI = 1.082-1.198) times more likely to have been diagnosed with hypertension compared to non-users. Males were 1.252 (95% CI = 1.196-1.309) times more likely to have been diagnosed with hypertension than females. Increasing BMI by one kilogram/meter squared (kg/m^2) was associated with 1.103 (95% CI = 1.098-1.107) times the odds and increasing age by one year was associated with 1.070 (95% CI = 1.068-1.072) times increased odds of hypertension diagnosis (Table 1).

Dual users were 2.396 (95% CI = 2.011-2.855) times more likely to have had a stroke compared to non-users. Current combustible cigarette users were 2.114 (95% CI = 1.815-2.463) times more likely to have had a stroke than non-users. There was no difference in stroke occurrence among e-cigarette users compared to non-users; however, former combustible cigarette users currently using e-cigarettes were 1.652 (95% CI = 1.245-2.191) times more likely to have had a stroke compared to non-users. Males were 1.114 (95% CI = 1.014-1.224) times more likely to have had a stroke than females. Increasing BMI by one kg/m^2 was associated with 1.032 (95% CI = 1.024-1.040) times increased likelihood, and increased age by one year was associated with 1.067 (95%; CI = 1.063-1.070) times increased likelihood of a prior stroke (Table 1).

Compared to non-users, dual users were 1.219 (95% CI = 1.108-1.341) times more likely, and combustible tobacco users were 1.141 (95% CI = 1.023-1.274) times more likely to have been diagnosed with DM. There was no difference between non-users and e-cigarette users or former combustible cigarette users using e-cigarettes regarding likelihood of having been diagnosed with DM. Former combustible cigarette users not using e-cigarettes were 1.083 (95% CI = 1.010-1.162) times more likely to have been diagnosed with DM compared to non-users. Males were 1.124 times more likely to have been diagnosed with DM than females (95% CI = 1.067-1.183). Increased BMI and increased age also increased the likelihood of DM diagnosis (Table 1).

Compared to non-users, dual users were 2.211 (95% CI = 1.837-2.660) times more likely, and combustible cigarette users were 1.962 (95% CI = 1.611-2.151) times more likely to have been diagnosed with CAD. There was no difference in CAD occurrence between e-cigarette users and non-users. Compared to non-users, former combustible cigarette users currently using e-cigarettes were 2.278 (95% CI = 1.791-2.898) times more likely, and former combustible cigarette users not using e-cigarettes were 1.531 (95% CI = 1.402-1.672) times more likely to have been diagnosed with CAD. Males were 1.973 (95% CI = 1.817-2.143) times more likely to have been diagnosed with CAD than females. Increasing BMI by one kg/m2 was associated with 1.047 (95% CI = 1.040-1.054) times increased likelihood and increasing age by one year was associated with 1.086 (95% CI = 1.082-1.090) times increased likelihood of CAD diagnosis (Table 1).

Dual users were 3.839 (95% CI = 3.232-4.560) times more likely to have had a MI compared to non-users. Combustible cigarette users were 2.836 (95% CI = 2.442-3.294) times more likely to have had a MI compared to non-users. There was no difference in likelihood of MI occurrence between non-users and e-cigarette users. Compared to non-users, former combustible cigarette users currently using e-cigarettes were 2.448 (95% CI = 1.880-3.189) times more likely, and former combustible cigarette users not currently using e-cigarettes were 1.752 (95% CI = 1.576-1.947) times more likely to have had a MI. Males were 2.142 (95% CI = 1.946-2.359) times more likely to have had a MI compared to females. Increasing BMI by one kg/m^2 was associated with 1.041 (95% CI = 1.034-1.048) times increased likelihood and increasing age by one year was associated with 1.077 (95% CI = 1.073-1.081) times increased likelihood of a prior MI (Table 1).

Table 1. Condition among e-cigarette and/or combustible cigarette users compared to non-users.

Group	Hypertension Odds Ratio (95% CI)	Stroke Odds Ratio (95% CI)	Diabetes Mellitus Odds Ratio (95% CI)	Coronary Artery Disease Odds Ratio (95% CI)	Myocardial Infarction Odds Ratio (95% CI)
E-Cigarette Only Users	1.244 (1.048-1.477)*	1.058 (0.586-1.911)	1.108 (0.972-1.263)	0.856 (0.519-1.412)	0.984 (0.555-1.747)
Combustible Cigarette Only Users	1.384 (1.277-1.499)*	2.114 (1.815-2.463)*	1.141 (1.023-1.274)*	1.862 (1.611-2.151)*	2.836 (2.442-3.294)*
Former Combustible Cigarette Users Currently Using E-Cigarettes	1.308 (1.162-1.472)*	1.652 (1.245-2.191)*	0.952 (0.831-1.091)	2.278 (1.791-2.898)*	2.448 (1.880-3.189)*
Former Combustible Cigarette Users Not Currently Using E-Cigarettes	1.139 (1.082-1.198)*	1.287 (1.151-1.436)*	1.083 (1.010-1.162)*	1.531 (1.402-1.672)*	1.752 (1.576-1.947)*
Dual Users of E-Cigarettes and Combustible Cigarettes	1.660 (1.519-1.814)*	2.396 (2.011-2.855)*	1.219 (1.108-1.341)*	2.211 (1.837-2.660)*	3.839 (3.232-4.560)*
Sex (males compared to females)	1.252 (1.196-1.309)*	1.114 (1.014-1.224)*	1.124 (1.067-1.183)*	1.973 (1.817-2.143)*	2.142 (1.946-2.359)*
Body Mass Index	1.103 (1.098-1.107)*	1.032 (1.024-1.040)*	1.056 (1.055-1.183)*	1.047 (1.040-1.054)*	1.041 (1.034-1.048)*
Age	1.070 (1.068-1.072)*	1.067 (1.063-1.070)*	1.030 (1.029-1.032)*	1.086 (1.082-1.090)*	1.077 (1.073-1.081)*

*Indicates significant difference.

DISCUSSION

The current study suggested that e-cigarette use, whether alone or combined with concurrent combustible cigarette use, increased the likelihood of a person being diagnosed with hypertension. Several small studies have evaluated the short-term effects of e-cigarette use on blood pressure with mixed findings;[15] however, this was the first large-scale study to analyze the prevalence of hypertension among e-cigarette users compared to non-users, while also analyzing hypertension among current and former combustible cigarette users. Due to the variability of ingredients in e-cigarettes,[16,17] it is difficult to pinpoint a common underlying component in both combustible and e-cigarettes that could be contributing to the increased occurrence of hypertension among combustible and e-cigarette users in the current study. However, because most e-cigarettes contain nicotine,[17] a sympathetic nervous system stimulant[7] and a component of combustible cigarettes,[18] the results of the current study could suggest that the consumption of nicotine in any form, including e-cigarettes, increases the chance of a person developing hypertension. Regardless of exactly which ingredient(s) of combustible and e-cigarettes contribute to the increased occurrence of hypertension observed among users in the current analysis, these results indicated a need for public health action, as hypertension is a major risk factor for stroke,[19] CAD,[19] and MI.[20,21]

Compared to non-users, dual users had more than twice the likelihood of previously having a stroke. Combustible cigarette users, both current and former, also had increased likelihood of having a stroke compared to non-users. However, e-cigarette users did not demonstrate an increased likelihood of stroke compared to non-users, which supported previous findings.[9,22] Prior research identified an increased likelihood of CVDs (stroke, CAD, and MI) among dual users compared to non-users, but no difference between e-cigarette users and non-users.[9,22] However, one previous study did not evaluate each CVD individually,[9] as did the current analysis. Another previous study identified the control group as individuals who previously had tried e-cigarettes but were not current e-cigarette users,[22] rather than the current study's control group who had never used combustible or e-cigarettes. The lack of an association between e-cigarette use and stroke occurrence in the current analysis could be due to differences in age between combustible and e-cigarette users. E-cigarette users tended to be younger; more than 85% of e-cigarette users who have never smoked combustible cigarettes were younger than 35 years.[23] Most combustible cigarette users, on the other hand, were 45 to 64 years.[24] Because stroke risk was greater among older individuals,[25] it was possible that the younger age of e-cigarette users in the current analysis was protective against stroke. Additionally, older individuals were more likely to have been diagnosed with conditions that are predisposed to stroke, like hypertension,[26] and an increased duration of uncontrolled hypertension increases one's risk for having a stroke.[27] Therefore, the currently young population of e-cigarette users, who were more likely to have hypertension than non-users based on the current analysis, could go on to experience a greater frequency of strokes than non-users. Continued monitoring of stroke occurrence among e-cigarette users is needed to observe if the findings of the current study change as e-cigarette users age.

In addition to hypertension, DM was another stroke risk factor.[28,29] The current analysis was the first large study to analyze associations between e-cigarette use and diagnoses of DM while adding analyses of DM among current and former combustible cigarette users. Compared to non-users in the current analysis, dual users, combustible cigarette users, and former combustible cigarette users not currently using

e-cigarettes were more likely to have been diagnosed with DM. However, when compared to non-users, there was no difference in association between having a prior diagnosis of DM and e-cigarette use, nor former combustible cigarette use with current e-cigarette use. The lack of association between former combustible cigarette users currently using e-cigarettes and DM diagnosis was unique from the trends observed for the other CVDs analyzed in the current study, where a lack of association generally occurred among e-cigarette users when compared to non-users. This could be due to potential differences in weight gain after cessation of combustible cigarettes, as individuals who stop using combustible cigarettes were most likely to experience weight gain and be diagnosed with DM within seven years of cessation.[30] If, in fact, the cessation of nicotine, generally present in both combustible and e-cigarettes, was associated with weight gain and increased risk of DM development, then use of e-cigarettes among former combustible cigarette users potentially could explain these study findings. More research is needed to understand the associations between DM occurrence, combustible cigarette cessation, and e-cigarette use.

DM is a risk factor for CAD,[31] and the current analysis investigated associations between diagnoses of CAD and combustible and e-cigarette use. Compared to non-users, dual users and former combustible cigarette users currently using e-cigarettes were twice as likely to have been diagnosed with CAD. Although there were increased odds of CAD among current combustible cigarette users and former combustible cigarette users not using e-cigarettes compared to non-users, there was no difference in the likelihood of CAD among e-cigarette users compared to non-users. These findings supported previous research.[9,22] However, the current study was unique from previous research in its separate evaluation of CAD[9] and its control group that included respondents who never used combustible or e-cigarettes.[22] Similar to stroke, the lack of association between CAD and e-cigarette use in the current analysis could be related to age differences between combustible and e-cigarette users. CAD was most prevalent among older adults, affecting 19.8% of adults older than 65 years compared to 1.2% of adults 18 to 44 years;[32] however, most e-cigarette users were younger than 35 years.[23] Thus, as e-cigarette users age and as hypertension, a risk factor for CAD,[33] progresses in this group, it is possible that the occurrence of CAD among e-cigarette users will change. Because CAD was a risk factor for MI,[19] continued monitoring for the development of CAD among e-cigarette users is warranted.

MI occurrence has been analyzed previously among e-cigarette users,[8,9,22] and the current analysis built upon these findings from 2014 and 2016.[8] In the current analysis, compared to non-users, dual users were 3.839 times more likely to have had a MI, which was slightly lower than the 4.62 times increased odds of MI calculated among dual users in prior research.[8] Additionally, the current analysis suggested that, when compared to non-users, former combustible cigarette users currently using e-cigarettes were 2.448 times more likely to have had a MI, while former combustible cigarette users not currently using e-cigarettes were 1.752 times more likely to have experienced a MI. This was consistent with previous estimates that, when compared to non-users, the odds of MI were greater among former combustible cigarette users currently using e-cigarettes than among former combustible cigarette users not using e-cigarettes.[8] Unlike previous research,[8] the current analysis did not identify an association between exclusive e-cigarette consumption and likelihood of experiencing a MI compared to non-users. This could be due to differences in how analyses were conducted, as the previous study stratified e-cigarette users by daily and non-daily consumption in an adjusted model.[8] Alternatively, these findings could be due to changes in e-cigarette consumption trends in the U.S. in 2017 and 2018. E-cigarette use increased 2.4% among adults 18 to 24 years in the U.S. from 2017 to 2018, while e-cigarette use among adults 45 or older decreased.[34] Thus, because e-cigarette users tend to over-represent younger generations, who are less likely to experience a MI based on age alone, it was possible that the differences observed between the current analysis and the former study[8] could reflect these changing trends in e-cigarette use. More research is needed to understand the effects of exclusive e-cigarette use on cardiovascular health better, including MI.

Limitations. The results of this study relied on survey responses, which were affected by recall and non-response biases.[35] Additionally, e-cigarettes have been available commercially in the U.S. for 15 years,[5] limiting the time for long-term observation on the association of e-cigarette use and chronic health conditions. However, the limited knowledge of the long-term effects of e-cigarettes on CVDs validated the need for the current and future analyses.

CONCLUSIONS

The analyses of each cardiovascular condition in the current study suggested that, compared to non-users, dual users of combustible and e-cigarettes had the greatest likelihood of reporting having been diagnosed with hypertension, stroke, DM, CAD, and MI. The current analysis extended previous research findings regarding associations between e-cigarette use and these CVDs. The increased occurrence of hypertension observed among all forms of e-cigarette use was concerning for future development of CVDs among the generally young population of e-cigarette users. The findings of this study indicated that e-cigarettes were not a cardiovascular risk-free alternative to combustible cigarettes.

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Clinical Outcome of Different Post-operative Prophylactic Strategies on Symptomatic Venous Thromboembolism after Total Knee Arthroplasty

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ABSTRACT

Introduction. The objective of this study was to evaluate the use of different post-operative prophylactic strategies on the rates of symptomatic venous thromboembolic events (VTE) incidence after primary total knee arthroplasty (TKA).

Methods. A retrospective study of patients who underwent primary TKA procedure was performed from January 2015 through July 2020. Outcomes examined prophylaxis medication used during inpatient and outpatient care, amount of medication, length of medication, complications occurring within 90 days post-operatively, including symptomatic VTE (deep venous thrombosis (DVT), and pulmonary embolism (PE)), gastrointestinal (GI) bleeding requiring medical attention, change in management protocols after post-operative complications, and mortality.

Results. In total, 5,663 cases were included (mean age 66 ± 10 years, mean BMI 34.1 ± 7.1kg/m^2). The overall post-operative complication rate was 0.9% (DVT: 0.5%, PE: 0.3%, VTE: 0.04%, and GI bleeding: 0.09%). Enoxaparin use as inpatient anticoagulation medication was reduced significantly (67% vs. 13%, $p < 0.001$), and apixaban was increased significantly (6% vs. 49%, $p < 0.001$). Average hospital stays were reduced significantly among the years (3 ± 2 days vs. 2 ± 1 days, $p < 0.001$), and complication rates were not significantly different between the five years (~1%, $p < 0.001$). Most post-operative complications occurred on either aspirin 325 mg (36%) or apixaban (26%). However, the relative risk ratio results indicating that utilization of warfarin, rivaroxaban, and aspirin 81 mg as outpatient anticoagulation medication were more likely to increase the risk of symptomatic VTE incidence compared to other anticoagulants. The average time of complication detected was 21 ± 21 days (range: 1 - 87 days). More than 54% of complication events occurred after the patient had completed their medication (enoxaparin, rivaroxaban, and apixaban).

Conclusions. The observed incidence of symptomatic VTE in this study was similar to previous studies regardless of the type of post-operative inpatient or outpatient prophylaxis prescribed. The ultimate choice of prophylaxis should remain with the treating physician and their knowledge of a particular patient's medical history.

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INTRODUCTION

Total knee arthroplasty (TKA) is one of the most common orthopedic surgical procedures whereby the diseased knee joint is replaced with artificial material. This procedure accounts for more than one million cases annually in the U.S., and a dramatic increase in the number of TKAs will likely be seen.[1] Patients undergoing this procedure are at high risk of venous thromboembolic events (VTEs), including deep venous thrombosis (DVT) and pulmonary embolism (PE), post-operatively.[2-7] VTE after TKA is of great concern because of the associated increases in morbidity and mortality reported in the literature.[2,3,5,6] To prevent VTE after TKA, administration of prophylaxis is recommended by both the American Academy of Orthopaedic Surgeons and the American College of Chest Physicians.[8-11]

Prophylactic strategies to prevent VTE after primary TKA vary widely and are influenced by surgeon experience, current research, and historical precedent. Aspirin, enoxaparin, apixaban, rivaroxaban, and coumadin are the most common methods of DVT chemoprophylaxis used by orthopedists.[3,5,10,12-16] However, anticoagulation after TKA can pose unique challenges because anticoagulation medications must balance the reduction in blood clot formation, with the risk of post-operative bleeding, hematoma formation, revision surgery, and infection.[17-19] Despite decades of clinical experience, new technology on implant design, better surgical procedure, improved physical therapy protocol, and hundreds of studies, the ideal method of VTE prophylaxis remains controversial. This has resulted in variability and inconsistency of prophylaxis for TKA patients and a concern that many patients may be left at risk with no prophylaxis or suboptimal prophylaxis. The specific aim of this study was to evaluate the use of different post-operative prophylactic strategies on the rates of symptomatic VTE incidence after primary TKA.

METHODS

Subjects. Institutional Review Board approval was obtained for this study. This retrospective study reviewed the clinical charts of patients (greater than 18 years of age) who had undergone primary TKA procedures from January 2015 through July 2020 from hospitals within a single institution in the Midwest region. Patients who underwent unicompartmental knee arthroplasty, revision knee arthroplasty, same day bilateral TKAs, or had less than 90 days follow-up without any complication were excluded from this study.

Variables. The retrospective chart review gathered patient demographic data including age, gender, body mass index (BMI), surgical date, site of procedure, prophylaxis medication used during inpatient care and outpatient care, amount of medication, length of medication, and length of hospital stay. Post-operative complications included those occurring within 90 days post-operatively including symptomatic VTEs and upper and lower gastrointestinal (GI) bleeding requiring medical attention. Change in management protocols after post-operative complications and mortality also were recorded.

Statistical Analysis. Descriptive statistics of the mean, standard

deviation, range, and percentages were determined for subject demographics, prophylaxis medication used during inpatient care and outpatient care, length of medication, and complications. One-way analysis of variance (ANOVA) with the Least Significant Difference (LSD) multiple comparisons post hoc test method was utilized to determine significant observed differences among different parameters (e.g., age, BMI, length of hospital stay, prophylaxis medication used during inpatient care, and post-operative complications) between the five years. All statistical testing methods were performed using IBM® SPSS Statistics software (version 24.0.0.0; IBM® Corporation, Armonk, NY), and the statistically significant relationships were defined as those with $p < 0.05$. Relative risk ratio with 95% confidence interval was utilized to compare complication rates among therapies. A risk ratio greater than 1.0 indicated an increased risk of complication compared among the other therapies.

RESULTS

There were 6,440 primary TKA cases identified, with only 5,663 of those cases (2,254 males and 3,409 females) included in this study due to exclusion criteria or incomplete inpatient medication. The mean age was 66 ± 10 years (range: 23 - 96 years) and the mean BMI was 34.1 ± 7.1 kg/m^2 (range: 17.7 - 79.1 kg/m^2). The mean hospital stay was 2.1 ± 1.3 days (range: 0 - 34; Table 1). There were 155 patient deaths recorded in this study, and 10% (n = 15) were within 90 days post-operatively due to natural causes or other medical conditions.

There were 0.9% (n = 50) post-operative complications including symptomatic DVT (0.5%), PE (0.3%), unspecified VTE (0.04%), and upper and lower GI bleeding (0.09%). The mean age for these complication groups was 65 ± 11 years (range: 41 - 83 years) and the mean BMI was 33.6 ± 6.0 kg/m^2 (range: 22.4 - 50.0 kg/m^2). The mean hospital stay for all complication groups was 3.1 ± 2.6 days (range: 1 - 12; Table 1).

There were seven different anticoagulants prescribed as inpatient medication in this study: enoxaparin, rivaroxaban, warfarin, apixaban, aspirin 325 mg, aspirin 81 mg, and heparin (Table 2). Enoxaparin (34% of the patients) was the most frequently used medication for inpatient anticoagulation for DVT chemoprophylaxis. Utilization of rivaroxaban, aspirin 325 mg, aspirin 81 mg, and heparin as inpatient anticoagulation medication were more likely to increase the risk of symptomatic VTE incidence compared to other anticoagulants.

When comparing the yearly breakdown, utilization of enoxaparin as inpatient anticoagulation medication was reduced significantly over the five years (67% vs. 13%, $p < 0.001$), except the years 2018 and 2019 ($p = 0.61$). The other inpatient anticoagulation medications were increased significantly over the years, especially apixaban (6% vs. 49%, $p < 0.001$; Figure 1). Average hospital stays were reduced significantly among the years (2.8 ± 1.7 days vs. 1.5 ± 1.0 days, $p < 0.001$), except the years 2018 and 2019 ($p = 0.61$). The complication rates were not significantly different across the five years (~1%), except the years 2016 and 2019 (0.4% vs 1.2%, $p = 0.04$; Table 3).

The three most common outpatient anticoagulation medications prescribed were apixaban (31%), aspirin 325 mg (38%), and enoxaparin (14%). Of the post-op complications, the most common outpatient medications used were apixaban (26%) and aspirin 325 mg (36%). However, the relative risk ratio results indicating that utilization of warfarin, rivaroxaban, and aspirin 81 mg as outpatient anticoagulation medication were more likely to increase the risk of symptomatic VTE incidence compared to other anticoagulants. The average time of complication detection was 20.8 ± 21.1 days (range: 1 - 87 days), and 40% of the complications found occurred after the patient had completed their anticoagulation medication (Table 4).

When comparing the time of complication and length of time on outpatient anticoagulation medication, the results of this study demonstrated that when enoxaparin, rivaroxaban, and apixaban were used as outpatient anticoagulation medications, more than 54% of complication events occurred after the patient had completed their medication (Table 5).

Table 1. Patient demographics.

Variable	Overall (N = 5,663)	Complication (N = 50)	DVT (N = 28)	PE (N = 15)	VTE (N = 2)	GI Bleed (N = 5)
Gender, n (%)						
Female	3,409 (60%)	30 (60%)	14 (50%)	12 (80%)	2 (100%)	2 (40%)
Male	2,254 (40%)	20 (40%)	14 (50%)	3 (20%)	-	3 (60%)
Age, mean years ± SD (range)	66 ± 10 (23 - 96)	65 ± 11 (41 - 83)	65 ± 12 (41 - 82)	63 ± 10 (47 - 77)	70 ± 4 (67 - 72)	73 ± 11 (56 - 83)
BMI, mean kg/m^2 ± SD (range)	34.1 ± 7.1 (17.7 - 79.1)	33.6 ± 6.0 (22.4 - 50.0)	32.2 ± 5.1 (22.4 - 49.0)	35.5 ± 6.1 (23.8 - 43.9)	41.0 ± 12.6 (32.1 - 50.0)	32.9 ± 5.7 (26.8 - 40.3)
Site of Procedure, n (%)						
Left	2,743 (48%)	25 (50%)	15 (54%)	8 (53%)	-	2 (40%)
Right	2,920 (52%)	25 (50%)	13 (46%)	7 (47%)	2 (100%)	3 (60%)
Hospital stay, mean days ± SD (range)	2.1 ± 1.3 (0 - 34)	3.1 ± 2.6 (1 - 12)	2.3 ± 1.7 (1 - 9)	4.7 ± 3.7 (1 - 12)	2.5 ± 0.7 (2 - 3)	2.8 ± 1.1 (1 - 4)

Table 2. Inpatient medication effects on complications.

Inpatient Medication	Overall (N = 5,663)	Complication (n = 50)	Relative Risk Ratio (RR)	95% RR Confidence Interval	DVT (n = 28)	PE (n = 15)	VTE (n = 2)	GI Bleed (n = 5)
Enoxaparin	1,941 (34%)	16 (32%)	0.9	(0.6 - 1.6)	9 (32%)	4 (27%)	1 (50%)	2 (40%)
Rivaroxaban	484 (9%)	6 (12%)	1.5	(0.4 - 3.4)	6 (21%)	-	-	-
Warfarin	182 (3%)	1 (2%)	0.6	(0.1 - 4.4)	-	1 (7%)	-	-
Apixaban	1,785 (32%)	10 (20%)	0.5	(0.5 - 1.1)	2 (7%)	4 (27%)	1 (50%)	3 (60%)
Aspirin (325 mg)	1,140 (20%)	13 (26%)	1.4	(0.5 - 2.6)	9 (32%)	4 (27%)	-	-
Aspirin (81 mg)	122 (2%)	2 (4%)	1.9	(0.3 - 7.7)	1 (4%)	1 (7%)	-	-
Heparin	9 (0.2%)	2 (4%)	26.2	(0.3 - 91.8)	1 (4%)	1 (7%)	-	-

Table 3. Yearly comparison of complication to hospital stay time and complication rate.

	Year 2015 (n = 1,020)	Year 2016 (n = 1,089)	Year 2017 (n = 1,094)	Year 2018 (n = 1,203)	Year 2019 (n = 1,032)
Hospital stay (days)	2.8 ± 1.7 (1 - 34)	2.6 ± 1.2 (1 - 20)	2.2 ± 1.0 (0 - 10)	1.5 ± 1.1 (0 - 14)	1.5 ± 1.0 (0 - 9)
Complication	10 (1.0%)	4 (0.4%)	8 (0.7%)	11 (0.9%)	12 (1.2%)

Note: Year 2020 was excluded due to only have four months of data.

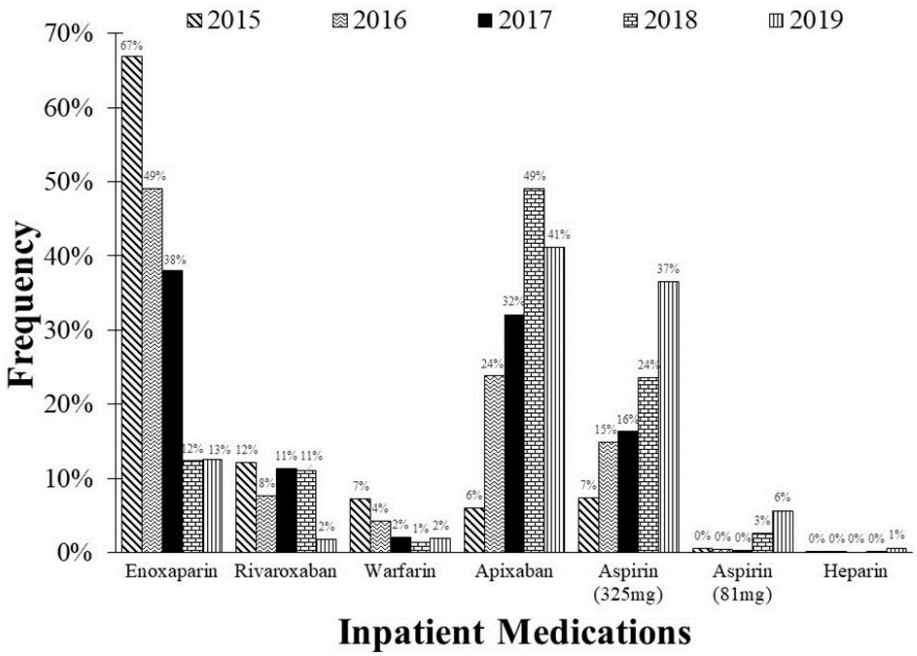

Figure 1. Yearly comparison of inpatient medications.

Table 4. Outpatient medication effects on complications.

	Overall (N = 5,663)	Complication (n = 50)	Relative Risk Ratio	95% RR Confidence Interval	DVT (n = 28)	PE (n = 14)	VTE (n = 2)	GI Bleed (n = 5)
Outpatient Medication								
Enoxaparin	800 (14%)	7 (14%)	1.0	(0.5 - 2.2)	3 (11%)	1 (7%)	1 (50%)	2 (40%)
Rivaroxaban	266 (5%)	3 (6%)	1.3	(0.3 - 4.1)	3 (11%)	-	-	-
Warfarin	284 (5%)	5 (10%)	2.1	(0.4 - 5.3)	1 (4%)	4 (27%)	-	-
Apixaban	1,766 (31%)	13 (26%)	0.8	(0.5 - 1.5)	5 (18%)	5 (33%)	1 (50%)	2 (40%)
Aspirin (325 mg)	2,167 (38%)	18 (36%)	0.9	(0.6 - 1.6)	14 (50%)	3 (20%)	-	1 (20%)
Aspirin (81 mg)	295 (5%)	4 (8%)	1.6	(0.4 - 4.4)	2 (7%)	2 (13%)	-	-
Time to Complication	-	21 ± 21 (1 - 87)	-	-	23 ± 23 (2 - 87)	14 ± 14 (2 - 54)	51 ± 16 (40 - 62)	19 ± 19 (1 - 50)
Complication vs. on/off regimen								
On	-	30 (60%)	-	-	17 (61%)	11 (73%)	-	2 (40%)
Off	-	20 (40%)	-	-	11 (39%)	4 (27%)	2 (100%)	3 (60%)

Table 5. Outpatient medication regimen on complications.

	Time on Outpatient Medication (Days)	Time of Complication (Days)	On Regimen	Off Regimen
Overall complication (N = 50)	22.2 ± 18.0 (0 - 90)	20.8 ± 21.1 (1 - 87)	30 (60%)	20 (40%)
Outpatient Medication				
Enoxaparin (n = 7)	8.4 ± 1.7 (7 - 12)	16.0 ± 15.8 (1 - 40)	3 (43%)	4 (57%)
Rivaroxaban (n = 3)	11.0 ± 2.7 (9 - 14)	39.3 ± 19.7 (26 - 62)	-	3 (100%)
Warfarin (n = 5)	50.0 ± 45.8 (0 - 90)	8.6 ± 7.8 (2 - 22)	4 (80%)	1 (20%)
Apixaban (n = 13)	19.1 ± 17.7 (9 - 60)	25.9 ± 23.2 (2 - 75)	6 (46%)	7 (54%)
Aspirin (325 mg) (n = 18)	26.2 ± 7.8 (6 - 32)	22.1 ± 24.2 (2 - 87)	13 (72%)	5 (28%)
Aspirin (81 mg) (n = 4)	30.0 ± 0.0 (30 - 30)	8.3 ± 4.2 (4 - 14)	4 (100%)	-

DISCUSSION

The specific aim of this study was to evaluate the use of different post-operative prophylactic strategies on the rates of symptomatic VTE incidence after primary TKA. Complication rates were not significantly different across the five years despite which inpatient or outpatient anticoagulation prophylaxis was used. Forty percent of the complications took place after patient had completed their anticoagulation medication, and when looking specifically at enoxaparin, rivaroxaban, and apixaban as outpatient prophylaxis, more than 54% of complications occurred after the patient had completed their medication.

Patients undergoing TKA are at high risk of VTE if they do not receive anticoagulation as it is considered as the third most frequent cause for hospital readmission after TKA.[20] There is considerable debate regarding the appropriate post-operative prophylactic agent for patients undergoing primary TKA,[21-23] with many surgeons making decisions based on anecdotal evidence and historical precedent. As VTE is an uncommon event with reported rates of symptomatic VTEs within 90 days of TKA at less than 2%,[24,25] and the mortality rates from VTE following lower limb arthroplasty low (less than 1%),[25-28] it is difficult to acquire sufficient statistical power to discern differences between agents.

Over the five-year study period, there was a transition from using enoxaparin to oral anticoagulation therapy such as apixaban, rivaroxaban, and aspirin. At the end of the study period, some surgeons' preference was to prescribe all their patients one of the direct oral inhibiters (e.g., apixaban, rivaroxaban), whereas others were risk stratifying based on patients' history. Due to this study being a retrospective review, there was no standardization of medication or length of time. Patients that were on anticoagulation before the procedure also were restarted on their previous regimen after surgery.

Two previous meta-analyses found that low-dose aspirin has a similar efficacy in the prevention of VTE when compared to enoxaparin.[29-31] Recently, there has been more literature comparing low dose aspirin to high-dose aspirin. In a study by Faour et al.[32], low-dose aspirin was found to be as efficacious to high-dose aspirin in the prevention of VTE following TKA. In another study by Parvizi et al.[33], the efficacy and adverse event profiles of low-dose (81 mg twice daily) versus high-dose aspirin (325 mg twice daily) regimens were examined

high-dose aspirin (325 mg twice daily) regimens were examined for patients undergoing total hip and knee arthroplasty and they also found that low dose aspirin was as efficacious to high-dose aspirin in the prevention of VTE. A meta-analysis of randomized controlled trials comparing dabigatran, rivaroxaban, apixaban, and enoxaparin reported incidence of symptomatic VTE as 0.7%, 0.5%, 0.5%, and 0.8%, respectively.[34] None of these studies mentioned compared prophylaxis regimens in patients with known hypercoagulable risk factors such as those with inherited blood clotting disorders, history of previous VTE, obesity, malignancy, estrogen therapy, and varicose veins and increased age.[35]

One result of this study captured VTEs occurred at an average of 20 days after discharge, and 40% of those patients had completed their anticoagulation medication at the time of VTE complication. Specifically, the average length of apixaban, rivaroxaban, and enoxaparin dosing were 17, 10, and 8 days, respectively, while 54% of the apixaban, 100% of the rivaroxaban, and 57% of the enoxaparin post-op symptomatic VTEs occurred after medication completion. These findings were similar to a study by Warwick et al.[36] in 2007, where they found that mean times to VTE after TKA was 9.7 days (SD 14.1 days), but 27% of patients who received the recommended forms of prophylaxis were no longer receiving it after 7 days. Current treatment guidelines for patients following TKA recommended the routine administration of a prophylactic anticoagulant for at least 10 days after the operation.[37] The American Academy of Orthopaedic Surgeons (AAOS) and the American College of Clinical Pharmacy (ACCP) guidelines for VTE prophylaxis for patients undergoing elective TKA also stated the duration must be at least 10 to 14 days, and up to 35 days regardless of the medication being used.[19] This indicated it was likely some complications could have been avoided by extending the duration of the medications.

One possibility for the average time to VTE to occur after average medication completion could be due to a rebound hypercoagulable effect. In 2018, Li et al.[38] reported that although a rebound effect is controversial, physicians should be aware of the possibility. The mechanism behind this rebound hypercoagulable phenomenon after discontinuation is uncertain. It has been suggested for rivaroxaban that decreased plasma concentration after its discontinuation results in loss of prothrombinase/factor Xa inhibition at the thrombotic sites, thus leading to prothrombotic activity.[39] Another possibility is the anticoagulation medications were masking the symptoms of the VTE or preventing it from enlarging. Often DVTs are created intraoperative, confirmed by venographic and leg-scanning studies, but are asymptomatic or silent until they can enlarge due to prolonged impairment of venous function, sustained hypercoagulability, or impairment of the endogenous anticoagulant systems.[40]

Limitations. This study had certain limitations. First, a small sample size of post-operative complications found made applying tests of significance to certain variables difficult. A total of 3,400 patients would afford an adequate trial at 95% power and 5% significance, assuming a baseline symptomatic VTE event rate of 1%. Second, this study was a retrospective chart review study that introduced the possibility of selection and/or observation bias, as it was neither randomized nor blinded. Third, patient compliance (or lack thereof) to the post-operative prophylactic regime was not available. Fourth, the information in this study was limited to the specified time within a single institution and there is a possibility of under-reporting that may have played a role, as many DVTs are diagnosed in the outpatient clinic or in the community. Fifth, minor bleeding complications, such as surgical site hematoma and post-operative transfusions, were not recorded in a consistent manner, therefore not included in this study. Sixth, medications purchased over the counter (e.g., aspirin) or provided as samples by physicians were not available in the recorded data. Lastly, a power analysis was not performed since the data were reviewed retrospectively. Further evaluation in a larger randomized controlled study is required to support the findings of this study. The plan is to use these data and perform a quality improvement project to standardize prophylactic anticoagulation strategies after primary TKA in the future.

CONCLUSIONS

Choice of post-operative prophylaxis agents after primary TKA remains an important issue. The observed incidence of symptomatic VTE events in this study is similar to previous literature, regardless of the type of post-operative prophylaxis regimen prescribed after TKA procedure. A higher rate of VTE incidence was observed after completion of apixaban, rivaroxaban, and enoxaparin therapies, suggesting that a longer treatment course may reduce VTE incidence further. In conclusion, the ultimate choice of prophylaxis remains with the treating physician and his or her unique knowledge of a patient's medical history, especially for patients with known risk factors for VTEs.

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Patient Controlled Analgesia and an Alternative Protocol: A Comparison of Outcomes After Thoracic and Lumbar Surgery

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ABSTRACT

Introduction. Patient controlled analgesia (PCA) is a common form of pain management after spine surgeries, in which patients get custom control of their opioid dose. PCA has been demonstrated as a safe form of analgesia; however, use of PCA comes with risks that can be mitigated by opting for alternative pain management. This study aimed to compare the outcomes of patients using PCA to those with an alternative analgesia protocol that does not involve PCA.

Methods. A retrospective chart review from January 2017 to July 2018 was conducted. Patients included in this study were those 18 or older who were admitted to a large midwestern tertiary medical center in Wichita, Kansas, and underwent thoracic or lumbar spinal surgery from a single spine surgeon. Data from patient demographics, comorbidities, and type of procedure were collected and compared to control for possible confounding variables. Patients were divided into two groups: patients receiving a PCA pain protocol post-operatively and those receiving a non-PCA protocol. Statistical analyses were performed and all tests with $p < 0.05$ were considered significant.

Results. This study found patients in the PCA protocol had similar outcomes to those in the alternative analgesia protocol. This was true for both primary and secondary outcomes. The primary outcome was patient length of stay after the operation. Secondary outcomes included readmission rates, frequency of naloxone rescue, transfers to higher levels of care, and total opioid consumption.

Conclusions. This study supported that a non-PCA protocol for post-operative pain management yields similar outcomes to a PCA protocol in the setting of thoracic and lumbar surgery.

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INTRODUCTION

More than 238 million opioids were prescribed in the U.S. in 2011[1], with opioid abuse costing $78.5 billion in healthcare and criminal justice expenditures.[2] In response to an epidemic of opioid-overdoses, government regulations have been tightened, proposals have been made to reduce opioid manufacturing, and there have been manufacturing problems in several pharmaceutical companies.[3] This has resulted in an abrupt shortage of three of the most commonly used parenteral opioids, including hydromorphone (i.e., Dilaudid®).[4]

The sudden shortage required physicians to adjust their opioid prescribing and find alternative ways to manage patient pain. The Enhanced Recovery After Surgery (ERAS) guideline recommendations urged multimodal analgesia to reduce opioid use post-operatively.[5] The best alternatives, non-steroidal anti-inflammatory drugs (NSAIDs), are a known impedance to bone and ligamentous healing[6] and prevents spinal fusions, which is problematic in the context of spine surgery. A recent study has shown little effect on bone healing in using NSAIDs in the short term.[7] Spine protocols have been slow to add multimodal analgesia, but Cozowicz et al.[7] noted that adding NSAIDS/COX-2 inhibitor to opioids was associated with reduction in opioid prescriptions, cost, and length of hospitalization, and there was an increased use of naloxone by 50% when gabapentinoid was used.

Effective opioid analgesia administration is a difficult balancing act, challenging physicians to ensure proper stewardship of these drugs.[8] On one hand, a large portion of those who become opioid dependent are first exposed in the perioperative period.[7] Conversely, inadequate perioperative analgesia is a risk factor for developing chronic pain, which itself contributes to opioid abuse.[9]

One way to administer opioids in the hospital is by patient-controlled analgesia (PCA). PCA involves patient self-administration (by pushing a button) of small doses of opioids intravenously by means of a programmable pump.[10] Though PCA generally is characterized as being safe,[11,12] potential problems arise, like pump programming errors,[13] activation of the PCA pump by others (i.e., family members),[14,15] and equipment failure, resulting in spontaneous activation of drug delivery.[16]

Although studies have demonstrated the risks and benefits of PCA opioid administration, the literature was lacking information comparing patient outcomes between PCA protocols to non-PCA protocols within spine surgery. Specifically, there was limited information comparing the effectiveness of using different administration modalities of opioids post-operatively.

This was a retrospective study to compare patient outcomes from thoracic and lumbar surgeries between patients using a PCA pain control protocol and patients using a non-PCA pain control protocol. The primary outcome used to assess the differences in analgesia was patient length of stay in the hospital. Secondary outcomes included total opioid consumption and the proportion of patients who were readmitted, required naloxone rescue, and transferred to higher levels of care.

METHODS

Participants. Patients included in this study were those 18 years or older who were admitted to a large midwestern tertiary medical center in Wichita, Kansas that performs more than 500 thoracic and lumbar procedures annually. These patients underwent thoracic or lumbar spinal surgery between September 1, 2016 and July 31, 2018. Patients who underwent a thoracic or lumbar procedure between September 1, 2016 and November 16, 2017 used PCA for pain control post-operatively. Patients who underwent a similar procedure between

November 30, 2017 and July 31, 2018 predominantly were given oral analgesia (non-PCA) to control pain post-operatively. Patients with the non-PCA protocol could receive parenteral morphine for pain that was not controlled sufficiently on oral analgesia, but this morphine was not administered via PCA. Patients with kidney disease (defined as a glomerular filtration rate less than 60 mL/min) required restricted opioid use, so these patients were excluded from the study.

Opioid Protocols. The non-PCA pain management protocol was standardized to the patient taking 1-2 tablets orally every 4-6 hours PRN of hydrocodone 10/325 mg for pain on a scale of 1-5. If the patient still had pain, the hydrocodone 10/325 mg could be switched with 1-2 tablets orally every 4-6 hours PRN of oxycodone (Percocet®) 10/325 mg, for pain on a scale of 1-5. Intravenous (IV) pain medications included 2-4 mg of morphine every hour PRN for pain on a scale of 6-10. However, if pain continued, then the morphine could be switched out with 0.2-0.5 mg every hour PRN of hydromorphone for pain on a scale of 6-10. Lastly, a cyclobenzaprine, or muscle relaxer, was added for the patient to take 10 mg orally every 8 hours to help with muscle spasms.

The PCA pain management protocol was standardized to allow the patient to self-administer IV opioid analgesics via pump and was used as the basis of protocol for this research. There was no loading dose or continuous IV fusion used. The patient was able to self-administer 0.1-0.4 mg of hydromorphone at a range of 5-15 minutes. With PCA, 0.5-2 mg of morphine at a range of 5-15 minutes was a rare substitute for hydromorphone.

Data Collection. The abstracted data included patient characteristics such as age, sex, race, and body mass index (BMI); the type of procedure performed; comorbidities (smoking, diabetes, hypertension); and the method of analgesia used post-operatively. Outcome data included: patient length of stay (from surgery to discharge), unplanned hospital readmission within 30 days after discharge, requirement of pain management from the emergency department of one facility within 30 days of the procedure, transfer to a high level of care (intensive care unit, ICU) post-operatively, post-operative naloxone use, and total opioid consumption.

Six different narcotic drugs were abstracted. Four of the narcotics administered were given orally (hydrocodone/Norco®, oxycodone/Percocet®, tramadol, and oxycodone as single formulation), and two were given intravenously (hydromorphone and morphine).

Procedures. This project was approved by the Wichita Medical Research and Education Foundation's Institutional Review Board and the Human Subjects Committee at the University of Kansas School of Medicine-Wichita. Data were collected through a retrospective chart review of eligible patients' electronic medical records and entered into Research Electronic Data Capture (REDCap®)[17] hosted at University of Kansas School of Medicine-Wichita.

Statistical Analysis. Descriptive statistics were summarized using frequencies (percentages) and means (standard deviations). Differences in study variables were compared according to the method of analgesia used post-operatively and analyzed using Pearson's chi-square, likelihood ratio chi-square, and Fisher`s exact tests, as appropriate. Mean comparisons were conducted using independent t-test, Mann-Whitney U test, and one-way ANOVA was used to compare the means differences as appropriate. 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 $p < 0.05$ were considered to be significant. SAS version 9.4 was used for data analysis (SAS Int. Inc., Cary, NC).

RESULTS

Of the 269 patients who met the inclusion criteria, 18 had kidney disease due to the interference with drug metabolism and were excluded. The remaining 251 patients were included in the study analysis: 48.2% (n = 121) in the PCA protocol group and 51.8% (n = 130) in the non-PCA protocol group.

Most patients were Caucasian (92%, n = 231) and female (62%, n = 155), and the average age was 62 years (SD = 13; Table 1). There were no significant differences between the two groups. Other patient characteristics (type of procedure performed, BMI, smoking, diabetes, and hypertension status) were also similar between groups.

The amount of orally administered drugs was similar between the two groups (Table 2), whereas the amount of intravenously administered drugs differed between groups. Those on the PCA protocol received more hydromorphone and less morphine than those on the non-PCA protocol ($p < 0.0001$).

The average length of stay was 3.66 (95% CI: 3.39-3.93) days for those on the PCA protocol and 3.41 (95% CI: 3.18-3.63) days for those on the non-PCA protocol ($p = 0.15$). The proportion of 30-day emergency department visits for pain, 30-day inpatient readmission, transfers to the ICU, and naloxone use were not significantly different between the two groups (Table 3).

DISCUSSION

The purpose of this study was to compare outcomes between patients using a PCA pain control protocol versus patients using a non-PCA pain control protocol. Findings revealed there were no differences in patient lengths of stay, readmission rates, transfers to higher levels of care, and frequency of naloxone rescue between patients on the PCA and non-PCA protocols. The average amount of narcotic received between the two groups was also similar, except for morphine and hydromorphone. Patients on the PCA protocol received more hydromorphone than patients on the non-PCA protocol due to the hydromorphone shortage; those on the non-PCA protocol received more morphine than those on the PCA protocol since morphine was the parenteral drug used in place of hydromorphone.

There are some advantages of a non-PCA protocol versus a PCA protocol. Although PCA pumps generally are regarded as safe and effective,[10,11] there have been PCA pump mishaps that have led to patient harm.[13,15,16,18] Though these instances were relatively rare, their risk of occurring was null by removing the PCA pump altogether. Another possible advantage of a non-PCA protocol is a reduced cost compared to using a PCA protocol. By not using the PCA pump, this infers a lower cost compared to a non-PCA alternative because the cost of the pump is avoided. Furthermore, the cost of the drugs between the

Table 1. Demographics and clinical characteristics of sample population.

	Total (n = 251)	PCA (n = 121; 48%)	Non-PCA (n = 130; 52%)	p Value
Demographics				
Mean age, years; (SD)	62 (13)	62 (12)	61 (14)	0.65
Age, range (years)	19-86	22-86	19-83	
Sex, female (%)	155 (62)	73 (60)	82 (63)	0.65
Race (%)				0.59
White	231 (92)	113 (93)	118 (91)	
Other	20 (8)	8 (7)	12 (9)	
Body Mass Index (%)				0.12
Underweight (< 18.5)	5 (2)	2 (2)	3 (2)	
Normal weight (18.5-25)	29 (12)	12 (10)	17 (13)	
Overweight (25-30)	64 (25)	24 (20)	40 (31)	
Obese (> 30)	153 (61)	83 (68)	70 (54)	
Clinical Characteristics				
Diabetic (%)	61 (24)	33 (27)	28 (22)	0.29
Hypertension (%)	160 (64)	81 (67)	79 (61)	0.31
Smoking Status (%)				0.17
Never smoked	134 (54)	72 (60)	62 (48)	
Former smoker	81 (32)	34 (28)	47 (36)	
Current smoker	36 (14)	15 (12)	21 (16)	
Procedure Type (%)				0.8
Non-fusion	50 (20)	26 (21)	24 (18)	
1-2 level fusion	159 (63)	76 (63)	83 (64)	
3+ level fusion	42 (17)	19 (16)	23 (18)	

Table 2. Comparison of narcotics used between PCA and non-PCA groups.

	PCA	Non-PCA	MME	p Value
Oral				
Hydrocodone (Norco®)	99.86 (80.06-119.70)	101.90 (83.21-120.60)	40-120	0.86
Oxycodone (Percocet®)	51.90 (35.28-68.52)	52.00 (34.30-69.70)	60-180	0.99
Tramadol	5.38 (-2.32-13.08)	16.73 (4.78-28.68)		0.12
Oxycodone (single formulation)	5.08 (-0.50-10.67)	0.58 (-0.56-1.72)	60-180	0.12
Intravenous				
Hydromorphone (Dilaudid®)	6.59 (5.08-8.09)	1.01 (0.50-1.51)	19.2-48	< 0.0001
Morphine	0.08 (-0.08-0.25)	4.63 (2.82-6.44)	48-96	< 0.0001

Note: All values presented in means and 95% Confidence Intervals; all narcotic values in milligrams. MME stands for Morphine Milligram Equivalence. The Opioid Conversion Calculator from Oregon Pain Guidance was used to calculate the MME per day.

Table 3. Outcomes of primary and secondary endpoints.

	Total (n = 251)	PCA (n = 121; 48%)	Non-PCA (n = 130; 52%)	p Value
Outcomes				
Mean Hospital Length of Stay (days), (SD)	3.53 (1.40)	3.66 (1.49)	3.41 (1.29)	0.15
Naloxone Use (%)	6 (2)	3 (2)	3 (2)	0.92
Transfer to ICU (%)	5 (2)	4 (3)	1 (1)	0.15
30-day ED visit for pain (%)	6 (2)	4 (3)	2 (2)	0.36
30-day Readmission (%)	9 (4)	3 (2)	6 (5)	0.36

two protocols was similar due to each group using a similar amount of narcotics. However, the PCA protocol used more hydromorphone, the non-PCA protocol used more morphine. Morphine is a significantly cheaper opioid than hydromorphone (at this institution, 4 mg of morphine cost $1.67 and 4 mg of hydromorphone cost $7.32); it was also a less potent sedative.[19] Hydromorphone delivers 4 morphine milligram equivalents (MME).[20] This means hydromorphone is four times as potent as morphine, therefore, the PCA protocol received a higher dosage of narcotic overall. The PCA protocol received 26.36 MMEs in hydromorphone, compared to 4.04 MMEs in the non-PCA protocol, making morphine both a cheaper and safer[20] option in comparison to hydromorphone.

An advantage to using a PCA instead of a non-PCA protocol is patient satisfaction. Patients generally are satisfied with the PCA and the feeling of autonomy it provides.[10]

A disadvantage of a non-PCA protocol is an increased burden on the nursing staff caring for these patients. Since patients without a PCA pump can receive their pain medications only when they are administered by a nursing staff member, an assumption can be made that nursing workloads would increase. Further studies could test this assumption. However, patients on PCA or non-PCA protocols still required routine monitoring.

Decreasing length of stay has been identified as an important measure for increasing hospital efficiency and reducing iatrogenic morbidity and mortality and was a leading factor in the development of current Enhanced Recovery After Surgery (ERAS) guidelines.[9,21] Our study found no difference in the length of stay between a PCA and non-PCA protocol, adding to previous studies that suggested there was no difference in length of stay between patients on PCA and non-PCA protocols.[10,22]

Limitations. Some limitations of the current study included sample size. For a difference of 0.25 days in hospital length of stay to be statistically significant, 500 patients' data would have to be abstracted (power = 0.80). Adequacy of analgesia in the acute period after surgery is especially important to prevent chronic pain in the context of the current opioid crisis,[5] however, our study was not designed to assess this. The current study also failed to distinguish between those patients who were opioid naïve and those who had significant prior exposure. Stratifying according to opioid naïveté versus tolerance would have allowed for elimination of this as a cofounder.

CONCLUSIONS

This study suggested a non-PCA analgesia protocol can result in similar outcomes to a PCA protocol among patients undergoing thoracic or lumbar surgery. A surgeon considering avoiding PCA postoperatively can do so with similar outcomes.

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Keywords: patient controlled analgesia, opioids, thoracic, lumbar, surgery, length of stay

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The Association of Metabolic-Associated Fatty Liver Disease with Clinical Outcomes of COVID-19: A Systematic Review and Meta-Analysis

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ABSTRACT

Introduction. Metabolic-associated fatty liver disease (MAFLD) is a hepatic manifestation of metabolic syndrome (MS). MAFLD patients have a higher prevalence of COVID-19. MAFLD also is associated with worse clinical outcomes of COVID-19, such as disease severity, intensive care unit (ICU) admission rate, and higher mortality rates. However, this evidence has not been well characterized in the literature. This meta-analysis aimed to determine the clinical outcomes of COVID-19 among MAFLD patients compared to the non-MAFLD group.

Methods. A comprehensive search was conducted in the Cumulative Index of Nursing and Allied Health (CINAHL), PubMed/Medline, and Embase for studies reporting MAFLD prevalence among COVID-19 patients and comparing clinical outcomes such as severity, ICU admission, and mortality among patients with and without MAFLD. The pooled prevalence of MAFLD among COVID-19 patients and the pooled odds ratios (OR) with 95% confidence intervals (CI) for clinical outcomes of COVID-19 were calculated.

Results. Sixteen observational studies met inclusion criteria involving a total of 11,484 overall study participants, including 1,746 MAFLD patients. The prevalence of COVID-19 among MAFLD patients was 0.29 (95% CI: 0.19-0.40). MAFLD was associated with the COVID-19 disease severity OR 3.07 (95% CI: 2.30-4.09). Similarly, MAFLD was associated with an increased risk of ICU admission compared to the non-MAFLD group OR 1.46 (95% CI: 1.12-1.91). Lastly, the association between MAFLD and COVID-19 mortality was not statistically significant OR 1.45 (95% CI: 0.74-2.84).

Conclusions. In this study, a high percentage of COVID-19 patients had MAFLD. Moreover, MAFLD patients had an increased risk of COVID-19 disease severity and ICU admission rate.

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INTRODUCTION

The novel severe acute respiratory syndrome coronavirus (SARS-CoV-2) is the cause of coronavirus disease (COVID-19), a pandemic that represents a global health challenge. COVID-19 is usually a self-limiting disease; however, it is associated with a significant (3-7%) mortality rate.[1] The excessive production of pro-inflammatory cytokines because of SARS-CoV-2 infection mainly is associated with high mortality due to multiple organ failure.[2] Acute respiratory distress syndrome (ARDS) resulting from the cytokine storm is the primary cause of mortality among COVID-19 patients.

Advanced age and specific co-morbidities, such as cardiovascular diseases (CVD), chronic obstructive pulmonary disease (COPD), diabetes mellitus type 2 (DM2), and hypertension, were the main risk factors for the development of COVID-19 and increased mortality.[1,3-5] Patients who have metabolic syndromes (MS) components such as hyperlipidemia, diabetes mellitus, and obesity were more likely to develop COVID-19 infection and have a higher mortality rate.[6,7] Chronic low-grade inflammation associated with the metabolic syndrome has been known to cause compromised body immune system, resulting in microvascular endothelial dysfunction, contributing to poor health outcomes among COVID-19 patients.[8,9]

Metabolic-associated fatty liver disease (MAFLD) is the most common cause of the chronic liver disease (CLD) and affects approximately 30-40% of the world population.[10] MAFLD is also a well-known risk factor for cardiovascular disease and diabetes mellitus, resulting in higher morbidity and mortality.[4,10] Lately, a consensus of international experts has proposed to change the disease acronym from NAFLD (i.e., non-alcoholic fatty liver disease) to MAFLD due to the strong association of NAFLD with the metabolic syndrome components.[10] The criteria to diagnose MAFLD are based on the presence of hepatic steatosis and three other measures, including the presence of DM2, obesity, and evidence of body metabolic dysregulation. Pre-existing liver disease, such as metabolic-associated fatty liver disease, could increase the risk of hospitalization and severity of COVID-19.[11] Moreover, the presence of MAFLD could release more pro-inflammatory cytokines to exacerbate the SARS-CoV-2 induced inflammatory response in COVID-19 patients. SARS-CoV-2 uses angiotensin-converting enzyme 2 (ACE 2) receptors for cellular entry, and the patients with MAFLD had increased expression of ACE 2 receptors, leading to more severe COVID-19 disease.[12] Furthermore, the increased production of reactive oxygen species among the MAFLD patients further stirs the inflammatory storm leading to the severity of the infection in certain patients.[13]

Recent observational studies have demonstrated that not only the presence of liver disease such as MAFLD may influence the COVID-19 disease course, SARS-CoV-2 infections also can affect the progression of liver disease (e.g., MAFLD, nonalcoholic steatohepatitis).[14,15] Other studies have reported that the existing hepatic steatosis was associated with further significant liver injury and disease severity among

COVID-19 patients.[16] Similarly, metabolic diseases also were associated with adverse COVID-19 outcomes.[17] However, limited data were available on how MAFLD was associated with the increased prevalence, severity, hospital course, and mortality of COVID-19. Therefore, this meta-analysis evaluated the prevalence of MAFLD among COVID-19 patients and how MAFLD influenced the hospitalization course and severity of COVID-19. The effect of MAFLD on the rate of intensive care unit (ICU) admission and mortality outcomes among COVID-19 patients also was evaluated.

METHODS

Study Search and Selection. The systematic review and meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 Statement.[18] The study search was conducted in the Cumulative Index to Nursing and Allied Health Literature (CINAHL), PubMed/Medline, Google Scholar, LILACs, and Embase from the database inception through May 28th, 2021. Potentially relevant articles also were identified by the manual search of the references of the selected articles. The search strategy was designed using keywords to retrieve the articles that demonstrated the association between MAFLD and COVID-19. Moreover, the bibliographies of relevant and review articles were searched manually to include any other studies of interest. The literature search was restricted to the English language articles. The initial screening of the retrieved articles was conducted based on their title and abstracts for possible eligibility. Furthermore, title and abstract-based retrieved articles were assessed for inclusion based on their full-text review. Covidence software (Covidence systematic review software; Veritas Health Innovation: Melbourne, Australia) was used by the two independent researchers (UH, MZA) to assess the eligibility of articles for final inclusion.

Inclusion Criteria. The studies were included in the final meta-analysis if they met the following inclusion criteria: (a) epidemiological studies involving patients older than 18 years of age, (b) reported laboratory-confirmed COVID-19 cases, (c) reported prevalence of MAFLD among the COVID-19 patients, (d) reported possible association risk between MAFLD and COVID-19 disease severity, ICU admission, and mortality. The following keywords were used for search strategy in PubMed, CINAHL, and Embase: "COVID-19" or "COVID-19/mortality", and "COVID-19" or "coronavirus", and "NAFLD" or "non-alcoholic fatty liver disease", and "MAFLD" or "metabolic associated fatty liver disease", and "fatty liver" and "metabolic fatty liver disease".

MAFLD was defined by the presence of hepatic steatosis and three other measures, including the presence of DM2, obesity, and evidence of body metabolic dysregulation. COVID-19 patients were considered to have the severe disease when they met the following criteria: (1) hypoxia (oxygen saturation less than 92%), (2) increased respiratory rate (greater than 35 per minute), (3) decreased consciousness: somnolence, apathy, convulsions, and coma, (4) certain specific manifestations, such as bleeding, coagulation disorders (deep venous thrombosis, pulmonary embolism), cardiovascular manifestation such as myocardial infarction, abnormally raised liver enzymes, rhabdomyolysis, and gastrointestinal dysfunction such as severe diarrhea.

Exclusion Criteria. The studies with patients younger than 18 years, pregnant patients, and those lacking informed consent were excluded. Also, those studies with a secondary cause of fatty liver diseases, such as alcoholic liver disease, autoimmune liver disease, drug-induced liver injury, cholestatic liver disease, and viral hepatitis, were excluded. Furthermore, interventional trials, animal studies, reviews, case reports, genetic studies, commentary, and study protocols were excluded. Lastly, this meta-analysis did not include the studies with incomplete literature data or information, study definitions, or unclear descriptions of outcomes.

Data Extraction. The following data were collected from each publication selected: (1) the characteristics of the study population including age, sex, body mass index (BMI), MAFLD and COVID-19 assessment methods, and population co-morbidities, (2) author name, study year, country of publication, trial registration, type of observational studies, source of the included database, duration of study follow-up, and the proportion of COVID-19 study population with metabolic associated fatty liver disease, and (3) study outcomes such as effect estimates of odds ratio (OR), risk ratio (RR), and hazard ratio (HR) were reported. To conform with the newer MAFLD definition, unadjusted ORs (not adjusted for other covariates such as age, sex, ethnicity, race, BMI, and other co-morbidities (e.g., hypertension, diabetes mellitus, obesity smoking, cardiovascular diseases, hepatocellular carcinoma (HCC), dyslipidemia, COPD, and alcohol consumption)) were used from those studies which reported the association between NAFLD and COVID-19 clinical outcomes. The absolute number of COVID-19 patients within the MAFLD and non-MAFLD group, along with the study conclusion, also were extracted. Any conflicts in the initial study screening process and data extraction phase were resolved by consensus and discussion with the senior author (MA).

Quality Assessment. The included studies were assessed for quality. The Newcastle-Ottawa scale (NOS) was used.[19] Three parameters of the scale, such as selection, comparability, and outcome/exposure, were applied to assess the quality of the publications. The studies were classified as low, medium, or high quality according to the NOS scale achieved based on the three parameters (e.g., selection, comparability, and outcome/exposure). The quality assessment was performed by two authors (UH, MZA) independently, and any discrepancies were resolved through mutual consensus. All studies with a higher NOS score (based on selection, comparability, and outcome/exposure) were selected. A high score indicates a high study quality.

Statistical Analysis. Meta-analysis was performed using the RStudio software (RStudio, v4.1.0; University of Auckland, New Zealand). The pooled prevalence of MAFLD among COVID-19 patients was calculated. The study used the published studies' available effect estimates of OR, HR, and RR. Absolute numbers were used to calculate the unadjusted ORs if the effect estimate was not reported. Pooled OR with 95% confidence intervals (CI) were calculated to assess the pooled estimates of odds of COVID-19 disease severity, ICU admission rate, and mortality (reference group: patients without MAFLD). A random-effect model was used to pool the effect estimates, based on the heterogeneity assessment of the individual study effect

estimate. A p value of < 0.05 was considered statistically significant for the pooled effect estimates. Forest plots were utilized to demonstrate the results of the meta-analysis.

Heterogeneity between the studies was tested with I^2 and X^2 tests for Cochran Q statistics. According to Cochran's handbook, I^2 value of (0-40%) was interpreted as "might not be important," (30-60%) as "moderate," (50-90%) as substantial, and (70-100%) as considerable heterogeneity.[20,21] The statistical review of this study was conducted by author UH.

RESULTS

The search results covered the period of database inception from December 2019 through May 2021. The total search results were 244 items, and after removing duplicates, it was reduced to 203. Fifty-eight studies were included in the full-text review process (by UH and MZA). After a full-text review of the extracted articles, sixteen studies were selected for the final meta-analysis, involving 11,484 overall study participants, including 1,746 MAFLD patients (Figure 1).

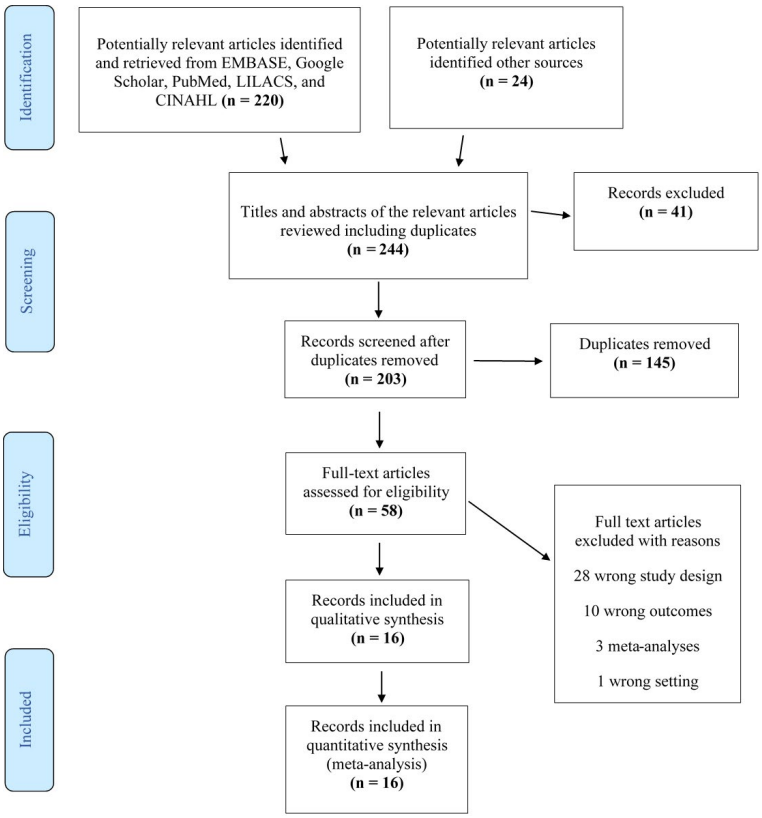

Figure 1. PRISMA flow chart of the studies.

Characteristics of the Studies Included. Three studies were cross-sectional or case-control studies,[23-25] and 13 articles were retrospective cohort studies,[22,26,28-33,35,37-40] Eight studies were reported from China,[24-26,29,31,41,43] three were from the U.S.,[21,29,36] two from the UK,[32,35] one from Turkey,[35] one from Mexico,[38] and one from Israel.[23] All studies were conducted between December 2019 and May 2021. The data sources for all studies were mainly electronic medical records/health records (EMR/HR).

Of the total, eight studies confirmed fatty liver disease based on ultrasound or computer tomography (CT).[23,24,26,28,30,31,35,36] Three studies used new consensus definition of MAFLD for diagnosis,[23,26,30] four studies used hepatic steatosis index (HIS),[29,38-40] one study used international classification disease code (ICD).[21] Two studies reported MAFLD based on the confirmed diagnosis of DM2 and obesity.[25,32] One study reported MAFLD based on EMR/HR.[33] The significant co-morbidities reported across all the included studies were obesity, DM2, hypertension, dyslipidemia, ischemic heart disease, chronic lung disease, chronic kidney disease (CKD), and metabolic dysregulation (see Tables 1 and 2 available online only at journals.ku.edu/kjm). Ten studies used reverse transcriptase-polymerase chain reaction (RT-PCR) to diagnose COVID-19 infection.[23,26,29-33,35,36,38] Six studies used laboratory-confirmed cases of COVID-19 infection.[22,24,25,28,39,40] One study did not provide clear information about the COVID-19 diagnosis method.[26]

MAFLD prevalence in COVID-19 patients. All sixteen studies reported the MAFLD prevalence in COVID-19 patients. The pooled prevalence of COVID-19 among MAFLD patients was 0.29 (95% CI: 0.19-0.40; p < 0.001; Figure 2).

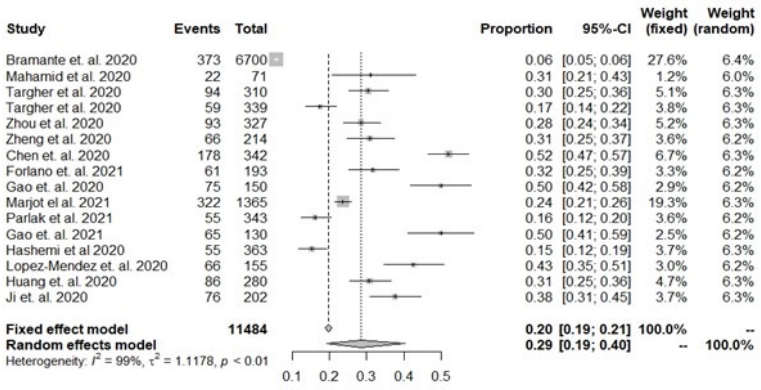

Figure 2. Forest plot of the pooled prevalence of the MAFLD among COVID-19 patients. OR, odds ratio; CI, confidence interval.

Clinical Outcomes

COVID-19 Severity in Patients with MAFLD. Twelve studies reported the severity of the COVID-19 symptoms related to MAFLD.[22-26,28-30,32,35,39,40] The pooled OR for severe COVID-19 symptoms in patients with MAFLD was 3.07 (95% CI: 2.30-4.09; p = 0.04) compared to those without MAFLD (Figure 3). Six studies reported the disease outcome as the severity of COVID-19 in MAFLD patients compared to those without MAFLD.[29-31,33,38,42] Another six studies reported the outcome as COVID-19 severity among NAFLD patients.[22,23,24,26,39,40] One study reported the association of obesity and metabolic dysregulation with COVID-19 severity.[35] Targher et al.[24] determined the association of COVID-19 severity with both low and high FIB-4 (hepatic fibrosis) scores. Also, Zhou et al.[26] reported the association of COVID-19 severity with NAFLD in both young and older patients separately.

COVID-19 Rate of ICU Admission in Patients with MAFLD. Overall, four studies reported the association between MAFLD and the rate of ICU admission among COVID-19 patients.[29,31,36,38] There was a significant increase in the rate of ICU admission among patients with MAFLD compared to those without. The pooled estimated OR was 1.46 (95% CI: 1.12-1.91; p = 0.28; Figure 4). The statistical heterogeneity for this analysis measured by I^2 was 22%. The clinical characteristics and quality assessment of the included studies have been described in Table 1 (available online only at journals.ku.edu/kjm).

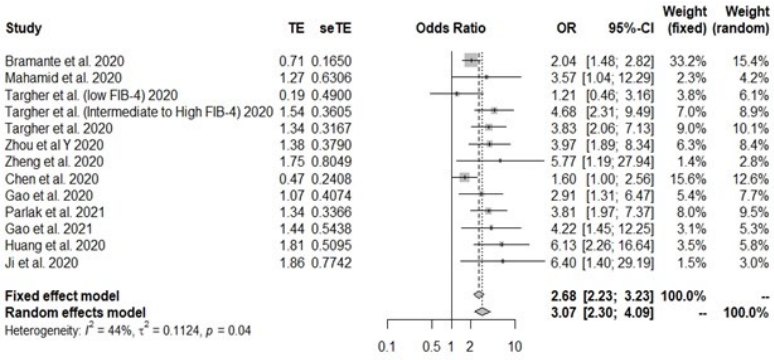

Figure 3. Forest plot of the pooled odds ratio of the association between MAFLD and COVID-19 severity. TE, treatment effect; seTE, standard error of treatment effect; OR, odds ratio; CI, confidence interval.

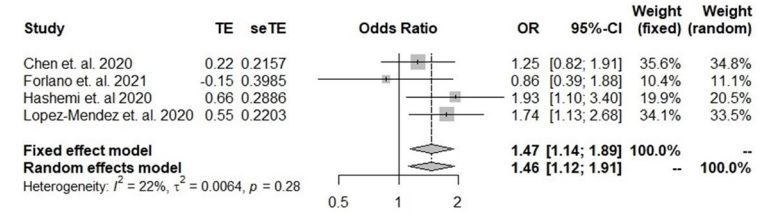

Figure 4. Forest plot of the pooled odds ratio of the association of MAFLD and ICU admission rate among COVID-19 patients. TE, treatment effect; seTE, standard error of treatment effect; OR, odds ratio; CI, confidence interval.

COVID-19 Mortality in MAFLD. Seven studies reported the COVID-19 mortality among MAFLD patients compared to those without MAFLD.[22,29,31,33,35,36,38] There was no observed statistical difference in the COVID-19 mortality among MAFLD patients compared to those without (OR 1.45; 95% CI: 0.74-2.84; p = < 0.01; Figure 5). The clinical characteristics and quality assessment of the included studies have been described in Table 1 (available online only at journals.ku.edu/kjm).

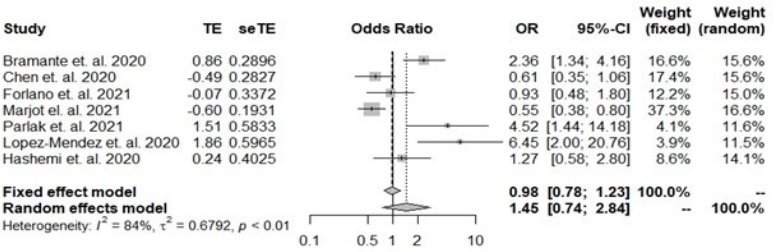

Figure 5. Forest plot of the pooled odds ratio of the association of MAFLD and COVID-19 mortality. TE, treatment effect; seTE, standard error of treatment effect; OR, odds ratio; CI, confidence interval.

The Assessment of Publication Bias. Based on the quality assessment criteria (i.e., NOS), all the included studies were observational and were moderate to high quality. The observational nature of the studies should be factored into in interpreting the results. Also, there was significant heterogeneity among the studies evaluating the COVID-19 prevalence among MAFLD patients (I^2 > 90%). There were several factors leading to this high heterogeneity. First, the studies included in this review have been conducted in different countries with different patient population demographics. Some countries were hit harder by the pandemic than others, leading to disparities in infection prevalence. Second, different data analysis parameters were used to adjust for confounders by different studies that might be the source of heterogeneity. Third, Bramante et al.[22] have the most skewed effect size in this analysis. It might be a source of high heterogeneity as their study has the highest study population among the studies included in this review. However, the point estimate effect was calculated by random effect model, taking on the higher heterogeneity between the studies, making the results significant. The publication bias was assessed using Egger's regression test methodology.[41] The p value was 0.025, suggesting the absence of publication bias in COVID-19 severity outcome. Egger's regression test was not performed for ICU admission and mortality outcomes because of the meta-analysis's limited number of studies (i.e., less than 10).

Both funnel plot and the ROBINS-E tool (The Risk of Bias in Non-randomized Studies of Exposures) were used to assess bias in the studies which reported the association of MAFLD with COVID-19 clinical outcomes (COVID-19 ICU admission and mortality). There are seven domains of bias assessment in this tool. These domains include the presence of confounding factors, selection of study participants, exposure classification, a patient departure from exposure, missing data, outcome measurement, and selection of the results reported in the study.[42] The individual judgments of each domain were taken and summarized to get an overall risk of bias assessment for the individual study. All those studies with a low risk of bias were selected and included in this meta-analysis. Two authors (UH, MZA) conducted the bias assessment and discussed any ambiguities with a senior author (HO).

DISCUSSION

The meta-analysis and systemic review have demonstrated the MAFLD prevalence and outcomes of COVID-19 among patients with MAFLD compared to those without. The study findings have established a high risk of COVID-19 disease severity and ICU admission among the patients with MAFLD than those without MAFLD. Moreover, there was an increased risk of COVID-19 mortality among MAFLD patients than those without MAFLD; however, this finding did not reach statistical significance.

COVID-19 is caused by SARS-CoV-2, which is genetically related to other coronavirus families such as SARS-CoV and Middle Eastern respiratory syndrome coronavirus (MERS-CoV).[43] These coronaviruses are known to affect liver function by different mechanisms. The direct effect of these viruses through translocation from the gut to the liver can spoil liver function. SARS-CoV-2 binds to the liver cells through angiotensin-converting enzyme receptors and causes direct toxicity through active viral replication within the hepatic cells. Furthermore, SARS-CoV-2 also can affect liver function through indirect mechanisms (e.g., causing ischemia, inflammation).[44] According to the cytokine storm hypothesis, SARS-CoV-2 infection can cause a severe immune-mediated cytokine storm because of inflammation that can damage the hepatocytes. This hypothesis was supported by the rise of the blood levels of the pro-inflammatory markers IL-2, IL-4, low-density lipoprotein, C-reactive protein, and serum ferritin in COVID-19 patients.[45] Among the other possible mechanisms of liver injury included drug-induced liver damage. Most of these patients were treated with antiviral drugs that can have harmful effects on hepatocytes, resulting in a rise in ALT and AST.[43,45]

The liver has an abundance of innate immune cells (e.g., macrophages, natural killer T cells, and γδ T cells).[46] Comorbid conditions such as obesity and MAFLD have been associated with the increased production of pro-inflammatory cytokines like tumor necrosis factor-α from Kupffer and adipose cells.[47] In MAFLD, free fatty acids flux in the hepatocytes and adipose tissue insulin resistance activates the liver macrophages. The dysregulated macrophages response in the liver of MAFLD patients promotes inflammation leading to the progression and severity of COVID-19.[4]

The presented meta-analysis revealed the high pooled prevalence of MAFLD among COVID-19 patients. This finding was comparable with the previously reported literature. In a meta-analysis of four studies, Pan et al.[50] reported a pooled prevalence of 0.31 (95% CI: 0.28-0.35) of MAFLD among COVID-19 patients. Moreover, the current study revealed a higher risk of COVID-19 disease severity among MAFLD patients than those without MAFLD. These findings were in alignment with other published studies. Hegyi et al.[51] reported an association of MAFLD with COVID-19. They demonstrated that MAFLD was associated with an increased risk of COVID-19 disease severity compared to the non-MAFLD group (OR = 2.61[95% CI: 1.75-3.91]).

Similarly, Singh et al.[52], in a pooled analysis, found that the presence of MAFLD among COVID-19 patients to be associated significantly with a higher risk of COVID-19 severity and ICU admission. Another study reported that obesity alone was associated with a significantly increased risk of COVID-19 disease severity even after adjusting for other confounders and co-morbidities.[53] The current meta-analysis revealed the effect of MAFLD on COVID-19 severity by using a large cohort of studies.

This study had limitations that need to be considered while interpreting the results. First, the respective studies included in this meta-analysis lacked a robust and consistent definition of COVID-19 disease severity. However, this limitation can be recommended for future epidemiological studies to contemplate while determining an association between COVID-19 outcomes and MAFLD. Furthermore, the various included studies did not adjust for confounding factors such as age, race, sex, and certain other co-morbidities, which can affect the study findings. Moreover, the study population had several co-morbidities, such as hypertension, obesity, DM2, CVD, and CKD, making it challenging to dissect the contribution of each co-morbidity towards COVID-19 outcomes, as previous studies have shown the negative association of these co-morbidities with COVID-19.[54] Lastly, fewer studies were included in the sub-group analysis of the effect of MAFLD on COVID-19 ICU admission rate and mortality, which made it challenging to analyze publication bias (less than ten articles). Despite the limitations, this study merits consideration. Foremost, to the best of our knowledge, this was the first study to report the MAFLD prevalence and COVID-19 outcomes together in a large-scale MAFLD population. In addition, this study is the first to report the COVID-19 mortality among MAFLD patients in a large cohort of studies.

CONCLUSIONS

In conclusion, MAFLD was more prevalent among patients with COVID-19. This meta-analysis and systemic review revealed a higher risk of COVID-19 disease severity and ICU admission in patients with MAFLD than their counterparts; however, the association between MAFLD and COVID-19 mortality was not significant. These findings suggested that the MAFLD patients should be followed closely for these complications if they develop COVID-19. The potential mechanism of COVID-19 severity among MAFLD patients remains illuminated by future studies. Furthermore, extensive prospective cohort studies are needed to include ICU admission rate and mortality outcomes in COVID-19 patients to elucidate the impact of MAFLD further.

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Keywords: non-alcoholic fatty liver disease, SARS-CoV-2, meta-analysis, critical illness, statistical data analysis

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Comprehension Profile of Patient Education Materials in Endocrine Care

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ABSTRACT

Introduction. The internet is an ever-evolving resource to improve healthcare literacy among patients. The nature of the internet can make it difficult to condense educational materials in a manner applicable to a worldwide patient audience. Within the realm of endocrinology, there is lack of a comprehensive analysis regarding these pathologies in addition to education materials related to their medical work-up or management. The aim of this study was to assess contemporary online patient education material in endocrinology and management of care.

Methods. Analysis of the readability of 1,500 unique online education materials was performed utilizing seven readability measures: Flesch Reading Ease (FRE), Flesch-Kincaid Grade Level (FKGL), Gunning Fog Index Readability Formula (FOG), Simple Measure of Gobbledygook Index (SMOG), Coleman-Liau Index (CLI), automated readability index (ARI), and Linsear Write Formula (LWF).

Results. The average grade level readability scores from six measures (e.g., FKGL, FOG, SMOG, CLI, ARI, LWF) was more than or equal to 11 which corresponds to a reading level at or above the 11th grade. The average FRE between adrenal, diabetes, and thyroid-related education material ranged between "fairly difficult" to "very difficult".

Conclusions. The readability of contemporary online endocrine education material did not meet current readability recommendations for appropriate comprehension of the general audience.

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INTRODUCTION

The internet remains a primary source for self-education among patients regarding health-related content. Moreover, the literature established a high level of patient satisfaction in the reported use of internet-based sources in seeking this self-education.[1] This satisfaction largely stems from the convenience of immediate information retrieval utilizing internet-based search queries. This convenience led to patients with a proactive approach to their own healthcare and ultimately greater involvement in making patient centered medical decisions with their healthcare providers.[2]

The concept of healthcare literacy is tied closely with the health of an individual. Poor healthcare literacy was associated with poor self-reported health conditions, increased risk for hospital admissions, and greater healthcare costs.[3-5] However, the ever-evolving material found through the internet can be difficult to condense in a manner applicable for the worldwide audience to work efficiently into their own healthcare literacy.[6] The concept of the readability of patient education material serves an important role in a person's ability to comprehend the material and plays a direct role in their healthcare literacy.[7] It is recommended that the readability of patient education materials should not be higher than sixth-to-eighth-grade reading level.[8] Moreover, the National Institutes of Health recommended the readability of self-administered patient questionnaires to be written no more than a sixth-grade reading level.[9] However, the implementation of this readability recommendation is more difficult with regard to the internet due to lack of peer-review and regulatory factors which can aid in the authentication and validity of online patient educational materials.[10]

This imbalanced relationship between the immense usage of the internet and readability recommendations highlighted the necessity for further understanding of this climate of online information.[11] The current literature, which investigated the readability of online patient education materials, have shown failure to meet these established readability recommendations, and it was supported that current healthcare literacy must be improved upon to improve healthcare outcomes holistically.[12-14]

Within the field of endocrinology, the use of information in real-time is key for providers to guide the management of patients with endocrine and metabolic diseases and has led to greater advancement of patient care technology (i.e., eHealth apps, advancements in continuous glucose monitors).[15-19] Despite this, there was a paucity of data which provided a comprehensive readability assessment of endocrine-related care. Moreover, current endocrine readability literature often was isolated to pathology or metabolic conditions.[20-28] This limited real time comparative analytic data which can help endocrine providers in providing improved health care education.[29-30] Therefore, the aim of this study was to assess contemporary online patient education material in endocrine disorders and management of care.

METHODS

Ethics. The data utilized in this study was entirely available for public use and did not involve human subjects. Therefore, Institutional Review Board approval was not required for this study.

Screening. Between November 2021 and January 2022, online education materials were extracted from Google® search queries (Google Inc., Mountain View, CA) for endocrine-related content areas of interest. Among these queries, three primary categories of content were of interest: adrenal, diabetes, and thyroid. These three categories of endocrine-related content were chosen due to perceived paucity of literature to date. Within each category, there were 10 common search items relevant for the category which were used in the queries as outlined in Table 1. These search items were chosen based on review of the most recent literature produced by the World Health Organization for the three categories.[31-33]

Each search item was entered individually as a search query and the first 50 site link results which met the study's inclusion and exclusion criteria were utilized in the analysis. For the purpose of this study, sites were included if they contained content that was pertinent towards providing general information on the search query of interests, as evaluated by the screeners (SPS, SS, KQ, SM). Sites met inclusion if

they were in the English language, contained over 250 words minimum, and publicly available without any form of subscription required. Sites were excluded if they underwent a formal peer-reviewed research process with scientific indexing, the site explicitly specified the intended audience is for healthcare providers only, nonfunctioning search links, duplicate links, and/or did not meet the inclusion criteria.

Table 1. Endocrine-related content areas of interest.

Adrenal	Diabetes	Thyroid
Addison's Disease	Type 1 Diabetes	Graves' Disease
Cushing's Disease	Type 2 Diabetes	Hashimoto's Thyroiditis
Cushing's Syndrome	Insulin	Thyroid Hormone
Conn's Syndrome & Hyperaldosteronism	Metformin	Thyroid Cancer
Congenital Adrenal Hyperplasia	Dipeptidyl Peptidase-4 (DPP-4) Inhibitor	Goiter
Pheochromocytoma	Sodium/Glucose Cotransporter (SGLT-2) Inhibitor	Levothyroxine
Multiple Endocrine Neoplasia	Insulin Pumps	Hypothyroidism
Neuroblastoma	Sulfonylureas	Hyperthyroidism
Paraganglioneuroma	Diabetic Ketoacidosis	Thyroid Biopsy
Hirsutism	Maturity Onset Diabetes of the Young	Thyroid and Iodine

Readability Quantification. Upon screening, the site content was reformatted to plain text in Microsoft Word®, as shown in previous literature methodology, to create efficient readability calculations later in the study.[34-38] During the reformat phase, content material was removed for plain text if the screeners identified the content was unrelated to patient education. This specifically included removal of acknowledgments, author information, copyright disclaimers, figures and related captions and legends, references, and any web page navigation text. Moreover, the remaining content was unchanged from its site's original format when converted to individual plain text documents for each site link.

After the reformat phase, each plain text document was evaluated quantitatively for its readability. This was performed through seven readability quantification measurements: Flesch Reading Ease (FRE), Flesch-Kincaid Grade Level (FKGL), Gunning Fog Index Readability Formula (FOG), Simple Measure of Gobbledygook Index (SMOG), Coleman-Liau Index (CLI), automated readability index (ARI), and Linsear Write Formula (LWF). The FRE was utilized in this study as it was one of the oldest and most used readability quantification measurement scales. FRE assesses the readability of the plain text using a scale of 0 to 100 where the higher the scaled number implies a higher readability of the plain text. For categorization purposes, the FRE in this study was scaled based off previous literature: very difficult (0-29), difficult (30-49), fairly difficult (50-59), standard (60-69), fairly easy (70-79), easy (80-89), and very easy (90-100).[29,34-38]

Similarly, the FKGL attempts to quantify the plain text by focusing on the average number of words per sentence and average number of syllables per word in the scale to correlate to a grade level (i.e., score of 9.4 would suggest a U.S. ninth grade reading level).[39] The SMOG scale focuses on the total polysyllabic word count of the plain text to correlate to a grade level (i.e., a SMOG of 40 would approximate a U.S. ninth grade reading level). The CLI scale focuses on the average number of characters and sentences per 100 words of plain text (i.e., a CLI of 9.5 would correlate to a U.S. ninth to tenth grade reading level). The ARI is the summation of word and sentence difficulty to quantify a reading level utilizing similar characters per word and words per sentence (i.e., an ARI of 9 would approximate a U.S. ninth grade reading level). The LFW scale focuses on per 100 word sets similar to CLI, but also categorizes syllable counties per word as "easy words" (two or less syllables) or "hard words" (three or more syllables).[27-29,39-40]

The date of the search queries was recorded to limit potential ambiguity in search comparisons. Additionally, the country of origin of the site link was recorded (i.e., United States, United Kingdom). All data were recorded using Microsoft Excel® (Microsoft Corporation, Redmond, WA).

Statistical Analysis. Statistical analysis of the seven readability quantification scales was performed using Stata 14 Statistical Package® (StataCorp, College Station, TX) for descriptive statistics on the variables of interest, including counts, percentages, means, and standard deviations, where appropriate. Confidence intervals (CI) for parametric distribution were set at 95%. One way analysis of variance (ANOVA) was performed to compare average FRE measurements among search items with each category. The level of significance was set at $p < 0.05$.

RESULTS

Between November 2021 and January 2022, a total of 1,500 education materials (500 diabetic, 500 adrenal, and 500 thyroid education materials) were quantified for all seven readability assessment measurements for a total of 10,500 calculated measurements. The origin of 88.2% of all education material was the U.S. (n = 1,323), followed by 6.3% of articles from the U.K. (n = 94). The average grade reading level of all education materials was 13.08 (n = 1,500). The average grade reading levels and FRE of each topic of educational material were as shown in Table 2.

Table 2. Average grade reading levels across categories.

Content of Education Materials	Average Grade Reading Level	Confidence Intervals
Diabetes-Related	13.54	(CI: 13.08 - 14.00)
Thyroid-Related	12.91	(CI: 12.56 - 13.26)
Adrenal-Related	12.78	(CI: 12.34 - 13.22)
Content of Education Materials	**Average Flesch Reading Ease Measurements**	**Confidence Intervals**
Diabetes-Related	40.29 ("difficult to read")	(CI: 34.45 - 46.13)
Thyroid-Related	39.82 ("difficult to read")	(CI: 36.43 - 43.21)
Adrenal-Related	32.57 ("difficult to read")	(CI: 28.17 - 36.97)

These results quantified all educational materials amongst the content categories as being "difficult to read" as per FRE measurements. Among the subgroup analysis of adrenal-related educational materials, no online education materials met at least one measurement of a sixth grade reading level or less (n = 50). In addition, content related to paraganglioneuromas had the highest grade reading level at 16.45 (CI: 15.01 - 17.89). Content related to neuroblastomas had the lowest grade reading level at 12.18 (CI: 11.84 - 12.54). The average grade reading level of all other adrenal-related content was as shown in Table 3.

Table 3. Reading level analysis of adrenal-related educational material.

Content Related To:	Grade Reading Level	Confidence Interval
Paraganglioneuroma	16.45	(CI: 15.01 - 17.89)
Conn's Syndrome	14.74	(CI: 14.30 - 15.18)
Congenital Adrenal Hyperplasia	14.48	(CI: 14.05 - 14.91)
Pheochromocytoma	14.22	(CI: 13.81 - 14.63)
Multiple Endocrine Neoplasia	13.94	(CI: 13.58 - 14.30)
Cushing's Disease	13.18	(CI: 13.14 - 13.22)
Addison's Disease	13.16	(CI: 12.84 - 13.48)
Cushing's Syndrome	13.12	(CI: 12.77 - 13.46)
Neuroblastoma	12.18	(CI: 11.84 - 12.54)

Among the analysis of FRE measurements for adrenal-related educational material, Addison's Disease had the highest FRE measurement at 45.07 (CI: 30.76 - 39.38), which would qualify as "difficult to read". Likewise, Conn's Syndrome had the lowest FRE measurement at 21.97 (CI: 16.55 - 27.40), which would qualify as "very difficult to read". The average FRE of all other adrenal-related content was as shown in Table 4.

Table 4. Average Flesch Reading Ease measurements of adrenal-related education materials.

Content Related To:	Flesch Reading Ease Measurement	Confidence Intervals
Addison's Disease	45.07 ("difficult")	(CI: 30.76 - 39.38)
Neuroblastoma	42.81 ("difficult")	(CI: 38.54 - 47.08)
Hirsutism	38.94 ("difficult")	(CI: 33.75-44.13)
Cushing's Disease	37.11 ("difficult")	(CI: 32.96 - 41.25)
Multiple Endocrine Neoplasia	33.73 ("difficult")	(CI: 29.87 - 37.59)
Congenital Adrenal Hyperplasia	29.32 ("very difficult")	(CI: 23.77 - 34.87)
Pheochromocytoma	26.07 ("very difficult")	(CI: 20.58-31.55)
Paraganglioneuromas	23.11 ("very difficult")	(CI: 17.76 - 28.45)
Conn's Syndrome	21.97 ("very difficult")	(CI: 16.55 - 27.40)

Among the subgroup analysis of diabetes-related educational materials, 10% of Type 1 diabetes online education materials met at least one measurement of a sixth grade reading level or less (n = 5), and all others were less than 10%. In addition, content related to sodium/glucose cotransporter 2 (SGLT2) inhibitors had the highest-grade reading level at 14.70 (CI: 14.33 - 15.08). Content related to type 1 diabetes had the lowest grade reading level at 11.15 (CI: 11.85 - 11.45). The average grade reading level of all other diabetes-related content was as shown in Table 5.

Table 5. Average grade reading level of diabetes-related educational material.

Content Related To:	Grade Reading Level	Confidence Interval
Sodium/Glucose Cotransporter 2 (SGLT2) Inhibitors	14.70	(CI: 14.33 - 15.08)
Sulfonylureas	13.87	(CI: 12.99 - 14.76)
Maturity Onset Diabetes of the Young	13.54	(CI: 13.15 - 13.93)
Metformin	13.33	(CI: 12.96 - 13.71)
DPP-4 Inhibitors	13.29	(CI: 12.88 - 13.70)
Type 2 Diabetes	12.04	(CI: 11.10 - 12.99)
Insulin	12.03	(CI: 11.67 - 12.39)
Insulin Pumps	11.91	(CI: 11.56 - 12.26)
Diabetic Ketoacidosis	11.61	(CI: 11.26 - 11.96)
Type 1 Diabetes	11.15	(CI: 11.85 - 11.45)

Regarding FRE measurements for diabetes-related educational material, Type 1 diabetes had the highest FRE measurement at 52.28 (CI: 48.52 - 56.03), which would qualify as "fairly difficult to read". Likewise, SGLT2 inhibitors had the lowest FRE measurement at 26.10 (CI: 22.80 - 29.39), which would qualify as "very difficult to read". The average FRE of all other diabetes-related content was as shown in Table 6.

Table 6. Average Flesch Reading Ease measurements of diabetes-related education materials.

Content Related To:	Flesch Reading Ease Measurement	Confidence Interval
Type 1 Diabetes	52.28 ("fairly difficult")	(CI: 48.52 - 56.03)
Type 2 Diabetes	49.46 ("difficult")	(CI: 46.35 - 52.58)
Insulin pumps	48.30 ("difficult")	(CI: 43.94 - 52.67)
Insulin	47.32 ("difficult")	(CI: 44.07 - 50.58)
Diabetic Ketoacidosis	44.91 ("difficult")	(CI: 40.44 - 49.41)
Metformin	38.71 ("difficult")	(CI: 34.36 - 43.06)
Maturity Onset Diabetes of the Young	34.69 ("difficult")	(CI: 30.51 - 38.87)
DPP-4 Inhibitors	32.92 ("very difficult")	(CI: 28.98 - 36.86)
Sulfonylureas	28.17 ("very difficult")	(CI: 24.25 - 37.59)
SGLT2 Inhibitors	26.10 ("very difficult")	(CI: 22.80 - 29.39)

Among the subgroup analysis of thyroid-related educational materials, 10% of hyperthyroidism online education materials met at least one measurement of a sixth grade reading level or less (n = 5), and all others were less than 10%. In addition, content related to hyperthyroidism had the highest-grade reading level at 13.73 (CI: 13.29 - 14.17). Content related to thyroid biopsy had the lowest grade reading level at 11.20 (CI: 10.86 - 11.54). The average grade reading level of all other thyroid-related content was as shown in Table 7.

Table 7. Average grade reading level of thyroid-related educational material.

Content Related To:	Grade Reading Level	Confidence Interval
Hyperthyroidism	13.73	(CI: 13.29 - 14.17)
Graves' Disease	13.18	(CI: 12.84 - 13.52)
Levothyroxine	12.97	(CI: 12.52 - 13.43)
Hashimoto's Thyroiditis	12.92	(CI: 12.58 - 13.26)
Thyroid and Iodine	12.91	(CI: 12.51 - 13.30)
Thyroid Hormone	12.48	(CI: 12.14 - 12.82)
Hypothyroidism	12.44	(CI: 12.13 - 12.75)
Goiter	11.61	(CI: 11.32 - 11.89)
Thyroid Cancer	11.36	(CI: 11.04 - 11.68)
Thyroid Biopsy	11.20	(CI: 10.86 - 11.54)

Thyroid cancer had the highest FRE measurement at 47.95 (CI: 44.20 - 51.70), which would qualify as "difficult to read". Likewise, hyperthyroidism had the lowest FRE measurement at 33.56 (CI: 29.15 - 37.97), which also would qualify as "difficult to read". The average FRE of all other thyroid-related content was shown in Table 8.

Table 8. Average Flesch Reading Ease of thyroid-related content.

Content Related To:	Flesch Reading Ease Measurement	Confidence Interval
Thyroid Cancer	47.95 ("difficult to read")	(CI: 44.20 - 51.70)
Thyroid Biopsy	47.80 ("difficult")	(CI: 43.43 - 52.16)
Goiter	45.98 ("difficult")	(CI: 42.50 - 49.46)
Thyroid Hormone	39.11 ("difficult")	(CI: 35.23 - 42.99)
Thyroid and Iodine	38.35 ("difficult")	(CI: 33.82 - 42.88))
Grave's Disease	37.81 ("difficult")	(CI: 33.83 - 41.79)
Hypothyroidism	37.51 ("difficult")	(CI: 33.64 - 41.39)
Levothyroxine	36.72 ("difficult")	(CI: 32.24 - 41.21)
Hashimoto's Thyroiditis	33.56 ("difficult")	(CI: 29.15 - 37.97)
Hyperthyroidism	33.44 ("difficult")	(CI: 29.15 - 37.72)

DISCUSSION

The internet remains a form of a "pseudo-provider" due to its essential usage in nearly a third of information-seeking individuals when trying to self-diagnose or manage care without professional consultation.[41-43] The growth of information-seeking behavior among individuals created both a beneficial effect in allowing extremely efficient dissemination of information than seen in previous years.[44] This allowed a greater number of individuals to become empowered and gain greater awareness, including in healthcare literacy. In addition, that information also may aid in alleviating patient anxiety and involved with risk reduction strategies.[45-49] However, this rise in information-seeking behavior has been suggested to cause cognitive changes in our ability to comprehend material and memory, and improper information seeking behavior may be related to risk behaviors including improper drug usage and potential addictions.[45,47-50] The rise in these neuropsychological changes make it critical that individuals must be exposed to appropriate, legitimate comprehension to protect themselves.

The findings were in concordance with prior studies on diabetes and management. Moreover, a readability analysis on monogenic diabetes noted search items included in their analysis had failed to meet recommendations of a grade reading level standards of less than the sixth grade.[21] While the presented study recorded 10% of online education materials (n = 5) meeting this readability recommendation, this growth may be negligible given the three years or more since the Guan et al.[21] publication. In addition, the average FRE measurement of Grave's disease is in concordance with previous literature in 2014 by Edmunds et al.[26] which employed a similar screening methodology. In this study, the FRE score of Grave's disease educational articles was found to qualify as "difficult to read" by FRE measurement. In fact, the current Grave's diseases FRE of 37.81 was lower than what was found in the Edmund's et al.[26] study. This was likely because the current study used a larger sample (n = 50) of online education materials which were dedicated to Grave's disease materials in comparison (n = 20). Regardless, this finding further compounded the need to attempt to simplify the readability of Grave's disease literature. To the best of our knowledge, there was no dedicated literature on the readability of adrenal-related endocrine care, so the findings of this study were novel without a comparison. Moreover, the lack of adrenal-related online patient education materials which met the grade level readability recommendations raised priority in emphasized improvement in these materials.[8-9]

This study had multiple aspects which strengthens its findings. For example, the screening methodology accounted for 1,500 total online education materials and 10,500 readability quantification measurements creating the largest sample related endocrine care to date. The employment of seven scales minimized any potential measurement bias between scales. Secondly, this sample size had characteristically included material which were not formally scientifically indexed to limit variation in grade level readability as the audience of literature in PubMed or other scientific indexes may not be intended for the general audience.

However, this study was not without its limitations. The methodology did not account for utilization of other internet search query programs other than Google®. Google® comprised over 90% of the internet search query market share in the past year,[51-53] so the methodology was believed to cover a valid portion of relevant online education materials. The methodology also implemented a plain text reformat of all included online education materials. This suggested that the study failed to account for an illustration or digital materials which has been shown to aid in improving healthcare literacy as well as patient-physician discussions.[53]

In addition, the inclusion criteria focused only on online education materials which were written in English and not formally peer reviewed. Thus, the results of this study may not apply to online education material which was not written in English. However, the increased use of online language translation applications raised the potential to investigate if there are any discrepancies in readability amongst foreign language texts.[54-56]

Another potential concern was consideration with temporal changes in search engine trends and the presence of a potential "bubble effect".[57]

Original literature on this form of selection bias was in the context of using internet search queries when screening literature for systematic reviews.[58] This was to account for how search query programs may tailor search results specific to the user's preferences. However, the ultimate purpose of a readability analysis is to focus on the online results of the general crowd, so various measures can be used to limit potential selection bias such as using a clear internet search cache or specifically establishing a period for which internet search queries are performed as seen in this study. Future directions to develop after this study may be to encompass a larger set of search terms (i.e., more than 30) and use search trend technology to collect the most relevant search queries by the general worldwide audience. In addition, a larger scope of endocrine care which includes pituitary-related online education material can validate current literature in the long term.[30]

CONCLUSIONS

Healthcare literacy remains an important driving factor in the prognosis of a patient's health condition and overall quality of life. Online education materials will continue to be a convenient source of information which can be used in the endocrinologist-patient relationship. However, the lifetime longitudinal care of patients with endocrine and metabolic diseases requires a greater awareness that the current climate of online educational materials do not meet readability recommendations for appropriate comprehension of the general audience.

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Keywords: diabetes mellitus, adrenal glands, thyroid, readability, patient education

KANSAS JOURNAL of MEDICINE

Bilateral Upper Lobe Collapse Secondary to Vaping

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INTRODUCTION

Vaping and electronic (e-cigarette) use have been marketed as a "healthier" nicotine product as well as a smoking cessation tool.[1,2] These products have been especially popular in younger populations, even as young as middle school-aged, and their use has been increasing over the past several years. There are many well-described pulmonary manifestations associated with e-cigarette or vaping product use-associated lung injury (EVALI), many of which are some degree of organizing pneumonia.[3,4] This commonly is seen as ground glass opacities to focal consolidation in various locations on computed tomography (CT) scans. EVALI also has been associated with other organ system dysfunction including the cardiovascular (CV) and immune systems.[5] Pneumothoraxes and/or lung collapse were observed less commonly.[6,7] When these findings were seen, they predominately were seen unilaterally.[8] In this case, we described a patient with bilateral upper lobe collapse secondary to EVALI.

CASE REPORT

A 23-year-old male with past medical history of asthma and remote substance abuse presented with a new onset of seizures. Initial history was provided by Emergency Medical Services (EMS) and family members. The patient was lying in bed vaping and talking on the phone when he spontaneously began experiencing seizures. It was unknown how long the patient was convulsing prior to being found by his family. Midazolam was administered by EMS upon their arrival, which halted the seizures. When the patient arrived in the emergency department, he was tachycardic (134 BPM), tachypneic (RR 25), and hypoxic, requiring a non-rebreather mask to maintain appropriate oxygen saturations. He was afebrile.

Physical exam was pertinent for altered mental status and inability to follow commands, subcostal retractions, and diffuse rhonchi on respiratory auscultation. A rapid arterial blood gas showed respiratory acidosis. The patient was intubated for airway protection. Initial laboratory results showed a leukocytosis of 19.4 cells per microliter and a creatinine of 1.69 milligram per deciliters. Electrocardiogram showed sinus tachycardia and post intubation chest x-ray showed collapse of bilateral upper lobes (Figure 1). Computed tomography (CT) of the brain was unremarkable. CT chest confirmed bilateral upper lobe collapse (Figures 2 and 3).

The patient appeared to meet criteria for sepsis on admission. However, no infectious etiology was identified. This included blood cultures, cerebral spinal fluid cultures, and viral tests for human immunodeficiency virus, hepatitis, COVID-19, and influenza A and B. As a result, the patient was diagnosed with systemic inflammatory response syndrome (SIRS). The patient was extubated one day after intubation.

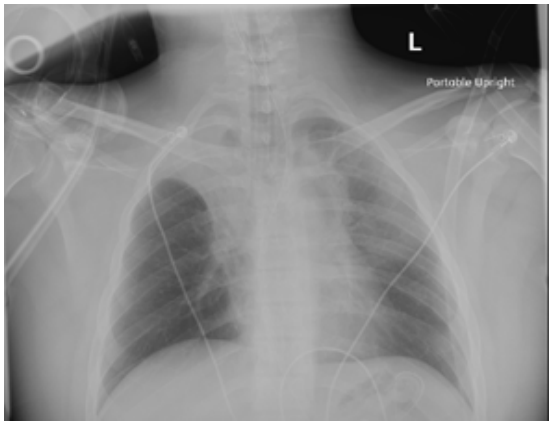

Figure 1. Anterior-posterior x-ray showing bilateral upper lobe collapse.

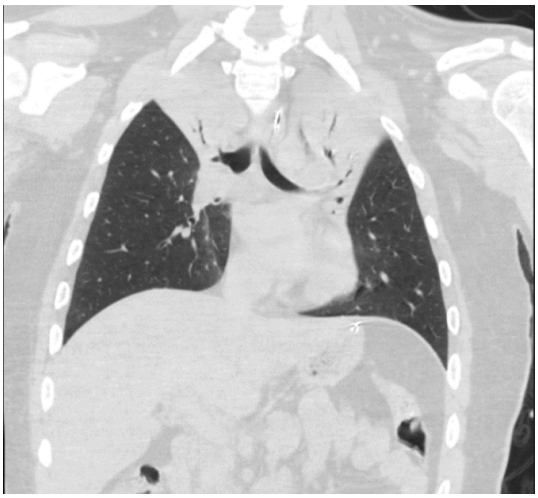

Figure 2. Coronal view of bilateral upper lobe collapse.

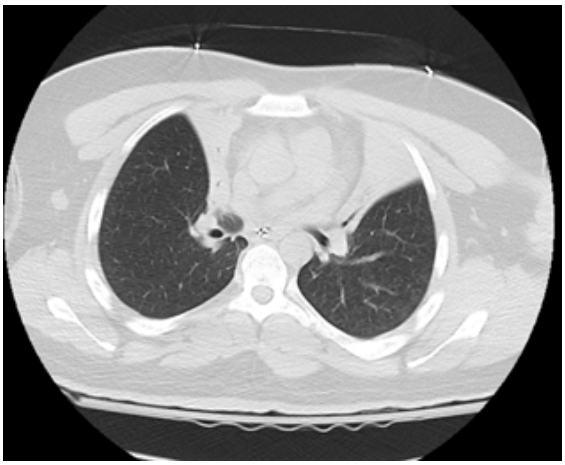

Figure 3. CT scan of bilateral upper lobe collapse.

Electroencephalogram was unremarkable for active seizures. The patient was treated with levetiracetam and was free of seizure activity for the remainder of his hospitalization. The patient's renal function improved with intravenous fluids and the patient was discharged on day five of admission. Given the patient's extensive workup and the unusual pattern of injury, it was concluded that his bilateral upper lobe collapse/atelectasis was secondary to vaping use.

DISCUSSION

EVALI is well-described with manifestations ranging from more benign with centrally located organizing pneumonia, to more severe with diffuse alveolar damage, which typically requires intensive care and ventilator support.[3,4] Respiratory failure secondary to vaping/e-cigarette use can be difficult to determine early in the course, as the acute presentation can be similar to that of respiratory viral infections.[4] This difficult diagnosis is especially pertinent in patients who require ventilator support and cannot provide a history of present illness, as seen in our patient. With increased vaping use being associated with more severe injuries and illness,[3] physicians should have a high index of suspicion of vaping/e-cigarette use in younger patients who present with respiratory failure.

EVALI likely will continue to be a diagnosis of exclusion, and this was seen in our patient, who required an extensive workup. The exact mechanism of EVALI remains elusive, but is suspected to be related to the vast number of chemical agents found in the smoking products.[9] This finding further emphasized the need for cessation and patient education.

CONCLUSIONS

In the presented case, an ostensibly rare complication of vaping use, bilateral upper lobe collapse/atelectasis, was described. Given our patient's young age and lack of prior lung injury and comorbidities, the differential diagnosis remained broad, thus necessitating an extensive work-up. EVALI is a diagnosis of exclusion and requires a high degree of suspicion. With more younger patients using vaping products, it is likely that lung injuries will continue to be seen. Cessation and education of these products should be a continued discussion between patient and physician.

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Keywords: vaping, lung injury, e cigarettes

KANSAS JOURNAL of MEDICINE

Takotsubo Cardiomyopathy in a Vaccinated Patient with Severe COVID-19

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INTRODUCTION

This case illustrated coronavirus disease-19 (COVID-19) induced interlukin-6 (IL-6) activation resulting in Takotsubo Cardiomyopathy (TCM) in a vaccinated patient. As noted by Kurowski et al.[1], the pathogenesis of TCM includes a high inflammatory state leading to increased myocardial stress and eventual transient dysfunction. As such, the patient may present with cardiac chest pain mimicking acute coronary syndrome and signs of clinical heart failure. This complication should be part of the differential in patients who present with acute ST-elevation myocardial infarction (STEMI), with no cardiac risk factors and suspicion for severe inflammation. The RECOVERY Collaborative Group[2] showed that the high inflammatory state seen in severe COVID-19 pneumonia can lead to major organ dysfunction, including TCM, and these patients also should be evaluated for immunomodulatory therapy targeting IL-6 as they may reduce mortality.

CASE REPORT

The patient was a 67-year-old female with a past medical history of chronic obstructive pulmonary disease, hypertension, and obesity who presented with 10 days of shortness of breath, fever, and fatigue. The patient received her second dose of the mRNA-1273 COVID-19 vaccine four days prior to admission, curiously while dyspneic, and when questioned further she was exposed by a family member who lives with her and subsequently tested positive for COVID during this period.

Physical exam was notable for irregular tachycardia and scattered rhonchi. Vitals were documented as blood pressure of 127/73 mmHg, heart rate of 127 beats/min, respiratory rate of 33 breaths/min, and oxygen saturation of 60% on room air improved to 92% on Bi-level Positive Airway Pressure. A computerized tomography chest scan with contrast was negative for an acute pulmonary embolism, but found bilateral interstitial opacities. Nasal swab polymerase chain reaction (PCR) testing was positive for COVID-19. Given this, she was admitted to the hospital for respiratory failure and management of her COVID. She was started on dexamethasone 10 mg once a day, with the intention of treating for 10 days, and a five day course of remdesivir. The patient was evaluated for tocilizumab, but she was not deemed a candidate due to hepatitis C antibody reactivity, positive methicillin-resistant Staphylococcus aureus respiratory culture with increasing oxygen requirements, and a large recent area of infarct in the left cerebellar hemisphere, as well as the left aspect of the brain stem.

On hospital day two, the patient complained of chest pain with an exam showing increasing respiratory effort, irregular tachycardia, no significant murmurs, and warm extremities. Vitals notable for blood pressure (147/75 mmHg) and heart rate (127 beats/min). Electrocardiogram (ECG) showed 1-mm upsloping ST elevations in leads II, III, and avF with a high sensitivity troponin found to be greater than 3000 ng/L (admission high sensitivity troponin less than 60 ng/l). Notable laboratory anomalies included IL-6 levels of 54.9 pg/mL, D-dimer levels of 28.45 mcg/mL, and C-reactive protein levels of 91.4 mg/L. Given the acute presentation, ECG findings, and troponin elevation, the differential diagnosis included STEMI, TCM, and myopericarditis.

The patient was intubated electively to reduce transmission and urgently taken for cardiac angiography. She was found to have no significant coronary artery stenosis with good thrombolysis in myocardial infarction (TIMI) 3 flow and a left ventriculogram with apical ballooning (Figure 1). A transthoracic echocardiogram with contrast showed ejection fraction 20-25%, normal left ventricular chamber size with basal wall hyperkinesis, and apical wall hypokinesis. The patient was admitted to the intensive care unit for her underlying COVID-19 pneumonia with findings consistent with TCM.

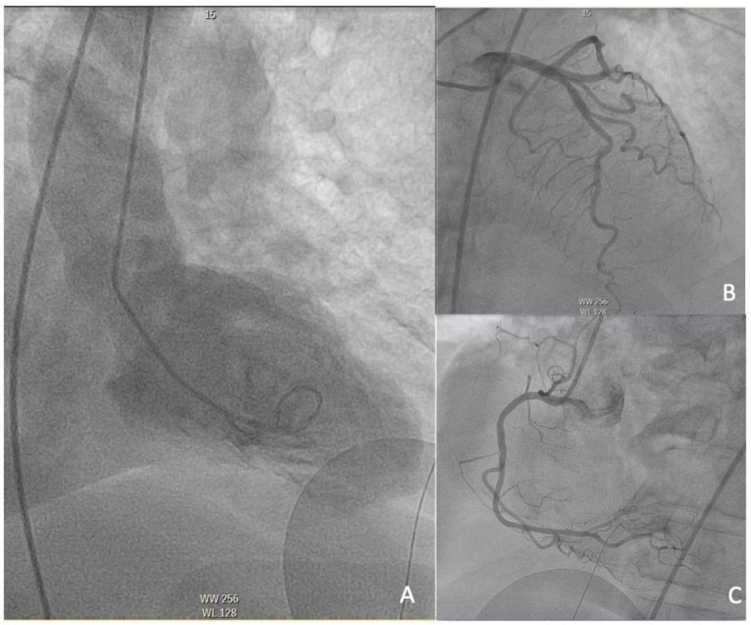

Figure 1. (A) Left ventriculogram consistent with apical ballooning. Angiogram showing good TIMI 3 flow in both the left (B) and right (C) coronary system.

Clinically, the patient continued to require high levels of oxygen via the ventilator with supportive care. Her inflammatory markers eventually trended down, as did her oxygen demand. A follow-up transthoracic echocardiogram showed return of normal cardiac function, ejection fraction of greater than 55%, and no regional wall abnormalities (Figure 2). Due to her lack of significant improvement and continued ventilator dependence, the multidisciplinary decision with the family was to have the patient undergo tracheostomy and percutaneous gastrostomy tube placement for long term convalescence.

Given the improvement of her cardiomyopathy with the improvement of her infection and the negative coronary findings on angiogram, the diagnosis of Takotsubo cardiomyopathy was believed to be most consistent.

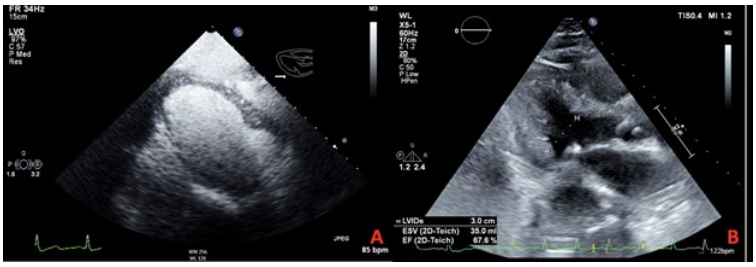

Figure 2. (A) Hospital day 2 ECHO with contrast showing an ejection fraction of 20-25%, normal left ventricular chamber size with apical hypokinesis and basal hyperkinesis consistent with TCM. (B) Hospital day 22 ECHO with contrast showing return of normal left ventricular function with no regional wall abnormalities. LVID: left ventricular internal dimension; ESV: end systolic volume; EF: ejection fraction.

DISCUSSION

Patients with Takotsubo cardiomyopathy classically present with typical chest pain and ECG findings of anterolateral ischemia. Of note, 1-2% of patients present with troponin positive suspected acute coronary syndrome or STEMI.[1] This finding was postulated to be due to direct left ventricular myocardial injury and resultant troponin leak appearing as ST elevations in the anterolateral precordial leads.[3] On ultrasound, the myocardial wall dyskinesis occurs over multiple coronary territories with no significant coronary stenosis seen on cardiac angiography further supporting a non-ischemic cardiomyopathy etiology.[1]

Stress, either psychological or physical, was thought to be a major contributor to TCM, with an 89.9% predominance for female patients.[3] A postulated theory includes increased levels of circulating catecholamines causing direct myocardial injury leading to classical left ventricular apical hypokinesis with basal hyperkinesis.[4] One such stressor may be the extensive inflammatory disease that occurs during an acute COVID-19 infection. It was believed to be a response to IL-6 activation through either the classical or trans signaling pathways.[2] IL-6 is produced transiently in response to infection and tissue injury, but prolonged inflammation can lead to continual synthesis leading to chronic inflammation and stress. A recent multicenter randomized control trial found a 4% reduction in all-cause mortality within the first 28 days for critically ill patients on tocilizumab with steroids against steroids alone.[2] In our case, the presentation with angiography and echocardiogram correlates with TCM, but the patients' comorbidities contraindicated tocilizumab.

Although novel therapies can be effective, the current strongest recommendation to prevent disease is vaccination. The two-part mRNA-1273 series provided viral protection with greater than 92% efficacy 14 days after the initial dose with greater than 94% efficacy two weeks after the second dose.[5] Although there have been reported cases of post-vaccine TCM, the timing and exposure with positive PCR seen in this case points to natural viral transmission leading to TCM.[6] Given the post-vaccination severe IL-6 mediated presentation by our patient, the importance of maintaining precautions prior to full vaccine series completion remains of utmost importance.

Although COVID-19 vaccinations have led to a significant decrease in severe disease, this case clearly demonstrated that vaccination, even complete vaccination, is not fully protective against severe disease. The patient had a severe IL-6 mediated disease despite the 92% efficacy rate with the vaccine after the first dose. Despite the high efficacy rate of these vaccines, it was essential to follow proper precautions as there was still a subset of those vaccinated who can develop severe COVID-19 pneumonia and can experience further complications due to the infection.

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Keywords: takotsubo cardiomyopathy, SARS-CoV-2 infections, myocardial infarction, treatment outcome, case study

KANSAS JOURNAL of MEDICINE

Scleroderma as an Uncommon Cause of Pericardial Effusion

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INTRODUCTION

Autoimmune diseases are a rare but important cause of recurrent pericardial effusions, and patients with scleroderma often present with pericardial effusion as their initial symptom.[1] Many patients with a rheumatologic condition go undiagnosed for years,[2] as with the presented case. With recurrent effusion, one must investigate the cause to prevent worsening morbidity, as simple drainage will not prevent reaccumulation of the fluid. Recurrent effusion in an elderly patient regularly indicates a workup for possible malignancy, but if tissue and cytology are negative for malignant cells, then autoimmune diagnosis should be ruled out. During the patient's hospital stay, she was found to have physical and laboratory findings consistent with scleroderma. Given her decompensated state after years of undiagnosed disease, little could be offered other than symptomatic relief. We stress the importance of considering rheumatologic causes of pericardial effusions, as early detection may change the clinical course of a patient significantly.

CASE REPORT

A 70-year-old female with recurrent pericardial and pleural effusions presented to the emergency department with bilateral lower extremity swelling. She recently was admitted for a similar presentation at an outside facility, treated with diuretics, and discharged. Notably, she had regular outpatient pulmonology appointments for recurrent pleural effusions with no known cause and negative malignancy workup.

On presentation, her temperature was 98.1° F, blood pressure 61/52 mmHg, heart rate 98 bpm, and respiratory rate 23 bpm saturating 95% on room air. Her physical exam was significant for cachexia with bitemporal wasting and bilateral elbow and distal interphalangeal joint edema without erythema. She exhibited jugular venous distension and distant heart sounds.

Initial lab findings were significant for mildly elevated B-type natriuretic peptide (450 pg/mL); troponins, creatinine, and lactic acid were within normal limits. An echocardiogram showed an ejection fraction > 55%, right ventricular systolic pressure > 60 mmHg, a moderate-sized pericardial effusion with right ventricular collapse during diastole, and mildly dilated right ventricle and bilateral atria (Figure 1).

Given her clinical deterioration with tamponade physiology, a decision was made to perform a fluoroscopy-guided pericardiocentesis. Fluid cytology and culture were negative, and cell count was significant for white blood cells with polymorphonuclear predominance (Table 1). Given her negative cytology and recurrent effusions with joint edema, further workup resulted in a normal ESR, elevated CRP (36), positive ANA antibody with a homogenous staining pattern (1:80), and positive scleroderma antibody (Table 2).

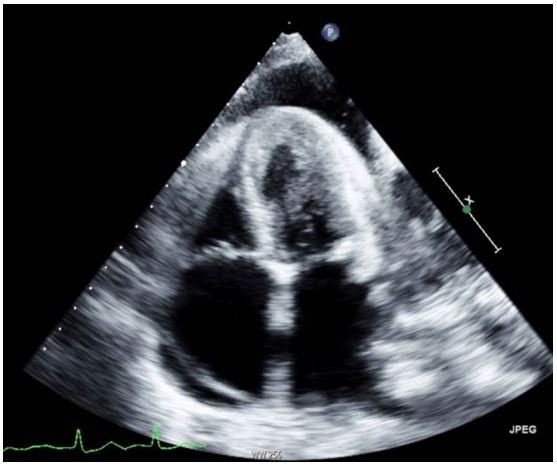

Figure 1. Transthoracic echocardiography showed fluid in the pericardium at the apex of the heart and right ventricular collapse.

Table 1. Laboratory analysis breakdown of contents in pericardial fluid.

White Blood Cell count	160 mm^3
Red Blood Cell count	< 2,000 mm^3
Polymononuclear Neutrophils	58%*
Mononuclear cells	42%*

*Values provided for informational purposes only, as there is no generally accepted reference interval.

Table 2. Laboratory result breakdown of autoantibodies present in patient's blood.

Antibody	Reference Range & Units	Patient Results
Antinuclear Antibody Screen	Negative < 1:80 Borderline 1:80 Positive > 1:80	Positive
Anti-DNA Antibody, double strand	0-9 IU/ml Negative < 5 Equivocal 5-9 Positive > 9	< 1
Jo-1 Antibody	0.0-0.9 AI	< 0.2
Anti-RNP	0.0-0.9 AI	< 0.2
Scleroderma Antibody	0.0-0.9 AI	2.8
SSA Antibody	0.0-0.9 AI	< 0.2
SSB Antibody	0.0-0.9 AI	< 0.2
Anti-Smith Antibody	0.0-0.9 AI	< 0.2

DISCUSSION

Autoimmune diseases are rare, and it is common for rheumatologic conditions to be either misdiagnosed or undiagnosed. Up to 25% of patients with rheumatologic diseases were unable to receive a definitive diagnosis, while others were undiagnosed for an average of 5 to 10 years.[2] The rheumatologic disorder diagnosed in this case study, scleroderma, has a prevalence of 135 million to 184 million cases in the U.S.[3] The majority of patients are female,[4,5] and those particularly with scleroderma present with a complication of pericardial effusion at an average age 52.2 ± 10.8 years.[1]

In scleroderma patients, pericardial effusions occur at a frequency of 17%, and pleural effusions occur less frequently at a rate of 7%.[6] Cardiac involvement at presentation (pericardial effusion or cardiac tamponade) was shown to be either prior to or simultaneous with a diagnosis of scleroderma in 32.5% of cases.[5] Cardiac symptoms of scleroderma were associated with an increase in mortality by 2.8 fold,[7] with a large portion due to arrhythmias or severe heart failure.[3]

Treatment options for pericardial effusion in scleroderma include medical management with steroids, non-steroidal anti-inflammatory drugs, colchicine, or surgical intervention through pericardiocentesis or pericardial window.[4] The majority of cases may be treated with medical therapy, reserving surgical intervention for more severe cases. Patients with pulmonary hypertension or an effusion causing hemodynamic compromise are advised to be optimized medically and managed cautiously to prevent cardiovascular collapse, reserving surgical intervention in cases that are absolutely necessary.

With our patient's advanced age, significant cachexia, and recurrent pleural effusions, clinical signs suggested the more common explanation of malignancy, and past encounters treated her accordingly. Her deviation from the typical age range of scleroderma and lack of other cardinal findings aside from her effusions did not fit the typical sclerodermal picture, possibly resulting in misdiagnosis and a likely more severe presentation during our encounter.

Because autoimmune diseases are rare, it is often the last etiology pursued, if at all. Yet, knowing that a significant percentage of scleroderma patients initially present with pericardial and/or pleural effusions was essential, and our decision to seek less common explanations led to her definitive diagnosis. Although our patient and family elected hospice, if her etiology was found earlier, it may have reduced her long-term morbidity and a more promising outcome may have been reached. We stress the importance of considering rheumatologic causes of pericardial effusions, as early detection can change the clinical course of a patient significantly.

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Keywords: systemic scleroderma, pleural effusion, autoimmune diseases, case report

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Mobile Health Clinics as a Healthcare Delivery Model to Address Community Disparities

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INTRODUCTION

The commentary by Rumalla et al.[1] observed the socioeconomic levels and corresponding healthcare disparities between Wyandotte and Johnson counties, which encompass the Greater Kansas City area. A salient observation was the notably higher exposure to primary care providers and lower preventable hospital stays in Johnson County, which also had a greater median household income and educational training. Since that commentary, there have been a number of public health initiatives that have been updated to improve concurrent local health disparities.[2-4] In particular, the Kansas City Community Health Improvement Plan (KC-CHIP) established numerous goals to improve public health infrastructure, which included educational funding in disinvested areas with lower property values for 2022-2027.[4] Moreover, there have been notable trends seen in the most recent data extracted from KC HealthMatters® (2015-2019) when compared to the 2014 extraction by Rumalla et al.[1] for the Wyandotte and Johnson counties (Table 1).[5]

In 2014, the median household income in Wyandotte County increased from $33,163 to $46,881.[5] Likewise, the median household income in Johnson County increased from $75,139 in 2014 to $89,087. What makes the income growth more encouraging, however, is that the Wyandotte County growth is over $10,000 more than the calculated United States Consumer Price Index inflation between 2014 to 2019 ($35,686).[6] The income growth in Johnson County was over $8,000 more than its inflation between 2014 to 2019 ($80,855).

The percentage of people aged 25 and older with a high school diploma or higher grew 0.3% in both counties (Wyandotte County: 78.9%; Johnson County: 96.0%).[5] However, the Wyandotte County growth rate can be of concern when considering that Wyandotte County has approximately 17% fewer people than Johnson County, therefore a greater increase would be desired to reduce healthcare disparity.

The number of primary care providers per 100,000 individuals has decreased 24.6% percent in Wyandotte County between 2014 and 2018, whereas this number has increased 19.2% in Johnson County.[5] This slower improvement seemed to make a weaker correlation to what was noted by Han et al.[7], which suggested income and resources for wealth were associated with educational success. From a primary care standpoint, a higher education attainment also was associated with higher measurements in health literacy, so the Wyandotte County measurements in health literacy were imperative to understand the socioeconomic climate.[8-10]

Moreover, poor health literacy was well established in literature to lead to increased hospital costs for the patient, as well as increased morbidity and mortality.[9-13] This issue further was compounded by the decrease in provider availability in Wyandotte County. This unfortunate decrease created a strain to the current network of available providers for patients in addition to the current healthcare infrastructure. This infrastructure included the concept of the healthcare safety net for first line emergency care in the form of emergency departments, emergency medical services providers (EMS), and public or free clinics.[11-13]

A potential solution provided by Rumalla et al.[1] was student-run free health clinics. This healthcare delivery model has been well-established in literature to address several healthcare disparities, including healthcare literacy, primary care screening, and education.[14-18] In addition, the student-run free health clinics create valuable learning opportunities for its student volunteers.[18,19] However, the growing strain on the local health safety net also may require additional interventions. This intervention could be additional student-run free health clinics.[20] This article aimed to provide a community level solution which may provide another distinctive solution that could work complementary to student-run free health clinics.

Mobile Health Clinics

A Mobile Health Clinic (MHC) is another community level intervention which can reduce the growing healthcare safety net strain.[21] Similar to student-run free health clinics, this intervention functions specifically as a delivery model for various medical services, including primary care and screening, preventative specialty care, and social interventions.[22-24] However, the unique quality which MHCs have is their ability to serve as a satellite medical facility that can allow for access to a wider demographic by geography. In addition, MHCs further remove the potential healthcare barrier of transportation for those who do not have a reliable source, and increase the convenience of healthcare access for the population who may have a reliable source of transportation.[23-25] The migratory characteristic carried by MHCs opens greater opportunities to establish patient rapport through a continued presence among communities which creates longitudinal care, and a foundation for greater provider trust by the patient.[26]

MHCs, by concept, create an environment which improves healthcare literacy for both the patient and provider.[22-25] Specifically, a patient having access to healthcare resources can create natural learning opportunities for themselves to improve healthcare literacy. However, the provider also gains a firsthand experience into physically being in their patients' community. This primary experience creates a greater sensory exposure which may not have been provided in the provider's training or a standard health clinic by being in one geographic location.

The fiscal implications of MHCs may create an encouraging proposition for their use in the community. In a community health survey by Attipoe-Dorcoo et al.[25], the types of healthcare services provided by 49 MHCs were recorded and an estimated mean cost range per patient visit was calculated to be lower than the standard costs for Medicare beneficiaries obtaining the same services at an institution. Community-level utilization of MHCs created a cost-savings environment in

Table 1. Temporal comparison of KC HealthMatters® data.[5]

	Wyandotte County		Johnson County	
	Measurement Period: 2014	Measurement Period: 2015-2019	Measurement Period: 2014	Measurement Period: 2015-2019
Median Household Income	$33,163	$46,881	$75,139	$89,087
People 25 and older with a High School diploma or higher	78.6%	78.9%	95.7%	96.0%
Primary Care Providers (per 100,000)*	61	46	104	124

*Most recent measurement period is 2018.

the form of reducing the number of avoidable emergency department visits.[22,27]

The current situation of MHCs in the state of Kansas is encouraging. According to the Mobile Health Map,[27] a collaborative network of MHCs in the United States which pool data on reported services and operation demographics (i.e., intended communities, mailing addresses, etc.), there are nine MHCs reported in Kansas. In comparison to the bordering states, Kansas had more reported MHCs than Nebraska (n = 6) and Oklahoma (n = 4), but far less than Colorado (n = 16) and Missouri (n = 27). Furthermore, six MHCs provided primary care services, and one also provided mammography screening, and another provided disaster relief services.[27] Based on the provided mailing address for each MHC, Johnson (n = 3), Shawnee (n = 3), Crawford (n = 1), Sedgwick (n = 1), and Saline (n = 1) provided MHCs. If an MHC will provide healthcare coverage to the county where it is located, then approximately 4% of the square area of Kansas is covered by at least one MHC. This implied that more MHC coverage, by county, could lead to more opportunities for individuals to receive healthcare services.

Additionally, these clinics rely on volunteers, including students, for day-to-day operative tasks like the student-run free health clinics discussed by Rumalla et al.[1] This volunteer opportunity provides students supplemental clinical exposure and practice to their medical training and was vital in exposing students to diverse patient populations. Finally, while MHCs create an overall beneficial healthcare delivery model, they also are not without limitations. The cost saving previously described also required an initial investment, which may require avenues to obtain this startup funding.[22-25,27] MHCs also must require carefully planned logistics and volunteers to provide equitable care for each location.[23,27] Despite these limitations, there were over 900 MHCs reported on Mobile Health Maps.[27]

CONCLUSIONS

Overall, the journey toward equitable health care will continue to require a multifaceted approach towards its delivery of care. Community level interventions such as MHCs are a promising concept which had unique characteristics that may lessen the burden on the healthcare safety net. This migratory delivery model allowed for greater geographic coverage, improvements in health literacy for both the patient and provider, fiscal impact, and education initiatives. Therefore, further studies to grow the literature on the community effects by MHCs is needed.

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Using the Residency Matched Method and Intent to Practice Method to Estimate Primary Care Workforce Production

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ABSTRACT

Introduction. Many medical schools overestimate the percentage of their graduates who enter the primary care workforce based on the "first-certificate" residency their graduates enter. To rectify this problem, Deutchman and colleagues proposed a new method of estimation. The objective of this study was to compare results from the traditional residency match and Deutchman methods to the actual percentage of University of Kansas School of Medicine (KUSM) graduates who practice primary care after completing medical school and all residency and subspeciality fellowship training.

Methods. A retrospective study was conducted using a convenience sample of KUSM graduates from 2003-2014. Percentages of graduates classified as primary care by the traditional Residency Match Primary Care Method (RMPCM) and the percentages of graduates identified as primary care by Deutchman's Intent to Practice Primary Care Method (IPPCM) were compared with the actual percentage of graduates who eventually entered the primary care workforce.

Results. Of the 1,944 KUSM graduates identified during the study period, the RMPCM predicted a 48.1% primary care output rate. The Deutchman's IPPCM predicted a 22.8% primary care output rate. The actual known percentage of graduates practicing primary care was 34.2%.

Conclusions. Neither the RMPCM nor the Deutchman's IPPCM performed well in predicting the percentage or number of KUSM graduates who eventually practiced primary care. Due to predictions for the shortage of primary care physicians, there is a need to identify a method that more accurately predicts the medical schools' contribution to the primary care workforce. ***Kans J Med 2022;15:262-266***

INTRODUCTION

Public policy leaders have requested an increase in accountability from medical schools and hospitals for their use of Medicare Graduate Medical Education (GME) funding used to train resident-physicians.[1] The Medicare program provides two types of extra funding to hospitals with residency programs. The first intends to offset the direct costs of residency programs, such as faculty salaries and administrative costs. The second provides a financial enhancement to a hospital's Medicare Prospective Payment System reimbursement that is intended to make up for additional patient care costs associated with inefficiencies in training resident-physicians.[2] The magnitude of these two payments is a driving force in the development of the physician workforce in the United States. The design of these payments may contribute to the national shortage of primary care physicians. It has been proposed that the current Medicare GME funding system incentivizes hospitals to preferentially support subspecialty training at the expense of primary care training.[1]

A source of controversy in determining accountability is the method of measuring workforce outcomes from each training program. One measure counts the number of medical school graduates who match into primary care residency programs; primary care generally is defined as family medicine, internal medicine, pediatrics, and medicine-pediatrics. This is known as the RMPCM.[3] However, because of the various subspecialty fellowships that residency graduates may enter after completion of their "first certificate" residency program, the RMPCM measurement magnifies the actual number of medical school graduates who eventually enter primary care practice at the conclusion of all their GME. For example, half of pediatrics residents and well over half of internal medicine residents enter subspecialty fellowships at the conclusion of their "first certificate" residency training.[4,5] Some have called this quandary the "Dean's lie"; double counting a significant number of medical school graduates as both primary care physicians at entry into residency and subspecialty physicians at the conclusion of their fellowship training.[6,7]

Understanding the final outputs of the entirety of the medical education process is important to meeting physician shortage and maldistribution problems. In 2013, Chen et al.[1] demonstrated a new way of determining the ultimate workforce specialty mix at the conclusion of GME training. Using the AMA Masterfile and data from the National Residency Matching Program (NRMP), this method measured a medical school's outputs five years after graduation, when primary care practices generally are established and subspecialty fellowship training has been completed.

Predicting the future primary care workforce and setting public policy on the use of funding for medical education is an important goal. An accurate predictive model based on NRMP match statistics would be useful and efficient and avoid the need to track all graduates of a medical school and determine their specialty-of-practice after completion of all their GME, years after they complete medical school.

In 2020, Deutchman and colleagues proposed another method of GME output measurement by limiting the determination of a medical school's primary care output to the match categories of family medicine, medicine-primary, pediatrics-primary, and medicine-pediatrics.[3] Deutchman and colleagues compared this method (IPPCM) to the traditional RMPCM, then used online resources to confirm the physicians' actual practice specialty at the conclusion of their medical school, residency, and subspecialty fellowship training. Deutchman and colleagues concluded that the new "Intent to Practice Primary Care Method more accurately predicted a medical school's actual primary care output than the Residency Match Primary Care Method".

This study applied the traditional RMPCM, as well as the new IPPCM, to determine the primary care production of graduates from the University of Kansas School of Medicine (KUSM) and compared them to the actual percentage of graduates who practice primary care.

METHODS

A retrospective study was conducted of the RMPCM and the IPPCM using a convenience sample of KUSM graduates. To allow time for completion of residency and entry into practice, physicians who had graduated from medical school between 2003 and 2014 were included, the same time period included by Deutchman and colleagues[3] in their study. The information available to us included the graduate's name, medical school graduation/match year, match specialty, city and state of the matched residency program, and current practice specialty. To determine the actual practice specialties of the physicians at the conclusion of all GME training, several methods were used, including internet resources such as Doximity, LinkedIn, and Google/Yahoo, as well as a residency graduate database available in the Department of Family and Community Medicine on the KUSM-Wichita campus. This was called the Actual Primary Care Method (APCM).

Table 1 outlines the specialties that Deutchman and colleagues[3] defined as primary care for the RMPCM, the IPPCM, and the APCM. Table 1 also includes those specialties that Deutchman and colleagues specifically defined as not primary care. The Deutchman IPPCM calculates primary care output using medical school match categories of family medicine, medicine-primary, pediatrics-primary, and medicine-pediatrics. Board certification in family medicine, internal medicine, and pediatrics through the American Board of Medical Specialties is sometimes referred to as a "first certificate".[8] Physicians with a "first certificate" may indicate that they are board-certified in one of those three primary care specialties. Many subspecialty fellowships require a "first certificate" for subsequent medical subspecialty board certification. In our study, the Deutchman and colleagues' definitions of primary care (Table 1) were used in our calculations of RMPCM and IPPCM.

Standard descriptive statistics were used to describe primary care for the RMPCM, the IPPCM, and the APCM. Chi-square tests were used to compare the proportion of graduates matched to primary care defined by RMPCM, the IPPCM, and APCM. Microsoft Excel and the IBM SPSS (Statistical Package for the Social Sciences; Armonk, NY) version 26 were used for these analyses. The University of Kansas Medical Center Institutional Review Board reviewed and granted an exempt status to the study.

RESULTS

Results of the Residency Match Primary Care Method. As Table 2 shows, data on 1,944 KUSM graduates were included in the study. The RMPCM yielded primary care match rates that ranged from 43.3% to 52.5% per year and an overall 12-year average of 48.1% (935 of 1,944) for the entire study cohort of KUSM graduates (Table 2).

Results of the Intent to Practice Primary Care Method. The new Deutchman and colleagues[3] IPPCM yielded primary care practice rates ranging from 17.1% to 27.9% per year and averaged 22.8% (443 of 1,944) for the entire study cohort of KUSM graduates over 12 years (Table 2).

Results of the Actual Primary Care Method. The practice specialty-of-choice of each KUSM medical school graduate between 2003 and 2014 was identified after completion of their graduate medical education "first certificate" residency and any subspecialty training. Actually practicing primary care was defined as those physicians who met the definition "Actual Primary Care" and who did not meet the definition of "Not Primary Care" (Table 1). Six hundred and sixty-four graduates were identified who ultimately practiced primary care based on the APCM, constituting 34.2% of the entire study cohort of 1,944 KUSM graduates (Table 2). The APCM practice rates ranged from 27.7% to 40.1% per year. We could not identify the primary care status of 3.5% of the entire study cohort.

Comparison of Results from the Three Methods. Twenty-nine percent ([935 - 664] = 271 of 935) of KUSM graduates labeled as primary care by the RMPCM actually were not practicing primary care, overestimating primary care output by 271 physicians or 13.9% (271 of 1,944) of the entire study cohort. Four hundred and forty-three KUSM graduates were labeled as primary care by the Deutchman and colleagues[3] IPPCM, underestimating primary care output by 221 (664 - 443 = 221) physicians or 11.4% (221 of 1,944) of the entire KUSM study cohort. As Table 2 shows, there were statistically significant differences between the overall proportion of graduates matched to primary care based on the RMPCM versus the IPPCM, the RMPCM versus the APCM, and the IPPCM versus the APCM.

Results of "First Certificate" Match Specialties of Physicians Who Actually Practice Primary Care. Table 3 shows the percentage of medical students matching into each NRMP primary care specialty who actually ended up practicing primary care at the conclusion of all of their residency and subspecialty medical education. Family medicine had the highest percentage (93.6%) of "first certificate" residents who actually practiced primary care, based on the APCM (Table 3). Table 4 shows the percentage of each specialty's contribution to the total primary care workforce produced by KUSM over the 12-year study period. A total of 336 family medicine "first certificate" physicians actually practice primary care, constituting 50.6% of the 664-total number of primary care physicians produced by KUSM during the study period (Table 4).

Nearly 76% of pediatrics (categorical) "first certificate" residents actually practice primary care (Table 3), making up a total of 141 (21.2%) physicians contributing to the primary care workforce (Table 4). Almost 47% of internal medicine (categorical) "first certificate" residents actually practice primary care (Table 3), making up a total of 152 (22.9%) physicians (Table 4). Medicine-pediatrics and medicine-primary together contributed less than 6% to the total primary care workforce. Interestingly, no one from a pediatric-primary or medicine-family medicine residency program practicing primary care was identified because few, if any, graduates of KUSM matched into these two graduate medical education programs. When combined, family medicine (50.9%), internal medicine categorical (22.9%), and pediatrics categorical (21.2%) programs contributed nearly 95% of the total primary care workforce produced by KUSM.

Table 1. Definitions of primary care used in this study.

Definitions Used at Entry into Residency after Medical School Graduation		Definitions Used at Time of Entry into Practice after Residency Completion	
Residency Match Primary Care Method	**Intent to Practice Primary Care Method**	**Actual Primary Care**	**Not Primary Care**
• Internal medicine (categorical) • Medicine-primary • Family medicine • Pediatrics (categorical) • Pediatrics-primary • Medicine-pediatrics	• Medicine-primary • Family medicine • Pediatrics-primary Medicine-pediatrics	• Family medicine • General internal medicine • General pediatrics • Medicine-pediatrics • Geriatrics	• Any medical or surgical subspecialty hospitalist • Emergency medicine • Urgent care • Hospice/palliative care

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Table 2. Residency Matched Primary Care Method, Intent to Practice Primary Care Method, and Actual Primary Care Graduates, 2003-2014 (N = 1,944).

Year	Total Graduates	Percentage of all Graduates Identified as Primary Care by Residency Match Primary Care Method	Percentage of all Graduates Identified as Primary Care by Intent to Practice Primary Care Method[¥]	Percentage of All Graduates Who Actually Practice Primary Care[§]	Percentage of Residency Match Primary Care Method Graduates Who Actually Practice Primary Care[€]	Percentage of Intent to Practice Primary Care Graduates Who Actually Practice Primary Care	Percentage Primary Care Status Missing
2003	164	72/164 = 43.9	38/164 = 23.2	49/164 = 29.9	49/72 = 64.8	36/38 = 94.7	4.9%
2004	152	72/152 = 47.4	40/152 = 26.3	53/152 = 37.5	53/72 = 72.2	33/40 = 82.5	4.6%
2005	167	79/167 = 47.3	46/167 = 27.5	57/167 = 34.1	57/79 = 71.6	40/46 = 87.0	6.6%
2006	172	84/172 = 48.8	48/172 = 27.9	59/172 = 34.5	59/84 = 66.7	37/48 = 77.1	3.5%
2007	160	79/160 = 49.4	35/160 = 21.9	51/160 = 32.5	51/79 = 73.8	29/35 = 82.9	3.1%
2008	155	67/155 = 43.2	29/155 = 18.7	43/155 = 27.7	43/67 = 63.2	25/29 = 86.2	3.2%
2009	152	67/152 = 44.1	26/152 = 17.1	47/152 = 30.9	47/67 = 67.1	23/26 = 88.5	5.9%
2010	163	83/163 = 50.9	30/163 = 18.4	60/163 = 37.4	60/83 = 74.1	28/30 = 93.3	4.3%
2011	160	77/160 = 48.1	43/160 = 26.9	52/160 = 33.1	52/77 = 60.4	30/43 = 69.8	1.9%
2012	162	85/162 = 52.5	41/162 = 25.3	64/162 = 39.5	64/85 = 74.1	40/41 = 97.6	1.9%
2013	155	75/155 = 48.4	29/155 = 18.7	56/155 = 36.8	56/75 = 66.2	26/29 = 89.7	1.3%
2014	182	95/182 = 52.2	38/182 = 20.9	73/182 = 40.1	73/95 = 72.6	36/38 = 94.7	1.1%
Total	1,944	935/1,944 = 48.1	443/1,944 = 22.8	664/1,944 = 34.2	664/935 = 71.0	383/443 = 86.5	3.5%

[¥]The difference between the overall proportion of graduates matched to primary care based on the Residency Match Primary Care Method vs the Intent to Practice Primary Care Method was statistically significant (χ^2, $p < .001$).
[§]The difference between the overall proportion of graduates matched to primary care based on the Residency Match Primary Care Method vs the graduates who actually practice primary care was statistically significant (χ^2, $p < .0001$).
[€]The difference between the overall proportion of graduates matched to primary care based the Intent to Practice Primary Care Method vs the graduates who actually practice primary care was statistically significant (χ^2, $p < .001$).

Table 3. Percentage of "first certificate" residency match specialties of physicians who actually practice primary care, 2003-2014.

Match Specialty[a]	Proportion of Match Specialty who Actually Practice Primary Care (N = 935)
Family Medicine	93.6% (336 of 359)
Pediatrics (categorical)	75.8% (141 of 186)
Medicine-Pediatrics	57.4% (31 of 54)
Internal Medicine (categorical)	46.5% (152 of 327)
Medicine-Primary	44.4% (4 of 9)
Pediatrics-Primary	0.0%
Medicine-Family Medicine	0.0%

[a]Number of graduates who matched in "first certificate" residency programs.

Table 4. Contribution of residency match specialties of physicians who actually practice primary care, 2003-2014.

Match Specialty	Contribution of Match Specialty to Actual Primary Care Physician Workforce (N = 664)
Family Medicine	336 (50.6%)
Internal Medicine (categorical)	152 (22.9%)
Pediatrics (categorical)	141 (21.2%)
Medicine-Pediatrics	31 (4.7%)
Medicine-Primary	4 (0.6%)
Pediatrics-Primary	0 (0.0%)
Medicine-Family Medicine	0 (0.0%)

Table 3 demonstrates that 24.2% of pediatrics (categorical) graduates, 42.6% of medicine-pediatrics, and 53.5% of internal medicine (categorial) graduates at KUSM did not practice in primary care. These drop-offs account for the inaccuracy of the RMPCM. On the other hand, not including internal medicine (categorical) programs and pediatrics (categorical) programs in the IPPCM calculation results in an underestimation of primary care output from KUSM. Furthermore, though the total numbers were small, only 44.4% of medicine-primary residents actually practice primary care (Table 3), making up only 0.6% of the primary care workforce in the sample (Table 4).

DISCUSSION

This study aimed to apply two methods of approximating the number and percentages of graduates from KUSM who actually practice primary care after graduation from medical school and after completing all of their GME. By tracking KUSM graduates and determining their specialty-of-practice using internet resources, 34.2% of KUSM graduates actually practiced primary care. The RMPCM overestimated primary care practicing physicians who graduated from KUSM by 13.9% (48.1% vs. 34.2%) while the new IPPCM underestimated the institution's primary care output by 11.4% (22.8% vs. 34.2%). The difference between both the RMPCM and the IPPCM was statistically different from the APCM. Our conclusion was that neither method of approximation provided accurate estimates for our institution.

A total of 93.6% of KUSM graduates who matched into family medicine residency programs actually practiced primary care. The finding that family medicine comprising the greatest percentage (50.6%) of the primary care workforce was in line with findings from previous studies.[1,3]

Data from KUSM were not included in the Deutchman and colleagues[3] original study. Comparing our institution's workforce output to that of the 14 medical schools in the Deutchman and colleagues' study, KUSM would rank first in the percentage of medical school graduates actually practicing primary care. In Chen's analysis of all graduate medical education programs in the country, the University of Kansas School of Medicine-Wichita campus alone ranked sixth nationally in the production of primary care physicians.[1]

This study confirmed that the "double-counting" of the traditional RMPCM contributed to an overestimation of a medical school's contribution to the primary care workforce. On the other hand, the IPPCM underestimated KUSM's contribution to primary care. This latter finding supported results from the Deutchman and colleagues[3] study, which underestimated the primary care workforce production at the majority of the 14 institutions studied. It would appear that including only internal medicine-primary and pediatric-primary residents while excluding internal medicine (categorical) and pediatrics (categorical) residents from the IPPCM was the major reason this method significantly underestimated the primary care workforce production from the KUSM.

A 2016 analysis by the U.S. Department of Health and Human Services estimated a shortage of over 5,000 primary care physicians for the Midwest region by 2025.[9] The need for accurate medical school graduation data is essential to enhance the prediction of the number of physicians who will practice primary care in the future and improve outcomes of GME funding policy decisions. The GME funding policy decisions could drive the necessary increase of the primary care physician workforce to meet societal needs. Unfortunately, neither prediction method used in this study provided an accurate estimation for our institution's contribution to the primary care workforce.

Additional steps are needed to develop new methods of accurate estimation of the future primary care physician workforce. Reliance on a single methodology may be inadequate. Perhaps an average of different methodologies will be required. Our findings showed that the RMPCM provided an overestimation of our institution's production by 13.9%, and the IPPCM underestimated our institution's production by 11.4%. The average of these two methodologies ([{935 + 443}/2] = 689/1,944 = 35.4%) more closely estimated the actual percentage (34.2%) of graduates from our institution practicing primary care. Alternatively, as Deutchman and colleagues[3] suggested, medical schools might develop an adjusted formula for the prediction of their future contributions to the primary care workforce based on historical averages of their institutions.

A limitation of this study was that it examined data over a 12-year period from 2003 through 2014. Repeat analysis that includes more data from more recent years, as it becomes available, will better reflect the percentage and number of graduates actually practicing primary care. Another limitation of the study was the accuracy of the assigned practice specialties that physicians actually were practicing using the search methodologies employed. Additional limitations were that the career pathways of medical students who entered subspecialty

residency programs and switched to primary care at some point during their GME were not followed, nor was the ultimate career pathways of residents who entered transitional or preliminary GME programs tracked, but these probably would have contributed little to overall primary care production.

Tracking the ultimate practice specialty of each graduate from a medical school or residency program is cumbersome and time intensive. An option to determine KUSM primary care production would be to use the AMA Masterfile and data from the NRMP, similar to the Chen methodology[1], but the AMA Masterfile is expensive to access and has limitations of its own. Ultimately, a simple and reproducible method of predicting workforce production would help to determine how institutions are meeting the primary care needs of the country.

CONCLUSIONS

Several methods have been proposed to estimate the percentage and number of medical school graduates who eventually will practice primary care. Our study compared the new IPPCM of Deutchman and colleagues[3] and the traditional RMPCM to the actual percentage of graduates who practice primary care for our institution. Neither method succeeded at closely estimating the primary workforce. More work is needed to find an accurate way to estimate primary care workforce production at KUSM.

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Racial/Ethnic Disparities and Determinants of Sufficient Physical Activity Levels

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ABSTRACT

Introduction. Adequate physical activity is an integral requirement for achieving cardiovascular health. Physical inactivity is the fourth leading cause of death worldwide. Hence, it is important to identify racial/ethnic groups that are less likely to achieve sufficient physical activity levels, and to address barriers to meeting physical activity requirements.

Methods. Cross-sectional data from the 2006-2015 National Health Interview Survey (NHIS) were used to compare self-reported sufficient physical activity among different racial/ethnic groups: non-Hispanic (NH) Whites, NH Blacks, NH Asians, and Hispanics in the United States. Sufficient physical activity was defined as ≥ 150 minutes per week of moderate-intensity physical activity, ≥ 75 minutes per week of vigorous-intensity physical activity, or ≥ 150 minutes per week of moderate and vigorous physical activity.

Results. The study sample consisted of 296,802 individuals, mean age ± standard error age 46.4 ± 0.10 years, 52% women, 70% NH White, 12% NH Black, 5% NH Asian, and 14% Hispanic. The prevalence of sufficient physical activity in the overall population was 46%, while it was 48% among NH Whites, 39% among NH Blacks, 45% among NH Asians, and 40% among Hispanics. In multivariable-adjusted models (odds ratio; 95% confidence interval), NH Blacks (0.79; 0.64,0.97), NH Asians (0.72; 0.62,0.85) and Hispanics (0.71; 0.61,0.82) were significantly less likely to engage in sufficient physical activity compared with NH Whites. Older age, women, and low income were inversely associated with sufficient physical activity, while a college education or higher was associated directly with it.

Conclusions. NH Black and Asian Americans and Hispanic adults were less likely to engage in sufficient physical activity levels compared with Whites. It is important to address barriers to meeting physical activity thresholds to help achieve optimal cardiovascular health.

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INTRODUCTION

There are well known racial/ethnic disparities in cardiovascular disease and cardiovascular risk factors.[1] Adequate physical activity is an integral requirement for achieving cardiovascular health[2,3] and physical inactivity is the fourth leading cause of death worldwide.[4] Hence, it is important to identify racial/ethnic groups that are less likely to achieve sufficient physical activity levels, and to address barriers to meeting physical activity requirements, especially among those with atherosclerotic cardiovascular disease (ASCVD).

A prior study showed that Blacks had a higher odds of physical inactivity compared with Whites even after adjusting for socioeconomic status.[5] However, these results were derived from a relatively small sample size in Baltimore. A study from the 2003-2005 National Health Interview Survey (NHIS) found that Asian Indians were less likely to be physically active compared with Whites, though this did not adjust for acculturation.[6] Another study from the 1998-2008 NHIS using age-adjusted prevalence estimates found that Hispanics were less likely to meet physical activity recommendations compared with Whites, though they did not account for other potential confounders in the association with physical activity.[7]

Herein, racial/ethnic differences in physical activity levels were examined in a more contemporary cohort, attempting to identify sociodemographic and cardiovascular risk factors that were associated with sufficient physical activity.

METHODS

Data were obtained from the 2006-2015 NHIS, a nationally representative health survey that has been conducted continuously since 1957 by the National Center for Health Statistics of the Centers for Disease Control and Prevention.[8] Detailed information on the survey design and methods can be found online: http://www.cdc.gov/nchs/nhis.html. The study was exempt from Institutional Review Board approval since it utilized deidentified data from a publicly available dataset.

All variables were self-reported. Sufficient physical activity was defined according to the 2019 American College of Cardiology/American Heart Association primary prevention of cardiovascular disease guideline as ≥ 150 minutes per week of moderate-intensity physical activity, or ≥ 75 minutes per week of vigorous-intensity physical activity, or ≥ 150 minutes per week of moderate and vigorous physical activity.[2] Race was reported as either White, Black, Asian, or Other, while ethnicity was classified as Hispanic versus non-Hispanic (NH). Race/ethnicity, therefore, was categorized as NH Whites, NH Blacks, NH

Asians, Hispanics, and Other. Asian race was classified further in NHIS as Chinese, Filipinos, and Asian Indians. Participants who identified as Japanese, Vietnamese, Korean, or other Asian subgroups were classified as "Other Asians".

ASCVD was defined as coronary artery disease (history of coronary heart disease, heart attack, or angina pectoris) or stroke (NHIS questionnaire did not have information on type of stroke). Cardiovascular risk factor burden in each participant was calculated as a cumulative cardiovascular risk factor score (0 to 4) based on the presence of hypertension, diabetes mellitus, current cigarette smoking, or hyperlipidemia. U.S. birth was classified as U.S. born versus foreign born. Time spent in the U.S. was categorized as < 10 versus ≥ 10 years.[9]

Study sample characteristics were summarized using mean (standard error) and numbers (weighted percentages) and compared by whether study participants engaged in sufficient physical activity. Study characteristics were stratified further by race/ethnicity.

Logistic regression models were used to study the association of race/ethnicity (NH White as reference group consistent with prior reports from NHIS[6,7]) and sufficient physical activity both in the overall study sample and restricting to individuals with prior ASCVD. Models were adjusted for age, gender, income, education, duration of time spent in the U.S., and cardiovascular risk factor score. To evaluate the determinants of sufficient physical activity in each racial/ethnic group, multivariable adjusted models were used to evaluate the association between each of age, gender, income, education, duration of time spent in the U.S., and cardiovascular risk factor score and sufficient physical activity stratifying by race/ethnicity.

To ascertain differences among NH Asians subgroups, multivariable-adjusted logistic regression models as above were used to study the association of Asian ethnic groups and sufficient physical activity (Chinese as reference given that they have a lower cardiovascular risk factor profile compared with other Asian groups[10]).

All analyses were conducted using Stata version 16.1 (StataCorp, College Station, Texas). A p value < 0.05 was considered statistically significant.

RESULTS

The study sample consisted of 296,802 individuals, mean age ± standard error 46.4 ± 0.10 years, 52% women, 70% NH White, 12% NH Black, 5% NH Asian, 14% Hispanic, and 1% Other. The prevalence of sufficient physical activity in the overall population was 46%, while it was 48% among NH Whites, 39% among NH Blacks, 45% among NH Asians, 40% among Hispanics, and 46% in other racial/ethnic groups (Table 1).

Compared with participants who did not engage in sufficient physical activity, those who did were younger (43 vs. 49 years), more likely to be men (58% vs. 42%), more likely to have college education or higher (54% vs. 46%), and have an annual income > $25,000 (65% vs. 35%). They were less likely to have spent greater than 10 years in the U.S. (40% vs. 60%), or have cardiovascular risk factors including current smoking (39% vs. 61%) diabetes (30% vs. 70%), hypertension (36% vs. 64%), hyperlipidemia (41% vs. 59%), and ASCVD (28% vs. 72%); all p < 0.001 (Table 2). Study characteristics stratified by race/ethnicity are displayed in the Table 1. The prevalence of current smoking was highest among NH Whites and Blacks, and diabetes was most prevalent among NH Asians. Hypertension was most prevalent among NH Blacks, and hyperlipidemia, coronary artery disease, and stroke were most prevalent among NH Whites; all p < 0.001.

Table 1. Baseline characteristics of the study sample stratified by race/ethnicity.*

	NH White (n = 179,239)	NH Black (n = 45,061)	NH Asian (n = 17,318)	Hispanic (n = 51,732)	Other (n = 3,452)	p Value
Age, years	48.4 ± 0.1	43.6 ± 0.2	44.0 ± 0.2	40.3 ± 0.1	42.3 ± 0.4	< 0.001
Women	97,738 (52%)	27,356 (55%)	9,269 (53%)	28,655 (49%)	1,940 (53%)	< 0.001
College education or higher	113,090 (63%)	22,713 (52%)	12,569 (74%)	18,353 (37%)	1,874 (53%)	< 0.001
Annual income > $75,0000	15,199 (16%)	1,550 (7%)	1,906 (23%)	1,487 (6%)	151 (9%)	< 0.001
Greater than 10 years in U.S.	6,755 (81%)	3,237 (72%)	8,835 (72%)	21,784 (76%)	186 (74%)	< 0.001
Sufficient physical activity	85,005 (48%)	16,446 (39%)	7,997 (45%)	19,777 (40%)	1,589 (40%)	< 0.001
Current smoking	36,130 (20%)	9,209 (20%)	1,813 (10%)	6,908 (13%)	976 (27%)	< 0.001
Diabetes	16,141 (8%)	6,242 (12%)	1,358 (8%)	5,221 (9%)	464 (14%)	< 0.001
Hypertension	59,572 (31%)	19,070 (37%)	4,029 (22%)	11,875 (21%)	1,159 (32%)	< 0.001
Hyperlipidemia	24,402 (29%)	4,793 (22%)	1,819 (24%)	4,600 (20%)	394 (23%)	< 0.001
Coronary artery disease	14,724 (7%)	3,104 (6%)	659 (3%)	2,344 (4%)	257 (7%)	< 0.001
Stroke	5,846 (3%)	2,020 (4%)	291 (2%)	1,052 (2%)	126 (3%)	< 0.001
ASCVD	18,081 (9%)	4,349 (8%)	821 (4%)	2,956 (5%)	337 (9%)	< 0.001

*Continuous variables are presented as mean ± standard error and categorical variables are presented as count (weighted row percentages). Abbreviations: NH (non-Hispanic), ASCVD (atherosclerotic cardiovascular disease).

Table 2. Baseline characteristics of the study sample stratified by sufficient physical activity.*

	Insufficient Physical Activity (n = 165,988; 54%)	Sufficient Physical Activity (n = 130,814; 46%)	Overall (n = 296,802)	p Value
Age	49.0 ± 0.1	43.3 ± 0.1	46.4 ± 0.1	< 0.001
Women	98,273 (58%)	66,685 (42%)	164,958	< 0.001
Race				< 0.001
NH White	94,234 (52%)	85,005 (48%)	179,239	
NH Black	28,615 (61%)	16,446 (39%)	45,061	
NH Asian	9,321 (55%)	7,997 (45%)	17,318	
Hispanics	31,955 (60%)	19,777 (40%)	51,732	
Other	1,863 (54%)	1,589 (46%)	3,452	
College education or higher	78,462 (46%)	90,137 (54%)	168,599	< 0.001
Annual income > $75,0000	6,984 (35%)	13,309 (65%)	20,293	< 0.001
Greater than 10 years in U.S.	24,896 (60%)	15,901 (40%)	40,797	0.03
Current smoking	33,911 (61%)	21,125 (39%)	55,036	< 0.001
Diabetes	21,139 (70%)	8,287 (30%)	29,426	< 0.001
Hypertension	62,772 (64%)	32,933 (36%)	95,705	< 0.001
Hyperlipidemia	21,991 (59%)	14,017 (41%)	36,008	< 0.001
Coronary artery disease	15,422 (71%)	5,666 (29%)	21,088	< 0.001
Stroke	7,277 (77%)	2,058 (23%)	9,335	< 0.001
ASCVD	19,523 (72%)	7,021 (28%)	26,544	< 0.001

*Continuous variables are presented as mean ± standard error and categorical variables are presented as count (weighted row percentages) Abbreviations: NH (non-Hispanic), ASCVD (atherosclerotic cardiovascular disease).

Table 3. Multivariable-adjusted[f] odds ratio (95% confidence interval) for the association of risk factors and sufficient physical activity by race/ethnicity.*

	NH White (n = 179,239)	NH Black (n = 45,061)	NH Asian (n = 17,318)	Hispanic (n = 51,732)	Other (n = 3,452)
Age, years	**0.984 (0.975,0.995)**	**0.980 (0.966,0.994)**	0.991 (0.981,1.001)	**0.982 (0.976,0.988)**	0.932 (0.857,1.012)
Women	0.88 (0.68,1.14)	**0.51 (0.35,0.73)**	**0.77 (0.64,0.92)**	0.87 (0.75,1.00)	0.75 (0.17,3.35)
College education or higher	**2.04 (1.48,2.82)**	**2.00 (1.40,2.85)**	**2.20 (1.69,2.87)**	**1.93 (1.65,2.26)**	2.37 (0.37,15.25)
Annual Income					
< $25,000	**0.63 (0.44,0.89)**	0.91 (0.47,1.73)	**0.69 (0.52,0.92)**	**0.44 (0.29,0.65)**	0.22 (0.01,5.89)
$25,000-$45,000	**0.48 (0.34,0.67)**	0.89 (0.47,1.68)	0.82 (0.63,1.08)	**0.50 (0.34,0.75)**	1.11 (0.01,147.0)
$45,000-$75,000	**0.71 (0.53,0.95)**	1.10 (0.54,2,23)	0.82 (0.61,1.10)	0.80 (0.52,1.22)	0.34 (0.01,12.19)
> $75,000	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
Greater than 10 years in the U.S.	1.14 (0.80,1.63)	1.04 (0.71,1.55)	**1.42 (1.08,1.87)**	1.16 (0.97,1.38)	3.63 (0.41,32.50)
Cardiovascular risk factor score**	1.09 (0.97,3.01)	1.01 (0.60,5.09)	1.04 (0.93,1.17)	0.96 (0.89,1.03)	1.09 (0.37,3.22)

[f]The above covariates were all present in the adjusted model.
*Abbreviations: NH (non-Hispanic). Bold items have significant p value.
**Cardiovascular risk factor burden score was based on the presence of hypertension, diabetes mellitus, current cigarette smoking, and hyperlipidemia and ranged from 0 to 4

In multivariable-adjusted models (odds ratio; 95% confidence interval), NH Blacks (0.79; 0.64,0.97), NH Asians (0.72; 0.62,0.85) and Hispanics (0.71; 0.61,0.82) were significantly less likely to engage in sufficient physical activity compared with NH Whites (Table 3). There were no significant racial/ethnic differences among those with ASCVD (results not shown).

Older age was inversely associated with sufficient physical activity among NH Whites and Blacks and Hispanic adults. NH Black and NH Asian women were less likely to engage in sufficient physical activity compared with men. A college education or higher was associated with higher likelihood of sufficient physical activity in all racial/ethnic group except in the "Other" group. Low annual income was associated inversely with sufficient physical activity except among NH Blacks and "Other" groups. There was a statistically significant association between living longer than 10 years in the U.S. and sufficient physical activity only among NH Asians (1.42; 1.08,1.87; Table 3).

Among NH Asians, 21% were Asian Indians, 20% were Chinese, 23% were Filipinos, and 36% were of another Asian ethnicity. In multivariable-adjusted models restricting to NH Asian individuals, there were no significant differences in odds of sufficient physical activity in Asian ethnic groups compared with Chinese (results not shown).

DISCUSSION

In a contemporary and representative sample of U.S. individuals (the majority of whom were NH White), less than half of U.S. adults engaged in sufficient physical activity. NH Black, NH Asian, and Hispanic adults were less likely to engage in sufficient physical activity compared with NH Whites. These differences persisted after adjusting for sociodemographic factors and cardiovascular risk factor burden. Older individuals, women, and those with low income were less likely to engage in sufficient physical activity levels, while educated individuals were more likely to be physically active.

The present study found that less than half of U.S. adults engage in sufficient physical activity. This was more pronounced among racial/ethnic minority groups including NH Blacks, Asians, and Hispanics who have a high burden of cardiovascular risk factors and ASCVD.[1] There were no significant differences in physical activity levels among those with ASCVD, though this analysis was likely underpowered. In addition to establishing clear guidance on physical activity thresholds that are necessary to achieve optimal cardiovascular health, it also was important to account for racial disparities and other barriers to achieving sufficient physical activity. Physical activity guidelines should acknowledge these cultural and socioeconomic factors in making their physical activity recommendations.

Physical activity should be addressed at each outpatient visit and adherence to activity recommendations should be reinforced for prevention of ASCVD. Clinicians and other healthcare providers also should consider tailoring their health recommendations to each patient's unique culture and their prevailing socioeconomic conditions. This will require training in culture-specific care where healthcare recommendations are delivered in a manner that is congruent with the values and lifestyles of a patient's specific culture. Prior research has shown the utility of a patient-centered culturally sensitive health care model for improving health care among ethnically diverse patients.[11] This may be especially important for recommendations pertaining to lifestyle habits such as diet, exercise, physical activity, tobacco, and alcohol intake.

Ethnic-specific research on values and preferences regarding lifestyle can inform culturally-sensitive recommendations. For example, a prior study of physical activity among South Asians in Scotland found that men were more likely to go to the gym and play football while women were more likely to walk and swim.[12] Both groups reported external motivators for taking part in physical activity such as social activity, enjoyment, weight reduction, and improving physical and mental health. Few respondents reported undertaking in physical activity for its own sake. Understanding which forms of physical activity are popular in a patient's culture and what are the barriers and motivators for physical activity will help patients be more engaged and adhere to lifestyle recommendations.

The South Asian heart lifestyle intervention (SAHELI) pilot study[13] and South Asians Active Together (SAATH; NCT04400253) trial were designed as culturally-targeted, community-based lifestyle intervention to improve physical activity and other lifestyle habits among South Asians. For example, South Asian women previously cited concerns about modesty gender norms, and lack of role models as reasons for not exercising. Therefore, men and women in SAHELI will exercise separately and participate in culturally-tailored exercise activities. Similarly, a randomized trial showed the effectiveness of pharmacist-led interventions among barbershop Black male patrons for reducing blood pressures in those with uncontrolled hypertension.[14]

The present analysis found that NH Black adults were less likely to engage in sufficient physical activity compared with NH Whites even after adjusting for income. A prior study found that Black individuals tended to be more physically inactive than Whites, but when adjusted for socioeconomic status, this difference was small.[5] However, that study was done in one low-income suburb in southwest Baltimore and cannot be extrapolated to a national level, as other studies have shown that physical activity varies significantly by geographical location.[15] In a prior study from NHIS, Black women were less likely to report physical activity compared with White women.[16] Black individuals may be more likely to work during non-conventional work hours and have less time to exercise or engage in physical activity.[17] Access to neighborhood greenspace and walkability, and crime also were potential contributors.[18]

Ye et al.[6] found that among Asian ethnic groups, only Asian Indians were more likely to report physical inactivity compared with Whites. In our study, all Asian American individuals were less likely to report sufficient physical activity compared to White Americans. There were no significant differences in physical activity comparing Asian ethnic groups to Chinese in the present study. Differences in physical activity among Asian Americans may be driven in part by acculturation, social and cultural norms, rigid gender roles, and difficulty defining mainstream approaches to physical activity.[19] In the present study, Asian Americans who lived in the U.S. longer than 10 years were more

likely to engage in sufficient physical activity. A previous study found similar results showing increased physical activity levels amongst third-generation Asian immigrants compared with their first-generation counterparts.[20] This could be due to an increased percentage of English speakers with each generation resulting in greater exposure to information and American social norms that promote physical activity.

In the current study, Hispanic adults were less likely to engage in sufficient physical activity compared with Whites. In a prior study from NHIS, Hispanic women were less active compared with White women.[16] In another study of Hispanic adults from South Texas, both Hispanic men and women were less likely to engage in physical activity compared with their NH White counterparts.[21] The most frequently reported barriers included "lack of time", feeling "very tired", and "lack of self-discipline" to exercise. Latino communities tended to live in areas with fewer parks, less access to recreational facilities, unsafe infrastructure, and higher crime rates.[22] Physical activity levels among Hispanic adults also were heterogenous depending on country of origin.[23]

By examining potential barriers and facilitators of physical activity, data from this study can inform large scale public, economic, and healthcare policy and guidelines to increase physical activity levels. Improving pedestrian infrastructure can be achieved by creating bicycle lanes, landscaping, pedestrian overpass or underpass, sidewalks, trails, or shared-use paths, and importantly signage to improve pedestrian safety. Subsidizing gym memberships may incentivize people to join the gym. Workplace wellness initiatives through tax credits and grants also can encourage physical activity to, from, and at the workplace.[24,25] Health insurance plans and employers may offer cash incentives to individuals who are physically active. Offering wearable fitness trackers also may help individuals meet their physical activity targets.[26]

The present results should be interpreted in the context of important limitations. All our variables were self-reported and may be prone to measurement error and recall bias. However, previous studies have shown that there was a high concordance between self-reported and objectively measured physical fitness.[27] There was no information on risk factors control. Small sample size likely underpowered our analysis to detect significant differences among those with prior ASCVD. As in any observational study, residual confounding may exist despite multivariable adjustment.

In conclusion, NH Black and Asian Americans and Hispanic adults were less likely to engage in sufficient physical activity levels compared with Whites. It is important to address barriers to meeting physical activity thresholds to help achieve optimal cardiovascular health.

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Epidermal Growth Factor Receptor Inhibitor Treatment Timing does not Impact Survival in Stage 4 Colon Cancer Treatment: A Retrospective Study

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ABSTRACT

Introduction. Colon cancer impacts the lives of Kansans and those across the United States. Epidermal growth factor receptor (EGFR) inhibitors, such as panitumumab and cetuximab, have gained popularity as first-line treatment for stage 4 colon cancer despite their toxicities and have been used by clinicians in later lines of therapy. EGFR inhibitors have been proven to be an efficacious first-line treatment for stage 4 colon cancer, but no study has investigated outcomes comparing EGFR inhibitors as first-line treatment to its use as second- or third-line treatment. This study investigated EGFR inhibitor therapy estimated overall survival when used as first-, second-, and third-line treatment for stage 4 colon cancer.

Methods. A retrospective review was done for patients with stage 4 colon cancer who underwent EGFR inhibitor treatment at a large academic center from November 2007 to August 2021. The patients were stratified into five groups by the line in which they received the EGFR inhibitor treatment. A log-rank test was used to analyze the groups, and the median survival for each group was determined.

Results. A total of 68 patients were reviewed; 18 received first-line, 23 received second-line, 18 received third-line, 6 received fourth-line, and 3 received sixth-line treatment with an EGFR inhibitor. Fourth- and sixth-line therapies were excluded due to small patient size. There was no significant difference in estimated survival time between any of the lines. Median survival of the therapies was found.

Conclusions. There was no statistical difference in survival between the first-, second-, or third-line groups, which may provide justification for its use as a second- or third-line therapy.

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INTRODUCTION

Colon cancer is the third leading diagnosis and cause of cancer death in Kansas and is expected to take 608,570 lives in the United States by the end of 2021.[1,2] Of the 1,300 new diagnoses each year in Kansas, half are diagnosed as late-stage. The Kansas Cancer Registry reported that colon cancer takes the lives of 500 Kansans annually and disproportionally impacts rural Kansans compared to those living in urban areas.[2] Rural Kansas has an increased total incidence, late-stage incidences, and mortality of colon cancer, and rural counties make up the highest incidences and mortality of colorectal cancer compared to their urban counterparts. Knowing the treatment efficacies for new chemotherapies for late-stage colon cancer and their justification for use in later lines of treatment is important for Kansas providers to understand.

Epidermal growth factor receptor (EGFR) inhibitors, such as panitumumab and cetuximab, have gained popularity as first-line treatment for KRAS wild type stage 4 colon cancer since the findings in several randomized control trials.[3-6] Other papers have found that EGFR inhibitors improve patient outcomes, such as progression free survival, overall survival, and tumor response rate, and recommend its use in stage 4 KRAS wild type colon cancer.[7-11] EGFR inhibitors commonly are combined with other chemotherapies and these regimens have shown positive patient outcomes.[8,12-22] EGFR inhibitors and KRAS screening have shown a cost benefit due to its effectiveness as a therapy by limiting chemotherapy changes.[23-27] This treatment was associated with many side effects, especially skin toxicity, that both the patient and all physicians on the care team must be aware of and its impact on patient's quality of life before starting and during treatment.[7,8,28-36] If these toxicities are not handled appropriately it can delay treatment.[35,37] There was no previous research that compared the patient outcomes of EGFR inhibitors in first-line to its use in later lines. Due to the large number of late colon cancer diagnoses in Kansas and EGFR inhibitors side effect profile and impact on the patient's quality of life, it is beneficial to understand if patient outcomes differ when prescribed as a first-line compared to a later line therapy.

This study compared the estimated overall survival from time of diagnosis of patients who received EGFR inhibitors as first-, second-, and third-line treatment for stage 4 colon cancer. This study investigated the justifications for the use EGFR inhibitor therapy in later lines. Due to its risk of toxicity and possibility of delayed treatment, its use in later lines may not outweigh the benefit of EGFR inhibitor therapy. One potential implication of this study was guiding the decision to consider, or not consider, selecting EGFR inhibitor as later line therapy and developing a better understanding of its efficacy in later lines.

METHODS

The Institutional Review Board approved a retrospective chart review on stage 4 colon cancer patients at our academic medical center. The initial lists of patients for screening were collected using a list of all patients who received EGFR inhibitor treatments cetuximab or panitumumab over the study's time period. Patients were divided into groups 1, 2, 3, 4, and 6 depending on which line they received cetuximab or panitumumab for their stage 4 colon cancer treatment. The study size was determined by the maximum number of patients who qualified for the study on this list. Patients who underwent treatment with cetuximab or panitumumab for stage 4 colon cancer and were at least 18 years of age were included. Patients with KRAS, NRAS, or BRAF mutations or those who did not undergo APC and TP53 testing were excluded. Chart reviewing was used to gather clinical information about the patients and reports from Next-Generation Sequencing (Illumina Inc., San Diego, CA, USA, 2021) and Caris Molecular Intelligence® (Caris Life Sciences, Irving, TX, USA, 2021) were used to determine KRAS, NRAS, BRAF, APC, and TP53 status.

Demographics collected included age, ethnicity, weight, height, medical comorbidities, and residence. The Eastern Cooperative Oncology Group (ECOG) Performance Status Scale at the time of starting EGFR inhibitor treatment was recorded. Dates of initial colon cancer diagnosis and stage 4 diagnosis, right or left tumor location, surgery dates, metastases, cancer's response to chemotherapy, date of recurrence or progression, date of last follow-up, and date of expiry was collected. First-, second-, and third-line chemotherapy regimens, start and end dates, and the number of cycles for each chemotherapy used were recorded. Fourth- and sixth-line chemotherapy were recorded when the therapy consisted of EGFR inhibitor use. "First-line" chemotherapy in this study was described as the first chemotherapy regimen the patient underwent after their stage 4 chemotherapy diagnosis. Overall survival was collected for patients and is defined as the length of time the patient is alive from the start of their initial treatment for metastatic colorectal cancer until date of last follow-up, and/or date of expiry. Overall survival is referred to as "survival" throughout the paper. The term "later-lines" in this paper referred to therapies after the "first-line" regimen. Research Electronic Data Capture (REDCap®) tools were used to collect the data.[38]

There was no protocol in the decision to start or discontinue the chemotherapy lines. The oncologist determined the chemotherapy regimens and number of cycles for each line. Some patients underwent EGFR inhibitor therapy concurrently with other chemotherapy drugs. Multiple oncologists treated the patients in this study.

Descriptive statistics were provided using the start date of EGFR inhibitor regimen, date of last follow-up, and/or date of expiry. Patients were divided into groups depending on which line they received the EGFR inhibitor. Appropriate data determined by a statistician was censored for analysis. Survival estimates for each EGFR inhibitor line was determined. Each EGFR inhibitor line was stratified and compared to one another using a log-rank test. The Chi-square test was used to find associations between the EGFR inhibitor treatment lines. Median survival for each EGFR inhibitor line was calculated for completeness. A p value greater than 0.05 was considered statistically significant. SAS v9.4 (Copyright 2002-2012 by SAS Institute Inc., Cary, NC, USA) was used to analyze data.

RESULTS

A total of 239 patients received cetuximab or panitumumab and these patients were reviewed. Of these 239 patients, 68 patients met the qualification for the study; 38 patients were observed and 30 were censored for statistical analysis. No significant difference of demographics, ECOG Performance Status Scale, and tumor location was found between each line of the patients reviewed. Demographics, ECOG Performance Status Scale, and tumor location are summarized in Table 1. There was a total of 18 patients who received EGFR inhibitor as a first-line therapy. Of these patients, 9 were observed and 9 were censored. The second-line group had a total of 23 patients; 13 patients were observed and 10 were censored. The third-line group had 18 total patients; 10 patients were observed and 8 were censored. The fourth-line group had a total of 6 patients (4 observed and 2 censored) and the sixth-line group had a total of 3 patients (2 observed and 1 censored). Total patients per EGFR inhibitor line and censor status is summarized in Table 2. The survival estimates for each EGFR inhibitor line is shown in Figure 1. The median survival of the groups was 1,444 days for the first-line group, 1,196 days for the second-line group, 1,402 days for the third-line group, 1,395 days for the fourth-line group, and 2,235 days for the sixth-line group. Median survival for each line is summarized in Table 3.

No patients were lost to follow-up during their EGFR inhibitor treatment. All lines of stage 4 therapy received at outside institutes were recorded. All start and stop dates and chemotherapy line number for EGFR inhibitor therapy were recorded. No patients were still receiving EGFR inhibitor treatment at the conclusion of the study. There were 27 patients still living at the conclusion of this study.

There was no significant difference in survival time between first- and second-lines ($p = 0.8639$), first- and third-lines ($p = 0.5239$), first- and fourth-lines ($p = 0.6380$), first- and sixth-lines ($p = 0.8223$), second- and third-lines ($p = 0.6755$), second- and fourth-lines ($p = 0.8239$), second- and sixth-lines ($p = 0.6649$), third- and fourth-lines ($p = 0.7462$), third- and sixth-lines ($p = 0.2870$), and fourth- and sixth-lines ($p = 0.3462$). The fourth- and sixth-lines sample sizes were very small and were considered unreliable for this study. Additional statistical information is shown in Table 4.

DISCUSSION

Stage 4 colon cancer is devastating and greatly impacts the lives of many in Kansas and in the U.S.[1,2] Fortunately, new chemotherapies, such as cetuximab and panitumumab, have shown positive patient outcomes.[3-22] EGFR inhibitors have shown to have severe toxicities which can influence the patient's quality of life and may affect the decision to begin treatment with these medications.[7,8,28-37] Inferior patient outcomes of EGFR inhibitor treatment in later lines might be an important determinant for the decision to choose a different chemotherapy to avoid the risk of these toxicities and potential treatment delays. It is also important for clinicians to have justifications for the use of EGFR inhibitors in later lines. This study demonstrated that there was no statistically significant change in estimate survival for patients receiving EGFR inhibitor therapy first-line compared to second- or third-line and clinicians may have justification for using these therapies as a third-line treatment.

This study showed that EGFR inhibitors may provide similar patient survival when used as second- or third-line therapy as it would first-line, and provided additional support for its clinical use as a third-line treatment option. The PRIME and PEAK randomized control trials have shown the effectiveness of first-line EGFR inhibitor use in metastatic colon cancer.[3,5] EGFR inhibitor use for metastatic colon cancer also has been shown to be effective in the treatment for metastatic colon cancer and is used as a third-line option by clinicians.[39-42] With findings similar to the first-line line patients, this study provided further justification for its use as a third-line treatment option.

The toxicities of EGFR inhibitors are well documented.[7,8,28-37] The toxicity profile EGFR inhibitors can evolve depending on the time and duration of its use, and can impact multiple organ systems.[43-45] Although

this study showed patients may have similar survival in later line treatments compared to first-line, accumulation toxicity of the therapy may impact the justifications for its use in later lines. Clinicians using EGFR inhibitors as a third-line treatment strongly should consider the accumulation toxicity.

Healthcare value should be considered when deciding on therapy. EGFR inhibitors reduced health care costs due to the decreased need to change therapy.[23-27] This study suggested that the healthcare value might be similar for first-, second, and third-line EGFR inhibitor use. Later line treatment may be beneficial to smaller treatment centers. Patients and physicians should consider this when they are deciding on using EGFR inhibitors as second- or third-line therapy.

This study had limitations. A larger patient population with less censored data would provide stronger evidence for this study. Although this study had only 68 total patients, the total number of patients and number of patients censored were distributed evenly throughout the groups. Performing a study with a controlled number of EGFR inhibitor cycles per patient along with controlling for any additional concurrent chemotherapy medications used in the patients' treatment would provide additional evidence that the EGFR inhibitor was impacting the patients' survival. This follow-up study would be difficult to conduct due to the unique treatment regimen every patient receives due to cancer response and change of medication due to patients' toxicities. This study was unable to adjust for prior lines of treatment for second- and third-lines, and we acknowledge that this impact places limitations on the results. Follow-up studies with larger studies with a more structured chemotherapy regimen at different institutions would increase external validity for our findings. Additional studies should continue to investigate how the side effect profile or toxicity frequency changes in later lines of EGFR inhibitor therapy, as this will impact its justification for its use in later lines. Despite its limitations, this study may provide justification for the use of cetuximab and panitumumab as a second- or third-line treatment for stage 4 KRAS, NRAS, and BRAF wild type colon cancer.

Table 1. Patient demographics, ECOG Performance Status Scale, and tumor location.

Characteristic	Statistic/Category	First Line	Second Line	Third Line	Overall	p Value
Number of Subjects	N	18	23	18	59	
Age	Mean	53.2	52.3	51.7	52.4	0.9351
	Std. Dev.	11.60	12.59	14.34	12.66	
	Median	53.5	52.0	49.5	52.0	
	Min, Max	32, 72	26, 69	27, 77	26, 77	
Sex [N (% of Column)]	Male	11 (61.11)	16 (69.57)	13 (72.22)	40 (67.80)	0.7547
	Female	7 (38.89)	7 (30.43)	5 (27.78)	19 (32.20)	
Ethnicity [N (% of Column)]	Hispanic	0	1 (4.35)	2 (11.11)	3 (5.08)	0.3096
	Non-Hispanic	18 (100.0)	22 (95.65)	16 (88.89)	56 (94.92)	
Race [N (% of Column)]	White	17 (94.44)	20 (86.96)	15 (83.33)	52 (88.14)	0.5683
	Asian	1 (5.56)	2 (8.70)	0	3 (5.08)	
	Other	0	0	1 (5.56)	1 (1.69)	
	Unknown	0	1 (4.35)	2 (11.11)	3 (5.08)	
Smoker [N (% of Column)]	Yes	6 (33.33)	8 (34.78)	7 (38.89)	21 (35.59)	0.9299
	No	11 (61.11)	14 (60.87)	10 (55.56)	35 (59.32)	
	Unknown	1 (5.56)	1 (4.35)	1 (5.56)	3 (5.08)	
ECOG Status [N (% of Column)]	0	8 (44.44)	12 (52.17)	9 (50.00)	29 (49.15)	0.8003
	1	10 (55.56)	10 (43.48)	8 (44.44)	28 (47.46)	
	Unknown	0	1 (4.35)	1 (5.56)	2 (3.39)	
Tumor Location [N (% of Column)]	Right	15 (83.33)	19 (82.61)	15 (83.33)	49 (83.05)	1.0000
	Left	3 (16.67)	4 (17.39)	3 (16.67)	10 (16.95)	

Table 2. Total patients per line.

Line	Total Patients	Observed Patients	Censored Patients	Percent Censored
First-Line	18	9	9	50.00
Second-Line	23	13	10	43.48
Third-Line	18	10	8	44.44
Fourth-Line	6	4	2	33.33
Sixth-Line	3	2	1	33.33
	68	38	30	44.12

Table 3. Median estimate survival.

Line	Estimate Survival (Days)
First-Line	1444.00
Second-Line	1196.00
Third-Line	1402.00
Fourth-Line	1395.50
Sixth-Line	2235.00

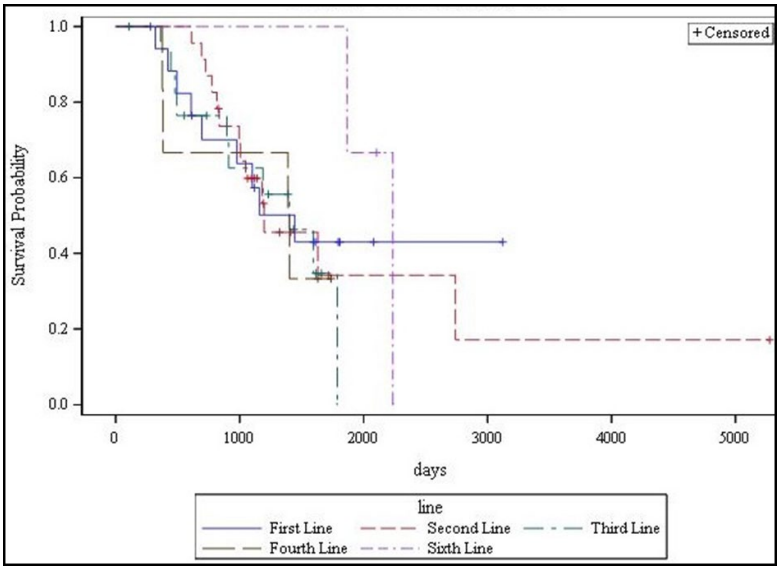

Figure 1. Product-limit survival estimates.

Table 4. Line survival comparison.

Strata Comparison		Chi-Square	p Values	
Line	Line		Raw	Tukey-Kramer
First-Line	Second-Line	0.0294	0.8639	0.9998
First-Line	Third-Line	0.4062	0.5239	0.9690
First-Line	Fourth-Line	0.2214	0.6380	0.9900
First-Line	Sixth-Line	0.0505	0.8223	0.9994
Second-Line	Third-Line	0.1752	0.6755	0.9936
Second-Line	Fourth-Line	0.0495	0.8239	0.9995
Second-Line	Sixth-Line	0.1876	0.6649	0.9927
Third-Line	Fourth-Line	0.1048	0.7462	0.9976
Third-Line	Sixth-Line	1.1337	0.2870	0.8246
Fourth-Line	Sixth-Line	0.8872	0.3462	0.8805

CONCLUSIONS

The EGFR inhibitors cetuximab and panitumumab used as a second- or third-line treatment may provide similar patient survival compared to its use as first-line therapy. No statistically significant difference in estimated survival was found when they were used as a first-, second-, or third-line therapy. This information may provide justification for EGFR inhibitors use as a second- or third-line treatment options for stage 4 KRAS, BRAF, and NRAS wild type colon cancer, although clinicians should continue to account for the changes in toxicity profile of the treatment.

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Preventive Care Utilization among Rural versus Urban Women 12 Months Prior to Pregnancy

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ABSTRACT

Introduction. Pregnancy-related mortality in the United States occurs in 32.3 per 100,000 live births. Rural maternal mortality rates were even higher, and these patients were less likely to receive routine care. The purpose of this cross-sectional study was to compare primary and prenatal care and health behaviors among perinatal mothers living in rural and urban Kansas.

Methods. Data were collected from 1,971 pregnant women who participated in Phase 8 Pregnancy Risk Assessment Monitoring System (PRAMS) for Kansas between 2016 and 2018. Respondent location (urban or rural based on NIH classification) was abstracted from birth certificates and frequencies of healthcare visits and secondary healthcare variables were compared.

Results. Most respondents (75.1%, n = 1,481) resided in an urban area. Most (84.4%, n = 1,664) women were Caucasian, and the largest category (31.1%, n = 613) was 25 to 29 years old. More urban women reported visiting an obstetrician/gynecologist within 12 months before pregnancy than rural women ($p < 0.0001$). Urban women reported attending pre-pregnancy dental visits ($p = 0.019$) and teeth cleanings ($p = 0.004$) more than rural women. Of the 35.7% of respondents (n = 516) who reported receiving pre-pregnancy counseling on folic acid, prenatal vitamins, or multivitamins, 78.9% (n = 407) resided in an urban area.

Conclusions. Rural women reported fewer routine primary and prenatal care behaviors compared to their urban counterparts. Efforts are needed to improve access to obstetrician/gynecologist services, especially for women in rural areas. ***Kans J Med 2022;15:278-284***

INTRODUCTION

Pregnancy-related mortality in the U.S. occurred in 32.3 per 100,000 live births between 2003 and 2016.[1] The leading causes of pregnancy-related mortality within this timeframe have been documented as cardiovascular as the leading cause at 15.5% of all deaths, followed by pre-existing chronic illnesses (14.5%), infection (12.7%), hemorrhage (11.4%), and cardiomyopathy (11.0%).[2] The majority of these causes are considered preventable with routine primary and prenatal care.[1,2] The proportion of chronic disease states (e.g., heart disease, obesity, hypertension) causing pregnancy-related death have notably increased compared to traditional pregnancy-related mortality causes, such as hemorrhage and thromboembolism.[2]

Women in rural areas with chronic conditions were more likely to have high-risk pregnancies and perinatal complications, and be less likely to receive vaccinations or take prenatal vitamins.[3-11] Women in rural areas also had higher rates of adolescent birth (49 vs. 27 per 1,000 live births) than their urban counterparts.[4] Moreover, rural patients were less likely to have "regular or routine" care in the 12 months leading up to conception compared to urban patients in one state, but other states have limited data on patient care uptake.[3] Despite a push in the 1980s to increase prenatal care focus, many women presented for prenatal care when most fetal organs have been formed and the interventions that can prevent adverse outcomes may be too late to benefit.[12]

There are limited U.S. data regarding rural maternal health outcomes and behaviors, and even fewer data in Kansas regarding rural and urban differences in perinatal utilization of primary and prenatal care. The purpose of this study was to compare the use of primary and prenatal care among perinatal mothers in rural and urban Kansas communities and determine the frequency of health behaviors (e.g., attending health visits, teeth cleanings before delivery, prenatal vitamin use, vaccinations, family planning) that could be impacted by primary and prenatal care.

METHODS

Participants. This study utilized data from Phase 8 (2016 to 2018) of the Kansas Pregnancy Risk Assessment Monitoring System (PRAMS).[12] Kansas PRAMS identified and collected data from women who have had a delivery in the past two to six months based on state birth certificates.[13,14] Every month, Kansas PRAMS conducted stratified random sampling of 140 mothers from the Kansas Vital Statistics Birth Certificate File to complete the questionnaire.[14] The PRAMS questionnaire administered to patients are a series of questions of categorical variables that is completed based on patient recall of their care from prenatal to postnatal period. Infants born with weight less than 2,500 grams were over-sampled compared to normal birth weight to gain sufficient data on this sub-group. Mothers were mailed PRAMS questionnaires up to three times. If there was no response via mail, telephone interviewers attempted to reach them. Survey data were weighted by the U.S. Centers for Disease Control and Prevention (CDC) to adjust for sampling, nonresponse, and non-coverage.[14] The PRAMS report statistics were reported as weighted estimates to account for sampling rates. Some participants did not answer every question of the survey; blank items were excluded from the report. No exclusion criteria were identified.

Instrument. The PRAMS database was developed by the CDC and included approximately 83% of all births in the U.S.[13] PRAMS abstracted the independent variable, respondent location (e.g., rural, urban), from newborn birth certificates based on county of residence at the time of birth. The definition of rurality was based on the National Center for Health Statistics' 2013 Urban-Rural six-tiered classification scheme.[15] Kansas PRAMS grouped large fringe metropolitan (1 million or more), medium metropolitan (250,000-999,999), and small metropolitan (49,999-249,999) counties as "urban" while micropolitan and noncore (less than 49,000) counties were coded as "rural".[14] The 10 outcome variables were centered around the use of primary

and perinatal healthcare visits [e.g., general healthcare, obstetrics and gynecology (OB/GYN), prenatal care visits, dental care visits, family planning visits, influenza vaccination counseling/receipt] as these variables have been reported as improving maternal outcomes.[2-4,6-9]

Additional variables included the coexistence and management of chronic conditions (e.g., diabetes, hypertension), substance use (e.g., tobacco, alcohol, illicit drugs), birth control use, sexually transmitted infection testing (e.g., HIV, hepatitis), potential abusers (e.g., partner, ex-partner, family member), and receipt of general counseling from a healthcare provider (e.g., recommendation for folic acid use, tobacco cessation). Breastfeeding duration and frequency also were analyzed in relation to the primary outcomes.

Procedures. This project was identified as "not human subjects" research by the local Human Research Protection Program. De-identified Phase 8 PRAMS data were requested from the CDC collected via self-assessment questionnaire or through telephone surveys. If no response was received, the state PRAMS team conducted a phone call to complete the questionnaire. Questionnaire responses were stored in an electronic database and made accessible to researchers via requests to the CDC.

Statistical Analysis. Data analyses were conducted with SAS 9.4 (SAS® Int. Inc., Cary, NC) using survey analysis procedures such as SURVEYFREQ, SURVEYMEANS, and SURVEYLOGISTIC to overcome complex survey structures, those rendering traditional procedures not useful for analysis. Descriptive statistics were presented as means and standard deviations for continuous variables (i.e., age), and proportions and frequencies for categorical variables (e.g., education level). Rao-Scott chi-square test, the Rao-Scott likelihood ratio test analyses were conducted to identify relationships associated with respondent characteristics and uptake of primary and prenatal care services. Multiple logistic regression analyses were used to analyze respondents' characteristics across study groups. Taylor series (linearization) method was used to estimate the covariance matrix of the regression coefficients. All statistical tests were two sided, and p values ≤ 0.05 were considered statistically significant.

RESULTS

Demographics. A total of 1,971 Kansas women completed the survey, most of whom (75.1%, n = 1,481) resided in an urban area. Most respondents were Caucasian (84.4%, n = 1,664), and the highest frequency of respondents, 31.1% (n = 613), were in the 25 to 29 years old age category (Table 1). The largest proportional difference in age between urban and rural women was in the 20 to 24-year category, with 24.1% (n = 118) of rural women reporting in this age range compared to 16.3% (n = 241) of urban women. Most women reported being married (67.4%, n = 1,329). More rural women acknowledged paternity of their child (84.5%, n = 147), compared to urban women (75.8%, n = 355; [$\chi^2(1, N = 642) = 5.54$]; p = 0.0186).

Table 1. Demographics of PRAMS survey respondents.

	Participants, n (%)			
Variable	**Urban n (%) n = 1,481**	**Rural n (%) n = 490**	**Overall n (%) N = 1,971**	**p Value**
Age				< 0.0001
≤ 17 years	14 (0.9)	4 (0.8)	18 (0.9)	
18-19 years	57 (3.8)	29 (5.9)	86 (4.4)	
20-24 years	241 (16.3)	118 (24.1)	359 (18.2)	
25-29 years	453 (30.6)	160 (32.7)	613 (31.1)	
30-34 years	476 (32.1)	119 (24.3)	595 (30.2)	
35-39 years	200 (13.5)	53 (10.8)	253 (12.8)	
40+ years	40 (2.7)	7 (1.4)	47 (2.4)	
Race				< 0.0001
White	1161 (79.3)	456 (93.1)	1617 (84.0)	
Black	152 (10.4)	8 (1.6)	160 (8.3)	
Other	80 (5.5)	10 (2.0)	90 (4.7)	
Asian/Native Hawaiian American Indian/ Alaska Native	54 (3.7)	3 (0.6)	57 (3.0)	
Marital Status				0.1094
Married	1013 (68.4)	316 (64.5)	1329 (67.4)	
Other	468 (31.6)	174 (35.5)	642 (32.6)	
Acknowledgement of Paternity*				0.0186
Yes	355 (75.9)	147 (84.5)	502 (78.2)	
No	113 (24.1)	27 (15.5)	140 (21.8)	
Place of Delivery				0.976
Hospital	1458 (98.4)	481 (98.2)	1939 (98.4)	
Birthing Center	15 (1.0)	6 (1.2)	21 (1.1)	
Other	5 (0.3)	2 (0.4)	7 (0.4)	
Residence	3 (0.2)	1 (0.2)	4 (0.2)	
Income 12 months before pregnancy				0.0008
$0 to $20,000	326 (27.5)	90 (35.4)	448 (31.1)	
$20,001 to $40,000	314 (26.5)	28 (11.0)	437 (30.4)	
$40,001 to $60,000	77 (6.5)	36 (14.2)	298 (20.7)	
$60,001 to $85,000	95 (8.0)	35 (13.8)	265 (18.4)	
More than $85,000	373 (31.5)	65 (25.6)	438 (30.4)	

Data are presented as n (%). Totals may not add up to 100% due to missing values.
*Variable only captured in P7 version of PRAMS.

Primary Outcomes: Healthcare Visits. A pre-pregnancy visit with an OB/GYN in the 12 months before pregnancy was more common in urban women (57.2%, n = 606) than rural women (44.1%, n = 149; [χ^2(1, N = 1,398) = 17.7]; p < 0.0001; Table 2). Urban women more commonly had pre-pregnancy dental visits (65.4%, n = 690) compared to rural women (58.3%, n = 198), and teeth cleanings (47.8%, n = 704) than their rural counterparts (40.4%, n = 196; [χ^2(1, N = 1,394) = 5.4]; p = 0.019 and [χ^2(1, N = 1,959) = 7.9]; p = 0.004, respectively). Urban mothers reported receiving an influenza vaccine before delivery (66.2%, n = 992) more than rural mothers (62.0%, n = 297; [χ^2(1, N = 1,934) = 6.3]; p = 0.042). More urban women participated in postpartum check-ups for themselves (91.5%, n = 1,340) than rural women (89.3%, n = 434; [χ^2(1, 1,951) = 2.07]; p = 0.15 (non-significant)), for an overall postpartum visit participation of 90.9% (n = 1,774).

Table 2. Primary outcomes: Healthcare visits.*

Variable	Urban Frequency n (%)	Rural Frequency n (%)	Overall Frequency n (%)	p Value
Pre-pregnancy OB/GYN visit	606 (57.2)	149 (44.1)	755 (54.0)	< 0.0001
Teeth cleaned during pregnancy	704 (47.8)	196 (40.4)	900 (45.9)	0.004
Pre-pregnancy visit with a dentist	690 (65.4)	198 (58.3)	888 (63.7)	0.019
Influenza vaccine received before delivery	992 (66.2)	297 (62.0)	1,289 (66.7)	0.042
Other pre-pregnancy healthcare visit	212 (20.1)	54 (3.9)	266 (19.1)	0.11
Postpartum check-up for self	1,340 (91.5)	434 (89.3)	1,774 (90.9)	0.149
Pre-pregnancy healthcare visit with a doctor	537 (50.2)	156 (46.0)	693 (49.2)	0.18
Pre-pregnancy healthcare visit	1,038 (52.9)	333 (16.9)	1,371 (69.9)	0.35
Pre-pregnancy healthcare visit for family planning/ birth control	209 (19.8)	60 (17.9)	269 (19.4)	0.46

*Data are presented as n (%). Some totals may not add up to 100% due to missing values.

Mental Health, Abuse, and Health Behaviors. During the pre-pregnancy visit interview, a minority of all women (45.9%, n = 664) reported being asked about emotional or physical abuse, with urban women reporting a higher frequency (50.7%, n = 540) than rural women (35.3%, n = 124; [χ^2(1, N = 1,447) = 20.8]; p < 0.0001; Table 3). A minority of women (48.1%, n = 695) reported being asked about feeling down or depressed before pregnancy; 50.3% (n = 551) of urban women were asked and 41.1% (n = 144) of rural women were asked ([χ^2(1, 1,444) = 9.03]; p = 0.0026). Women (35.7%, n = 516) reported counseling to take folic acid, prenatal vitamins, or multivitamins, with 37.1% (n = 407) of urban women reporting being counseled and 31.3% (n = 109) of rural women reporting receiving counsel on vitamin use. Depression and abuse reported during pregnancy were similar between demographics (Table 4).

Table 3. Topics discussed during pre-pregnancy health visits.*

Variable	Urban Frequency n (%)	Rural Frequency n (%)	Overall Frequency n (%)	p Value
Asked about emotional/physical abuse	540 (50.7)	124 (35.3)	664 (45.9)	< 0.0001
Asked if down/ depressed	551 (50.3)	144 (41.1)	695 (48.1)	0.0026
Asked if smoking cigarettes	826 (75.3)	246 (69.7)	1072 (73.9)	0.0368
Folic acid counseling	407 (37.1)	109 (31.3)	516 (35.7)	0.0512
Tested for HIV	238 (22.2)	63 (18.1)	301 (21.2)	0.1009
Expressed desire to have children	487 (44.4)	143 (41.0)	630 (43.6)	0.2618
Birth control use to prevent pregnancy	381 (35.0)	111 (31.7)	492 (34.2)	0.2662
Asked about type of work	660 (60.4)	200 (57.3)	860 (59.6)	0.3076
Counseling to control medical conditions	131 (12.0)	45 (12.9)	176 (12.2)	0.6349
Recommendation to improve health before pregnancy	280 (25.7)	88 (24.9)	363 (25.5)	0.7829
Discussion about STIs	197 (18.1)	62 (17.8)	259 (18.0)	0.8907
Weight counseling	343 (31.3)	109 (31.1)	452 (31.2)	0.9323

*Data are presented as n (%). Some totals may not add up to 100% due to missing values.

Table 4. Health problems during pregnancy.*

Variable	Urban Frequency n (%)	Rural Frequency n (%)	Overall Frequency n (%)	p Value
Depression	269 (18.4)	93 (19.3)	362 (18.6)	0.6663
Diabetes	141 (9.4)	48 (9.9)	189 (9.7)	0.8436
Hypertension	296 (20.1)	98 (20.2)	394 (20.1)	0.9682
Abuse by partner	25 (1.7)	11 (2.3)	36 (1.8)	0.4192
Abuse by ex-partner	17 (1.2)	7 (1.5)	24 (1.2)	0.6122
Abuse by another family member	10 (0.6)	6 (0.3)	16 (0.8)	0.2323

*Data are presented as n (%). Some totals may not add up to 100% due to missing values.

Prenatal healthcare outcomes included 70.4% (n = 1,355) of women being asked if they were experiencing emotional or physical abuse during pregnancy, with urban women (73.2%, n = 1,060) being asked more than rural women (62.0%, n = 295; [χ^2(1, N = 1,925) = 21.5]; p < 0.0001; Table 5). Most respondents (87.5%, n = 1,705) were offered information on an influenza shot during pregnancy; more urban women (89.0%, n = 1,307) reported having been offered the vaccine compared to rural women (82.7%, n = 398), χ^2(1, N = 1,949) = 13.08, p < 0.001. Most women (76.6%, n = 1,480) were asked if they were feeling down or depressed during pregnancy with more urban women (78.1%, n = 1,137) being asked compared to rural women (71.9%, n = 343), [χ^2(1, N = 1,933) = 7.65], p = 0.0057.

Table 5. Prenatal health characteristics and counseling.*

Variable	Urban Frequency n (%)	Rural Frequency n (%)	Overall Frequency n (%)	p Value
Asked if emotionally/ physically abused	1,060 (73.2)	295 (62.0)	1,355 (70.4)	< 0.0001
Received influenza vaccine information	1,307 (89.0)	398 (82.7)	1,705 (87.5)	0.0003
Asked if feeling down/depressed	1,137 (78.1)	343 (71.9)	1,480 (76.6)	0.0057
Asked if drinking alcohol	1,386 (95.3)	451 (94.2)	1,837 (95.0)	0.3373
Asked if respondent wanted HIV test	736 (51.0)	232 (49.2)	968 (50.6)	0.4765
Asked if planning to use postpartum birth control	1,135 (78.1)	367 (76.5)	1,502 (77.6)	0.4804
Asked if planning to breastfeed	1,336 (91.8)	446 (92.7)	1,782 (92.0)	0.4988
Asked if using drugs	1,163 (80.2)	377 (78.9)	1,540 (79.9)	0.5273
Weight gain counseling	836 (43.3)	283 (14.7)	1,119 (58.0)	0.6269
Prenatal counseling - asked if smoking	1,403 (96.2)	460 (95.8)	1,863 (96.1)	0.7477
Prenatal counseling - prescription medications	1,428 (98.1)	470 (97.9)	1,898 (98.0)	0.8263
Intention to become pregnant				0.6867
Later	264 (18.1)	97 (20.4)	361 (18.7)	
Sooner	231 (15.9)	73 (15.3)	304 (15.7)	
Then	667 (45.8)	221 (46.4)	888 (46)	
Did not want then or any time	88 (6.10)	23 (4.83)	111 (5.8)	
Was not sure	205 (14.1)	62 (13.03)	267 (13.8)	
Prenatal vitamin use in last three months of pregnancy				0.2534
Every day of the week	542 (36.77)	167 (34.2)	709 (36.1)	
4-6 times/week	116 (7.9)	30 (6.1)	146 (7.4)	
1-3 times/week	101 (6.9)	31 (6.3)	132 (6.7)	
Didn't take any vitamin	715 (48.5)	261 (26.7)	976 (49.7)	

*Data are presented as n (%). Some totals may not add up to 100% due to missing values.

Of postpartum visit variables (Table 6), 52.5% (n = 931) of women were asked about abuse, with urban women (55.0%, n = 739) reporting being asked more compared to rural women (44.8%, n = 192; [χ^2(1, N = 1,772) = 13.76]; p = 0.0002). Most women (83.9%, n = 1,487) reported being asked about depression at their postpartum visit, with urban women (85.0%, n = 1,142) being asked more compared to rural women (80.4%, n = 345; [χ^2(1, N = 1,773) = 4.98]; p = 0.026). A minority (25.4%, n = 498) of women reported smoking one or more cigarettes in the last two years, with more rural women (29.9%, n = 146) having smoked compared to urban women (23.7%, n = 352; [χ^2(1, N = 1,947) = 7.09]; p = 0.008).

Table 6. Topics discussed during postpartum health visits.*

Variable	Urban Frequency n (%)	Rural Frequency n (%)	Overall Frequency n (%)	p Value
Asked about abuse	739 (55.0)	192 (44.8)	931 (52.5)	0.0002
Tested for diabetes	222 (16.6)	48 (11.3)	270 (15.3)	0.0084
Asked about depression	1,142 (85.0)	345 (80.4)	1,487 (83.9)	0.0257
IUD/Implant inserted	296 (22.2)	75 (17.6)	371 (21.1)	0.0414
Diet and exercise counseling	659 (49.1)	231 (53.7)	890 (50.3)	0.0985
Birth control methods counseling	1,159 (86.4)	358 (83.5)	1,517 (85.7)	0.1339
Asked about smoking cigarettes	758 (56.6)	230 (54.1)	988 (56.0)	0.3673
Birth control prescribed	537 (40.2)	178 (41.5)	715 (40.5)	0.626
Pregnancy spacing counseling	619 (46.2)	203 (47.3)	822 (46.4)	0.675
Birth control use already	1,191 (81.4)	388 (80.5)	1,579 (81.1)	0.6774
Folic acid counseling	764 (57.1)	240 (56.2)	1,004 (56.9)	0.7336

*Data are presented as n (%). Some totals may not add up to 100% due to missing values.

Breastfeeding and Birth Control. At the time of this survey, 60.5% (n = 1,061) of women reported they currently were breastfeeding and fewer urban women (90.39%, n = 1,283) reported breastfeeding at any time than rural women (97.9%, n = 460; [χ^2(1, N = 1,932) = 5.94]; p = 0.0148; Table 7). A minority of women (21.1%, n = 371) reported having an intrauterine device inserted or birth control implant at their postpartum visit, with more urban women (22.2%, n = 296) reporting this compared to rural women (17.6%, n = 75; [χ^2(1, N = 1,761) = 4.16]; p = 0.0414). An overall of 40.5% (n = 715) of women were prescribed birth control at their postpartum visit, with 40.2% (n = 537) of urban women receiving prescription birth control compared to 41.5% (n = 178; [χ^2(1, N = 1,766) = 0.24]; p = 0.626) of rural women. Folic acid counseling was received by 56.9% (n = 1,004) of women, with 57.1% (n = 764) of urban women reporting receiving postpartum counseling compared to 56.2% (n = 240) of rural women ([χ^2(1, N = 1,764) = 0.116]; p = 0.734).

Table 7. Postpartum health characteristics and outcomes.*

Variable	Urban Frequency n (%)	Rural Frequency n (%)	Overall Frequency n (%)	p Value
Previous preterm births	55 (3.7)	29 (5.9)	84 (4.3)	0.036
Health problem - Diabetes	74 (5.0)	21 (4.3)	95 (4.9)	0.534
Health problem - Hypertension	111 (7.6)	34 (7.0)	145 (7.4)	0.694
Health problem - Depression	279 (18.9)	103 (21.1)	382 (19.4)	0.295
Health problem - Anxiety	400 (27.1)	138 (28.4)	538 (27.4)	0.57
Length of baby's hospital stay				0.0004
Not born in hospital	13 (0.9)	7 (1.5)	20 (1.0)	
<1 day	39 (2.7)	21 (4.4)	60 (3.1)	
1-2 days	580 (39.9)	241 (49.9)	821 (42.4)	
3-5 days	407 (28.0)	98 (20.3)	505 (26.1)	
6-14 days	153 (10.5)	45 (9.3)	198 (10.2)	
More than 14 days	243 (16.7)	68 (14.1)	311 (16.1)	
Infant living with mom	1,380 (98.2)	460 (97.9)	1,840 (98.1)	0.703
Breastfeeding - Ever	1,283 (90.3)	429 (90.7)	1,712 (90.4)	0.794
Breastfeeding - Still	802 (60.9)	259 (59.1)	1,061 (60.5)	0.502
Breastfeeding duration				0.918
Less than 1 week	62 (10.5)	18 (9.4)	80 (10.2)	
Weeks	256 (43.2)	83 (43.5)	339 (43.2)	
Months	275 (46.4)	90 (47.1)	365 (46.6)	
Depression level since birth of child				0.645
Never	468 (32.3)	146 (30.5)	614 (31.8)	
Rarely	500 (34.5)	176 (36.8)	676 (35.1)	
Sometimes	358 (24.7)	108 (22.6)	466 (24.2)	
Often/Almost Always	99 (6.8)	39 (8.2)	138 (7.2)	
Always	25 (1.7)	9 (1.9)	34 (1.7)	
Loss of interest/pleasure in things usually enjoyed since birth of child				0.826
Never	588 (40.1)	187 (38.5)	775 (39.7)	
Rarely	429 (29.2)	154 (31.8)	583 (29.8)	
Sometimes	303 (20.7)	93 (19.2)	396 (20.3)	
Often/Almost Always	103 (7.0)	35 (7.2)	138 (7.1)	
Always	44 (3.0)	16 (3.3)	60 (3.1)	

*Data are presented as n (%). Some totals may not add up to 100% due to missing values.

DISCUSSION

The current study's sample was representative of Kansas women.[16] Although the overall proportion of respondents and the proportion of urban respondents who reported seeing an OB/GYN in the 12 months before pregnancy was comparable to national data, the overall proportion of rural women who reporting seeing an OB/GYN was lower, suggesting rural women may be receiving inadequate care than is recommended for women of reproductive age in the American College of Obstetrics and Gynecology (ACOG) guidelines.[17,18] Additionally, despite a high proportion of reported general healthcare visits in our study, the proportion of visits with a doctor or OB/GYN was considerably lower among the rural population. Unfortunately, this disparity may explain rural respondents low reporting frequencies of being asked and counseled pre-pregnancy, prenatally, and postnatally about emotional or physical abuse, feeling down or depressed, and being asked about their smoking status.

Depression is a significant issue that poses a variety of problems which can impact pregnancy and infant outcomes.[19] Almost one-fifth of the respondents in our study reported depression during pregnancy. Depression before delivery and before pregnancy has been associated with preterm birth, low-birth weight, and postnatal emotional problems for the mother. Our study suggested women are asked about depression more frequently postnatally than before pregnancy or prenatally. Furthermore, rural women maintained significantly lower proportions of depression screening compared to urban women. Although the frequency of reported depression during pregnancy was similar between rural and urban women, it was unclear if patients would be aware of the nuances of possible depression without having had any screening. However, our study demonstrated not only the continued need for depression screening prenatally, but furthermore, rural women continued to report less preventive screening than their urban counterparts.

Despite high rates of influenza vaccination before delivery, the rural cohort had a significantly lower proportion reporting vaccination. Influenza virus is a significant threat to the pregnant mother and her fetus,[6] and influenza vaccination confers protection against complications. Multiple studies have sought to determine why vaccination uptake among pregnant women has remained low; the most common reason appeared to be the lack of vaccine being mentioned or recommended by physicians.[7-9,18] Our study suggested most women in Kansas reported receiving information about influenza vaccinations prenatally, but still report lower vaccination uptake. More information may be needed to discover why rural patients were not receiving information or vaccinations as often as their urban counterparts. Given the wide availability and acceptance of influenza vaccination, it is worth improving vaccination efforts in rural areas, and Kansas providers serving rural communities may provide insight into better rural vaccination strategies.

Despite obvious differences in preventive care and counseling between urban and rural women, there were some similarities and opportunities to improve care for both demographics of women. A history of emotional and physical abuse coincided with being low income and having an unwanted pregnancy and multiple health problems during pregnancy.[20,21] While similar proportions of rural and urban women reported abuse during pregnancy, fewer than half

reported being asked prior to their pregnancies, and, more concerning, the frequency of women being asked about abuse was even lower during the postpartum visit. This indicated a particular need to focus on abuse screening, especially before and after pregnancy. Additionally, few women reported being counseled about taking folic acid, multivitamins, or prenatal vitamins before and after their pregnancies despite the need and recommendation by ACOG for folic acid supplementation for all women of reproductive age. Adequate intake gave significant risk reduction of fetal neural tube defects, such as spina bifida and anencephaly, the latter of which is often fatal to the child.[5,18] Similarly, prenatal vitamin use also was associated with lower miscarriage rates.[18] Nearly half of respondents reported not taking any folic acid, prenatal vitamin, or multivitamin supplement during the last three months of their pregnancy indicating a significant area of risk for complications during pregnancy and for the infant postnatally. Further effort by providers to assess and promote nutritional status perinatally must be encouraged.

In this study, 38% reported they did not want to be pregnant at the time they were or were unsure if they wanted to be pregnant, which was lower than the national unintended pregnancy proportion of 45%.[18] However, fewer rural women reported discussing birth control or family planning during pre-pregnancy, and even fewer were asked about birth control methods or were prescribed birth control postpartum. Given that unintended pregnancy and closely spaced pregnancy can increase risk for pregnancy complications and mortality, and was associated with a high rate of abortion, providers must dedicate more time to address family planning, birth control, and pregnancy spacing with their patients.[17,22] Our study findings showing a discrepancy between rural and urban women in terms of postpartum family planning indicated there are opportunities for providers to discuss and assist rural women with family planning and future care during postpartum visits.

While most of women visited a dentist in the 12 months before pregnancy, fewer than half received teeth cleaning during their pregnancy. Rural women visited the dentist and received teeth cleanings significantly less than urban mothers. Poor dental health has been associated with negative outcomes during pregnancy, and the physiologic changes experienced by mothers leave them susceptible to poor dental health, which can have a negative impact on their own well-being after pregnancy.[23] The most common barrier to dental care was cost, and with more rural women reporting an income of less than $16,000 per year, it may be more apparent that cost would be a barrier. Supporting the need to prioritize dental care also falls on healthcare providers. While it has been cited that physicians appear to be well-informed about the importance of dental care perinatally, their practice of referring newly pregnant patients to receive dental care has been poor.[24]

This study's findings were limited by the nature of survey-collected data with recall biases being possible, as respondents answered questions regarding healthcare visits occurring as far as 27 months prior. Phase 8 PRAMS did not collect in-depth information regarding rurality factors such as access to healthcare (e.g., distance traveled for care, appointment availability, provider types in area), which prevented researchers from speculating further causes outside of the healthcare practices that may result in disparity of care, such as social determinants of health. Additionally, rurality was determined by residence at time of delivery, though respondents could have moved between rural and urban locations during the data collection window which might confound the results.

While this study utilized PRAMS data specific to Kansas, the disparities between rural and urban populations in some state-to-state and national reviews seemed to support the trends found in Kansas.[3-4,7] Future studies should attempt to use the PRAMS database in multi-state analyses to ascertain if the same outcomes remain when applied to larger populations.

CONCLUSIONS

Rural women reported fewer routine primary and prenatal care behaviors compared to their urban counterparts. Efforts are needed to encourage rural women to partake in preventive health behaviors, access OB/GYN and physician services, and help narrow the gap between care disparities between urban and rural populations. Further information must be explored to determine if access to healthcare is playing a substantial role in lower proportions of healthcare and health behavior uptake in Kansas, or if characteristics of rural populations like distance to healthcare services, play a unique role in preventive health behaviors. The method in which PRAMS asked respondents about the care visits gave the ability to evaluate the care that was being received by urban and rural women and determine their effectiveness.

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Rural and Urban Ecologies of Early Childhood Toxic Lead Exposure: The State of Kansas, 2005 to 2012

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ABSTRACT

Introduction. No safe detectable level of lead (Pb) exists in the blood of children. Until recently, U.S. Centers for Disease Control and Prevention (CDC) guidelines designated a blood lead level (BLL) ≥ 5 µg/dL as an elevated BLL (EBLL). For the State of Kansas, early childhood blood lead burdens lack reporting in the literature.

Methods. Secondary analysis was conducted of passively reported EBLL rates ≥ 5 µg/dL among children ages 0 - 5 years at the zip code-level in Kansas during 2005 to 2012. Data weights using corresponding population estimates were applied to produce statewide outcomes.

Results. Statewide estimates of annual testing coverage in Kansas among children ages 0 - 5 years were low (9.7%). Approximately 17,000 children ages 0 - 5 years developed an EBLL ≥ 5 µg/dL each year in Kansas with a 6.9% statewide EBLL rate compared to the national rate of 3.2% for the corresponding years. Significant variations in EBLL rates were found between suburban zip codes compared to urban, urban cluster, or rural at 3.1%, 7.2%, 8.8%, and 10.0%, respectively. Among the worst outcomes in EBLL rates was observed for zip codes in southeast Kansas (13.5%) and rural areas with < 500 persons (15.1%).

Conclusions. Young children in Kansas had twice the risk of developing an EBLL ≥ 5 µg/dL compared to the national rate, while higher rates consistently were seen outside of the suburbs and particularly in more rural and less populated areas. At-risk children and troubled areas of toxic lead exposure in the State of Kansas require increased recognition with improved targeting and interventions.

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INTRODUCTION

Lead (Pb) is a soft, dull gray-colored metal that poses significant systemic and neurotoxic properties that particularly are pronounced among young children.[1] Even at lower levels, exposure to lead during early childhood can result in a variety of negative outcomes to attention, behavior, cognition, decision-making, intellect, memory, and mental health.[2-14] Lead-induced neurotoxicity in children primarily impacts the cerebellum, hippocampus, and prefrontal cerebral cortex.[15] Decreased brain volume and lower structural brain integrity is found in adults with greater lead exposure during childhood.[16-18] Developing infants are the most vulnerable to lead and suffer more exposure in part from their comparatively greater body surface area, higher heart and respiratory rates, ingestion and inhalation of contaminated dust or soil from greater hand-to-mouth activity, pica, floor-level sitting and crawling, and low stature to the ground where lead dust settles.[19]

There has been a significant reduction of the early childhood blood lead burden from an average 16 µg/dL during 1976 to 1980 to a historic low of 2 µg/dL during 2007 to 2010 as a result of public health policies and interventions.[20-24] The CDC previously designated a blood lead level (BLL) ≥ 5 µg/dL as an elevated BLL (EBLL),[20] which recently was revised down to 3.5 µg/dL.[25] However, both the CDC and the American Academy of Pediatrics (AAP) officially recognize that there is no safe level of lead exposure or amount of lead in the blood of children.[26,27] In particular, there is a measurable loss of grade school intelligence quotient (IQ) points even with BLLs beginning at 2 µg/dL during the first two years of life.[4,14] Other negative outcomes associated with early childhood blood lead below the 5 µg/dL EBLL threshold include greater risk of attention-deficit/hyperactivity disorder (ADHD)-like symptoms,[28] childhood anemia and decreasing iron status,[29] and lower math and reading test scores in school.[30] In the U.S., billions of dollars a year in costs are estimated just from lost IQ points alone from early childhood lead exposure and present with significant racial disparities that disproportionately impact Black children as a result of greater amounts of lead exposure.[31]

For the State of Kansas, there is a paucity of published literature examining historical and ongoing lead hazards in the environment, in addition to burdens of lead exposure among the population. Only two descriptive studies published in the state medical and nursing journals for Kansas in 1993 and 1994, respectively, have assessed the early childhood blood lead burden in the state.[32,33] More recent research by the CDC in 2015 found that workers in Kansas ages 16 years and older have the second highest rate of an EBLL ≥ 10 µg/dL at 77.3 in 100,000 persons, followed by the State of Missouri with 106.7 in 100,000.[34] Two other studies of lead exposure in Kansas published in 1999 and 2016 examined early childhood BLLs and observed positive associations with increasing concentrations of soil contamination or anthropogenic lead emissions resulting from industrial activity.[35,36] Therefore, recent descriptions of the childhood blood lead burden in Kansas were lacking.

In 2016, the Reuters news agency reported that thousands of locales in the U.S. were experiencing early childhood EBLL rates that exceeded those which occurred in Flint, Michigan at the peak of its water crisis between 2014 and 2016.[37] The following year, Reuters published data for the State of Kansas after it was disclosed to the news agency. Therefore, these data were utilized to conduct an investigation of Kansas for the years of 2005 to 2012.

METHODS

Study Sample. Data of blood lead testing provided to Reuters were retrieved in their national reporting,[37] which originally were obtained from various state health departments and the CDC. For the State of Kansas, this included an eight year survey period between 2005 and 2012 of children ages 0 - 5 years. Tests for blood lead were reported

passively by providers to the Kansas Department of Health and Environment (KDHE), which discloses the data for the total number of overall tests and the total number of EBLL cases at the zip code-level. The KDHE uses CDC guidelines to identify an EBLL ≥ 5 µg/dL by rounding to the first decimal place and using values 4.5 µg/dL or higher.[20] However, the KDHE suppressed data for zip codes reporting > 0 but < 5 total tests or EBLL cases as a result of privacy concerns. Similar to other states, early childhood blood lead testing primarily involves an initial capillary blood test that typically is followed by a subsequent whole blood venous to confirm an EBLL identified via capillary testing. When multiple blood lead tests exist for an individual case in a given year, the highest blood lead value is identified, while other results are removed to prevent multiple entries in reporting. Lastly, nationwide reporting was retrieved for children ages 1 - 5 years from the 2005 to 2012 National Health and Nutrition Examination Survey (NHANES), which is a nationally-representative cross-sectional survey (www.cdc.gov/nchs/nhanes.htm).[38]

Geographic Designations. Zip codes in Kansas were categorized by their most populous city. Individual zip codes within multiple counties were designated to the county where the largest proportion of their population resided. Zip codes were categorized as either suburban, urban, urban cluster, or rural. As shown in Figure 1, urbanized metropolitan areas and urban clusters were defined using official designations from the 2010 census for the State of Kansas.[39] Urban zip codes included the three major urban cities of Kansas City, Topeka, or Wichita. Suburban designation was reserved for all other remaining zip codes within urbanized areas, in addition to the cities of Lawrence and Manhattan. Urban cluster cities are smaller urbanized capitals throughout the rest of Kansas that serve as the county seats for their respective counties, although not every county in the state has an urban cluster. Rural zip codes were designated as any other remaining zip codes that did not match one of the three aforementioned criteria. Lastly, the KDHE defines six different regions within the state along county lines. Zip codes were assigned to each region corresponding to their designated county.

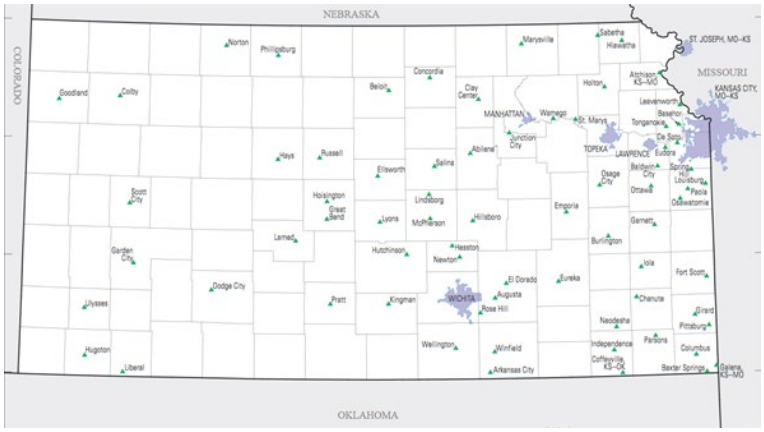

Figure 1. Urbanized metropolitan areas (dark blue) and urban cluster cities (green triangles) in the State of Kansas, 2010 census (US Census Bureau, 2012).

Statistical Design and Analysis. Early childhood EBLL rates were derived by dividing the total number of EBLL-positive cases by the total number of overall tests for each zip code. To produce statewide estimates, EBLL rates were weighted by total population estimates of children 0 - 5 years of age. Population weights were constructed by using five year estimates of the total population (all ages) for each zip code from the American Community Survey (ACS), which involved the survey years of 2015 to 2019 as a result of limited data availability. To construct childhood population weights, total population estimates were multiplied by the percentage of the population accounted for by children ages 0 - 5 years within each county corresponding to the zip code as reported from the 2010 census.[39] As previously mentioned, the KDHE suppressed the reporting of data when a zip code has > 0 but < 5 blood lead tests and/or EBLL cases over privacy concerns. To address this issue, data imputation was performed using a uniform distribution of values {1, 2, 3, 4} that conferred equal probability to each number being retrieved for suppressed data. Suppressed EBLL cases were not imputed for zip codes in which the total number of blood lead tests also had been suppressed, which were treated as unavailable data. Annual blood lead testing coverage was determined from multiplying estimated population totals for children 0 - 5 years of age by the eight survey years and dividing total BLL tests by that figure, while three zip codes were set to 100% as a result of exceeding that value. Simple regression analysis was used to assess linear trends while statistical significance was determined by a p value ≤ 0.05 for all testing.

RESULTS

Descriptive Statistics. As shown in Figure 2, unsuppressed data for blood lead testing rates were available from 662 zip codes (95.4%) and demonstrated a low average rate of testing statewide at 11.8%. Data including imputation for rates of an EBLL ≥ 5 µg/dL were available from 655 zip codes (94.4%) that included 45 suburban, 50 urban, 82 urban cluster, and 478 rural areas. As shown in Table 1, these examined zip codes represented an estimated 247,320 children 0 - 5 years of age (99.7%) residing in the State of Kansas in a given year. Within these zip codes, there was a total of 192,474 individual blood lead tests passively reported to the KDHE over the eight year survey period. Among the included blood lead tests, there were a total of 15,937 EBLL-positive cases at an 8.3% EBLL rate. A total of 635 EBLL-positive cases were imputed for 261 zip codes with suppressed data involving an estimated 22,449 children ages 0 - 5 years. There were seven zip codes with no blood lead testing involving an estimated 135 children ages 0 - 5 years, in addition to 32 zip codes with unavailable data as a result of suppressed data for both blood lead tests and EBLL-positive cases involving an estimated 628 children ages 0 - 5 years.

Weighted Outcomes. Weighted estimates for children ages 0 - 5 years were produced for blood lead outcomes among zip codes. As shown in Table 2, an estimated 16,928 EBLL-positive cases occurred each year in Kansas with an early childhood EBLL rate at 6.9% compared to the national rate at 3.2% produced from the NHANES data for the corresponding years of 2005 to 2012. Therefore, young children in the State of Kansas had more than twice the risk of developing an early childhood EBLL than their peers at the national level.

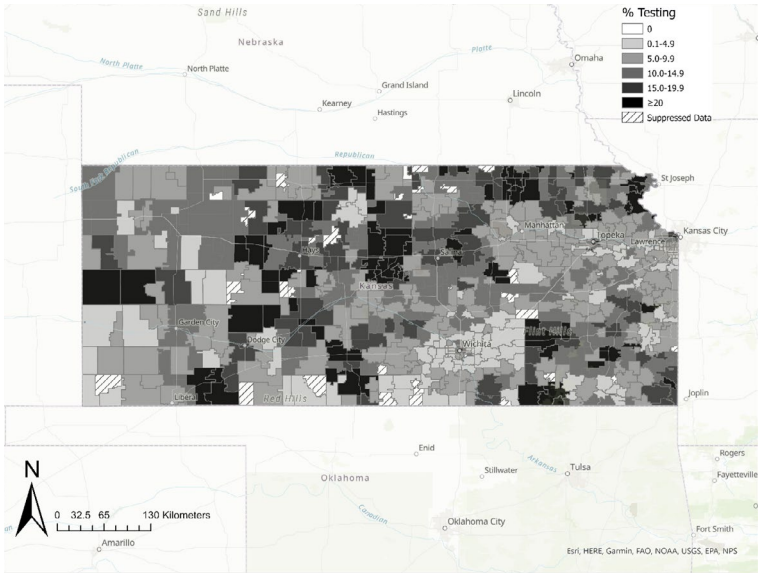

Figure 2. Passive reporting of blood lead levels among children ages 0 - 5 years to the Kansas Department of Health and Environment (KDHE), the State of Kansas, 2005 to 2012.

As shown in Table 2, risk was the lowest for suburban zip codes at an EBLL rate of 3.1%, which is where the lowest number of EBLL-positive cases occurs despite involving the greatest proportion of young children who reside in Kansas. In contrast, much higher rates were seen for urban and urban cluster zip codes at an EBLL rate of 7.2% and 8.8%, respectively. However, the highest rates were seen for rural zip codes at an EBLL rate of 10.0%, which was where the smallest proportion of young children in Kansas reside. Overall, the largest number of EBLL-positive cases occurred in urban cluster cities that stems from both their high EBLL rates and large proportional share of the total pediatric population.

The worst outcomes in EBLL rates observed in Table 2 were for zip codes in counties with a population density < 10 persons per square mile (11.0%), zip codes in counties with a ≥ 40% rural population (11.1%), urban cluster zip codes with a total population < 5,000 persons (12.0%), and rural zip codes that had a total population < 500 persons (15.1%). Regionally, the lowest rates at 4.9% were observed for the Northeast where Johnson County is located, which is predominately suburban and also the most populous county in the state. The highest rates were seen for Southeast Kansas at an EBLL rate of 13.5%, which is more than twice as high compared to the Northeast region.

As shown in Figure 3, there was a small yet significant linear association for Kansas zip codes between increasing early childhood EBLL rates and decreasing $\log^{10}$ total population estimates ($R^2 = 0.121$; $\beta = -0.349$; $B = -5.03$ [S.E. 0.53]; $p < 0.001$). Similar findings were seen in Table 2 in which increasing EBLL rates occurred in a stepwise fashion with categories of decreasing total population estimates among suburban, urban cluster, and rural zip codes. Significant yet weaker linear associations also were observed with $\log^{10}$ county-level population densities ($R^2 = 0.069$; $\beta = -0.262$; $B = -3.62$ [S.E. 0.52]; $p < 0.001$) and county-level rural population percentages ($R^2 = 0.040$; $\beta = 0.200$; $B = 0.60$ [S.E. 0.01]; $p < 0.001$).

It was hypothesized that rural and urban cluster zip codes located in areas that were more rural and isolated suffered from higher EBLL rates. As shown in Figure 3, the strongest linear associations with increasing EBLL rates were observed among urban cluster cities located in counties with greater percent rural population ($R^2 = 0.207$; $\beta = 0.455$; $B = 1.32$ [S.E. 0.03]; $p < 0.001$) or counties with decreasing $\log^{10}$ population densities ($R^2 = 0.200$; $\beta = -0.448$; $B = -4.98$ [S.E. 1.11]; $p < 0.001$). However, there was no association among rural zip codes between increasing EBLL rates and increasing rural population ($R^2 = 0.004$; $\beta = 0.061$; $B = 0.22$ [S.E. 0.02]; $p = 0.182$) and only a very weak significant association with $\log^{10}$ population densities ($R^2 = 0.018$; $\beta = -0.133$; $B = -2.83$ [S.E. 0.97]; $p = 0.004$)

As shown in Table 3, population estimates and total EBLL cases for zip codes in different categories for EBLL rates were examined. Based upon these categories, a visual illustration of varying EBLL rates among zip codes across the state is displayed in Figure 4. This revealed that more than 1 in 5 young children in Kansas (21.7%) lived in zip codes with an EBLL rate at least three times higher than the national average of 3.2% at the time, which accounted for nearly half of all EBLL cases (44.7%) across the state.

Lastly, as shown in Table 4, estimates for statewide blood lead testing coverage among children ages 0 - 5 years residing in the State of Kansas were low at 9.7% with the lowest testing in zip codes that were suburban (5.6%) compared to zip codes that were urban (11.5%) or urban clusters (12.3%) that had the greatest testing coverage. Furthermore, rural areas had lower testing rates (9.7%) despite having the highest rates of developing an early childhood EBLL.

DISCUSSION

Although our findings were somewhat dated, the current study involved the first descriptive examination of the early childhood lead burden for Kansas in nearly three decades. Compared to the national rate produced from NHANES data, young children in Kansas experienced twice the risk of developing an EBLL. This current study examined the early childhood lead burden in more detail and found that consistently higher rates of elevated blood lead were seen outside of the suburbs and particularly in areas that were more isolated or rural. Higher EBLL rates were correlated with lower population sizes and densities along with greater rural populations. Recently, another study of the national blood lead burden among young children found numerous zip codes in Kansas had the worst risks of developing an EBLL,[40] which were primarily located in rural areas of the state. This strongly suggested far greater early childhood lead exposure was occurring in rural Kansas.

In contrast to other states, higher EBLL rates were found in less urbanized and more rural areas in Kansas. Rural areas typically experience lower EBLL rates than urban cities,[41-44] although similar EBLL rates were found between rural and urban newborns in Iowa.[45] This may be unique to Kansas in part from a greater rural population, major urban cities that are comparatively smaller than others, much older and substandard housing, rural healthcare disparities related to access and affordability, and higher rates of soil contamination and industrial emissions as found in previous studies.[35,36] There also may be a lack of

Table 1. Blood lead testing and population characteristics in the State of Kansas, 2005 to 2012.

Setting		Variable	Summary Statistics			
			Sum	Mean ± S.E.	S.D.	Min-Max
Zip code	%	BLL testing coverage	–	11.8 ± 0.4	11.00	0 to 100
Zip code	%	EBLL-positive tests (≥ 5 µg/dL)	–	11.4 ± 0.4	10.2	0 to 66.7
County	%	Rural population	–	56.8 ± 1.3	34.0	4 to 100
Zip code	N =	BLL tests	192,396	294 ± 27	689	5 to 7,046
Zip code	N =	EBLL-positive tests (≥ 5 µg/dL)	15,937	24 ± 2	60	0 to 632
County	N =	Population density (persons/sq. mile)	–	137 ± 11	289	2 to 1,150
Zip code	N =	Population estimates (all ages)	2,898,982	4,426 ± 325	8,307	29 to 80,489
Zip code	N =	Population estimates (ages 0 - 5 years)	247,320	378 ± 29	741	1 to 6,954

Table 2. Weighted outcomes of elevated blood lead in the State of Kansas, 2005 to 2012.

Setting	Studied Sample Zip Codes N	Population Estimate Ages 0 - 5 Years N	Blood Lead ≥ 5 µg/dL Annual Incidence	
			Rate	N
Nationwide (NHANES)				
Total	–	6,673,044	3.2%	214,551
Statewide				
Total	655	247,320	6.9%	16,928
≥ 10,000 persons	94	176,377	6.0%	10,583
1,000 to 9,999 persons	246	60,442	8.2%	4,956
< 1,000 persons	315	10,501	13.0%	1,365
Suburban				
Total	45	74,265	3.1%	2,311
≥ 30,000 persons	5	20,863	2.4%	505
15,000 to 29,999 persons	18	32,972	3.1%	1,021
< 15,000 persons	22	20,430	3.8%	785
Urban				
Total	50	65,001	7.2%	4,693
Topeka, KS	17	13,766	6.5%	894
Kansas City, KS	9	16,156	7.1%	1,142
Wichita, KS	24	35,079	7.6%	2,657
Urban cluster				
Total	82	72,072	8.8%	6,315
≥ 15,000 persons	17	39,176	7.8%	3,035
5,000 to 14,999 persons	37	25,557	9.4%	2,398
< 5,000 persons	28	7,339	12.0%	882
Rural				
Total	478	35,982	10.0%	3,608
≥ 1,500 persons	111	20,498	8.3%	1,697
500 to 1,499 persons	170	11,430	11.4%	1,298
< 500 persons	197	4,054	15.1%	613
County rural population				
< 20%	138	164,455	5.1%	8,387
20 to 39%	94	32,144	8.8%	2,829
≥ 40%	423	50,721	11.1%	5,630

Table 2. Weighted outcomes of elevated blood lead in the State of Kansas, 2005 to 2012. *continued.*

Setting	Studied Sample Zip Codes N	Population Estimate Ages 0 - 5 Years N	Blood Lead ≥ 5 µg/dL Annual Incidence	
			Rate	N
County population density				
≥ 1,000 persons/sq. mile	42	68,208	3.6%	2,445
100 to 999 persons/sq. mile	86	83,520	6.3%	5,219
10 to 99 persons/sq. mile	308	80,398	9.5%	7,596
< 10 persons/sq. mile	219	15,194	11.0%	1,668
Region				
Northeast	175	112,731	4.9%	5,497
North Central	106	23,110	7.0%	1,606
Southwest	71	17,979	7.5%	1,340
South Central	106	66,499	7.7%	5,124
Northwest	93	9,158	10.3%	945
Southeast	104	17,843	13.5%	2,416

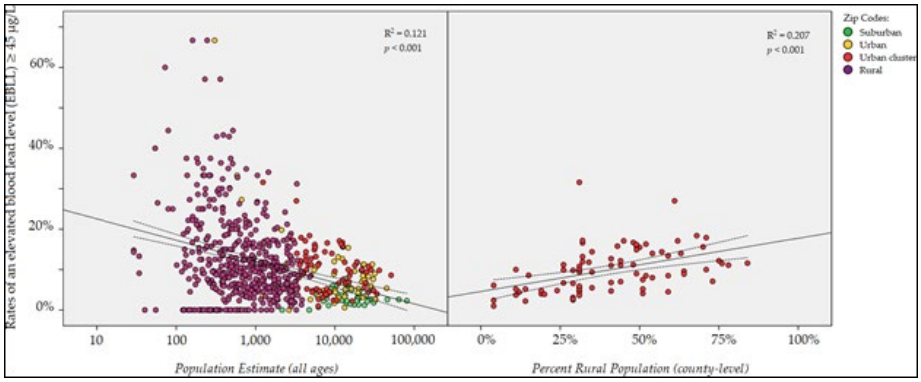

Figure 3. Scatterplots of zip codes with linear trends and 95% confidence intervals for elevated blood lead level (EBLL) rates ≥ 5 µg/dL among children ages 0 - 5 years in the State of Kansas, 2005 to 2012.

Table 3. Weighted outcomes of blood lead testing coverage in the State of Kansas, 2005 to 2012.

Setting	Studied Sample Zip Codes	Population Estimate Ages 0 - 5 Years		Blood Lead ≥ 5 µg/dL Annual Incidence	
	N	N	Percent	N	Percent
Statewide					
Total	655	247,320	–	16,928	–
0%	50	2,482	1.0%	0	0%
>0 to 5%	130	106,426	43.0%	3,147	18.6%
5 to 10%	178	84,896	34.3%	6,209	36.7%
10 to 15%	121	35,600	14.4%	4,143	24.5%
15 to 20%	74	13,769	5.6%	2,275	13.4%
20% or higher	102	4,147	1.7%	1,154	6.8%

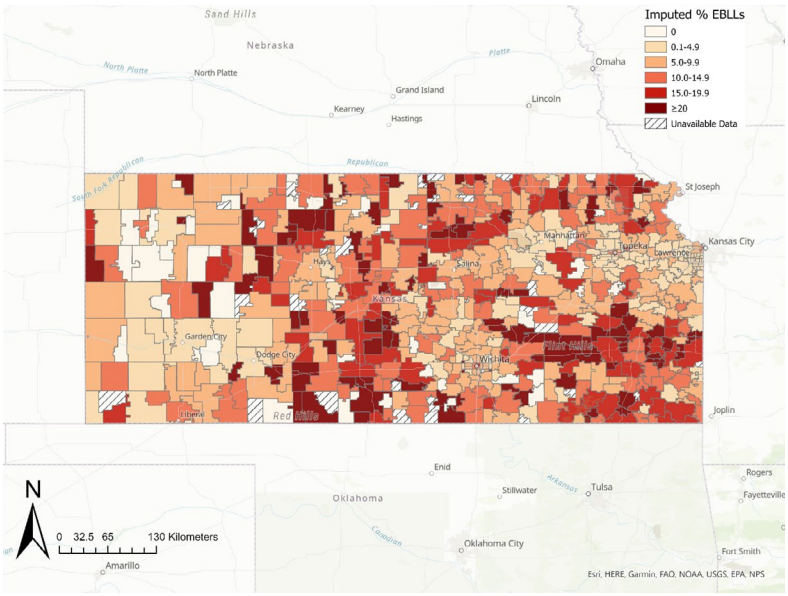

Figure 4. Zip code-level rates of an elevated blood lead level (EBLL) ≥ 5 µg/dL among children ages 0 - 5 years in the State of Kansas, 2005 to 2012.

Table 4. Weighted outcomes of blood lead testing coverage in the State of Kansas, 2005 to 2012.

Setting	Studied Sample Zip Codes N	Population Estimate Ages 0 - 5 Years N	Blood Lead ≥ 5 µg/dL Annual Incidence	
			Rate	N
Statewide				
Total	694	248,083	9.7%	192,474
Suburban	46	74,529	5.6%	33,475
Urban	52	65,067	11.5%	60,008
Urban cluster	82	72,072	12.3%	70,635
Rural	514	36,415	9.7%	28,356

awareness among the public and healthcare providers in rural areas with significant problems related to lead exposure and contamination. Underfunded public health institutions, hospital closures, and a low number of pediatricians and other clinicians in rural areas likely further compound these issues. Lastly, rural children with EBLLs ≥ 10 µg/dL were less likely to have a follow-up blood test,[46] while rural residents have been shown to be less knowledgeable about the prevention of lead exposure.[47]

However, while our findings for rural areas were unique, the findings for urban compared to suburban areas of the state were in agreement with those from other states. Higher early childhood lead burdens in urban areas are well-known and documented in states across the country, which were characterized by significant socio-economic and particularly racial/ethnic disparities that disproportionately impact Black children who are predominately African-American.[31,48] Sources of lead exposure in urban areas included industrial lead emissions,[49,50] soil contamination by industry and automobile traffic that can occur from both historical and ongoing sources of emissions,[51] and older housing containing higher rates of leaded paint and dust. Higher rates of industrial emissions, soil contamination, and household lead hazards still requiring cost-prohibitive remediation disproportionately impacted marginalized Black communities.[49-53] In contrast, suburban areas that typically are more affluent and predominately White were found to have much lower lead burdens compared to other areas outside of the suburbs.[43,44]

By region, the highest EBLL rates were found in Southeast Kansas, which is part of the Midwestern "lead belt" primarily located in Southwest Missouri and also includes Northeast Oklahoma. This region of Kansas has long been impacted by historical and ongoing issues of lead pollution largely resulting from mining and smelting operations centered around the urban cluster city of Galena, Kansas. Previously, two studies on industrial emissions in Kansas found a positive association between higher rates of lead exposure and greater amounts of lead in the blood of children,[35,36] in which a disproportionate share of these industries were located in Southeast Kansas. Workers in Kansas also suffered from the second highest rates of EBLLs ≥ 10 µg/dL in the U.S.,[34] which likely stemmed from greater employment in lead-related industries and can result in take-home contamination that results in childhood lead exposure.[54] Furthermore, many rural areas in Kansas have higher rates of older housing stock and substandard housing.[55] Lastly, the lack of investigations highlighted the need for further study.

Very low testing rates were observed for early childhood blood lead in Kansas, with lower testing rates in suburban and rural zip codes compared to zip codes that are urban or an urban cluster city. These findings revealed a gap between low testing rates and high EBLL rates among young children residing in rural areas of Kansas, which demonstrated the need for increased testing of rural households. Provider education and particularly the availability of point-of-care testing in Pennsylvania were found to increase blood lead testing rates at 1- to 2-year childhood well visits.[56] Such findings also were observed in New Hampshire after the implementation of provider education and point-of-care testing that served as a model for other rural areas.[57] In Ohio, blood lead testing at 1- and 2-year well visits greatly increased after the development of clinical decision-making support tools within the electronic health record.[58] Similar approaches in Kansas could increase early childhood blood lead testing in at-risk areas with low testing rates such as rural communities. Lastly, our findings strongly suggested that federally mandated blood lead testing among children ages 1 - 5 years who are enrolled in Medicaid, the State Children's Health Insurance Program (SCHIP), or other insurance programs that receive title XIX or XXI funding was not occurring frequently as has been seen with other states such as Minnesota and Wisconsin.[59,60]

Some limitations of the current study included a lack of reporting for early childhood EBLLs in zip codes with suppressed data, which led to the use of data imputation for assessing lead burdens in these areas. However, areas with suppressed data accounted for less than 10% of the total pediatric population in Kansas and predominately involved rural zip codes with a very small population. Therefore, this limitation largely involved rural areas that had the highest EBLL rates, while data imputation decreased EBLL rates when utilized and may have led to conservative EBLL estimates. Other limitations included low rates of blood lead testing, low ascertainment rates of EBLLs ≥ 5 µg/dL in Kansas,[61] and reliance on passive reporting to state public health authorities. Furthermore, zip code population estimates of children ages 0 - 5 years were limited by the use of county-level data for the total percent of the population represented by this age group as opposed to actual population counts, while population estimates from 2015 to 2019 were used as a result of limited availability of data regarding population counts for Kansas zip codes. However, the large sample size across several reporting years that was utilized in the present study increased our confidence in the robustness of these findings. Prospective studies still need to elucidate the impacts upon racial/ethnic groups overall and within differing settings. In particular, the conditions of Native children residing in largely rural tribal lands remain unknown.

CONCLUSIONS

Young children in Kansas have much higher EBLL rates than their peers at the national level. The risk of childhood lead exposure in Kansas increased when their residential setting was more rural and less populated, which was contrary to findings from other states in the nation. Wider recognition of at-risk children and troubled areas with regards to childhood lead exposure is needed among the populace, healthcare providers, and public health to address the disparately higher EBLL rates among children in Kansas. Furthermore, better prioritization and improved targeting is needed to identify early childhood lead exposure so that the proper preventative and mitigative interventions may take place. Low testing rates in Kansas could be improved through the promotion of both public and provider education along with greater availability of point-of-care testing. This may identify more EBLL cases among at-risk children while giving a clearer picture of troubled areas in the State of Kansas.

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Keywords: lead poisoning, adverse childhood experiences, epidemiology, public health, rural health

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Development of a Near Peer Clinical Anatomy Review Session during the Surgery Clerkship: Pre- and Post-Test Results among Third Year Medical Students

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ABSTRACT

Introduction. Our institution created a review of anatomy relevant to general surgery for third-year medical students. This study was designed to evaluate this review program and determine if participation increased third-year medical students' anatomy knowledge and confidence identifying anatomical structures in the operating room.

Methods. A formalin-embalmed cadaver-based review of anatomy was created and taught in near-peer fashion to third-year medical students. An anonymous survey and anatomy test were administered to participants pre- and post-session. The survey and test were designed to evaluate anatomy knowledge as well as student confidence identifying structures in the operating room. Survey data were compared using the Wilcoxon signed rank test.

Results. Seventy third-year medical students completed the anatomy review. There was a statistically significant improvement in students' confidence levels identifying structures in the operating room ($p < 0.001$) and in anatomy test scores ($p < 0.001$). Subjectively, students were thankful for the review session and found it helpful.

Conclusions. This near-peer review session designed at our institution was successful in improving immediate anatomy test scores and confidence levels identifying structures in the operating room. A course similar to this could be included at other medical schools to improve medical student confidence in identifying relevant anatomic structures in the operating room. ***Kans J Med 2022;15:293-297***

INTRODUCTION

Gross anatomy has been deemphasized in the modern medical education curriculum.[1,2] In the last century, hours of gross anatomy in a medical curriculum have dropped from approximately 550 hours in 1902 to 50 hours in 2000.[1] Reasons for this curriculum change included the rapid expansion of medical knowledge as well as the cost of cadavers and lab maintenance.

Many physicians, especially surgeons, consider this significant decrease in anatomy instruction to be inadequate.[1-3] In a 1999 survey, postgraduate residency program directors in general surgery ranked gross anatomy knowledge first in order of importance more often than any other basic science.[2] Additionally, in that same survey, 62% of the general surgery residency programs indicated that incoming residents need a refresher on gross anatomy and 24% reported that they were seriously lacking.[2]

Medical students, too, recognize the importance of gross anatomy and its relevance in clinical care.[4-5] However, knowledge retention and teaching context are potential barriers to the clinical application of anatomy knowledge. First, anatomy education commonly is consolidated to the first and second years of medical education, and the students' retention of basic science material after the preclinical years is generally poor.[3,6-7] Second, though students and faculty both acknowledge the effectiveness of gross anatomy dissection,[5,8-9] anatomy knowledge has been delivered more and more via computer learning, small group case studies, and problem-based learning, rather than by lectures and dissections.[2] While these case-based learning methods provide clinical context, gross dissection provides a physical context most like the identification of structures in surgery.

The combination of reduced hours spent in the gross anatomy lab, poor retention of basic science material including gross anatomy, and a different context of teaching contributes to difficulty in the transfer of gross anatomy knowledge to real-time application in the operating room. The aim of this study was to design a review of gross anatomy relevant to general surgery to help third-year medical students feel more confident identifying structures in the operating room. Acknowledging medical student perception of the surgery clerkship as being intimidating due to stereotypes of surgeons and of surgery,[10] the review sessions employed a near-peer teaching model to create a non-threatening learning environment and mentoring relationship.[11,12] The purpose of this study was to assess the ability of a near-peer anatomy review session to increase learner confidence in identifying anatomical structures during their surgery rotation. If a near-peer anatomy review session is shown to increase learner confidence in identifying anatomical structures during their surgery rotation, similar review sessions could be implemented in other medical school programs.

METHODS

This survey study was approved for implementation by the Ascension Via Christi Hospitals Wichita, Inc., Institutional Review Board with a waiver of informed consent. The development of this anatomy review session was prompted by medical student feedback and institutional curriculum changes including a reduction of anatomy teaching and lab hours. The anatomy review curriculum was prepared and taught by a team of nine fourth-year medical students. Five cases were identified as being relevant to general surgery based on our institution's medical student case logs and surgery clerkship oral board topics. The cases were inguinal hernia repair, trauma exploratory laparotomy, mastectomy, carotid endarterectomy, and thyroidectomy. With the guidance of surgery attendings and residents, relevant anatomy within the context of these cases was identified and surgical dissections were prepared on formalin-embalmed cadavers.

Participation in the anatomy teaching session was required of all third-year medical students during the first half of their eight-week, third-year surgery clerkship. Students were told that the session would be a review of anatomy relevant to general surgery but were not given the case topics ahead of time. Within each eight-week surgery clerkship, two teaching sessions were held in which the participating third-year medical students were split evenly between the two sessions to adhere to local COVID-19 gathering restrictions. The number of third-year

medical students per surgery rotation group ranged from 11 to 13 students and were split into groups of 5 to 7 per teaching session. Each teaching session lasted three hours during which the five cases were taught on two formalin-embalmed cadavers.

Pre-and post-session surveys, including an anatomy quiz, were administered to assess student level of confidence and to determine the level of student understanding before and after each teaching session. Completion of pre-and post-session surveys was voluntary, and students were assured that participation or non-participation would in no way affect their surgery rotation evaluations. One Likert-scale item was used to assess student level of confidence in identifying anatomic structures in the operating room (0 = poor, 1 = fair, 2 = okay, 3 = good, 4 = very good), and two multiple choice questions were created to assess knowledge of anatomy relevant to each teaching case for a total of ten multiple choice anatomy questions. One open-ended question was included for participants to leave feedback and additional comments (see Appendix).

Data Analysis. The Likert-scale and multiple-choice items were coded and compared with the Wilcoxon signed rank test to show the individual differences between the pre- and post-session survey responses. Responses from the open-ended question were compiled and analyzed using an inductive coding method. 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 IBM® SPSS Statistics Software (version 19.0; IBM® Corporation, Armonk, NY).

RESULTS

Seventy third-year medical students completed the anatomy review sessions and pre-/post-session surveys during the six eight-week surgery clerkship rotations held throughout the 2020- 2021 academic year.

Confidence. When comparing pre- and post-session Likert scale responses, there was a statistically significant improvement in participant confidence level identifying structures in the operating room ($p < 0.001$; Table 1). The pre-session median confidence level answer was "Fair", and most people answered between "Poor" and Fair" as the interquartile range was 0 - 1. The post-session median confidence level answer was "Okay", and most people answered between "Fair" and "Okay" as the interquartile range was 1 - 2.

Table 1. Overall assessment.

Parameter	Pre-Session Score Median (IQR)	Post-Session Score Median (IQR)	p Value
Confidence	1 (0 - 1)	2 (1 - 2)	< 0.001
Overall Index Scores	7 (6 - 8)	8 (8 - 9)	< 0.001

Anatomy Quiz Scores. The 10 multiple choice anatomy quiz responses were combined to make a pre-session index score and post-session index score. When the pre- and post-session indices were compared, there was a statistically significant improvement in anatomy quiz scores ($p < 0.001$; Table 1). The pre-session median score was 7 of 10 correct with an interquartile range of 6 - 8 and a range of 3 - 10. The post-session median score was 8 of 10 correct with an interquartile range of 8 - 9 and a range of 5 - 10.

When evaluating frequency of correct answers for individual anatomy quiz questions, 9 of 10 questions had improvement from pre-session to post-session; six demonstrated a statistically significant improvement (Table 2).

Table 2. Frequency of correct answers for individual questions.*

Question Number	Pre-Session Percent (n)	Post-Session Percent (n)	p Value
6	52.9% (37)	92.9% (65)	< 0.001
7	80.0% (56)	98.6% (69)	< 0.001
8	60.0% (42)	90.0% (63)	< 0.001
9	92.9% (65)	97.1% (68)	0.257
10	31.4% (22)	60.0% (42)	< 0.001
11	51.4% (36)	68.6% (48)	0.190
12	74.3% (52)	97.1% (68)	< 0.001
13	68.6% (48)	64.3% (45)	0.467
14	71.4% (50)	85.7% (60)	0.012
15	77.1% (54)	84.3% (59)	0.225

*See Appendix.

Quotes from Post-Session Surveys. A total of 49 third-year medical students left a comment on their post-session survey. Of those, one was "N/A", which was omitted from further analysis, leaving a total of 48 comments. Responses were compiled and coded using inductive coding. Each comment was coded into one of three categories (i.e., thankful, helpful, or suggestions). Since a single response may contain multiple sentiments, one comment could have up to three codes. With that in mind, 58.3% of comments by 28 medical students contained a sentiment categorized as "thankful". Just over one-half of comments (54.2%) by 26 medical students contained a sentiment categorized as "helpful". Approximately one-third of comments (35.4%) by 17 medical students contained a sentiment categorized as "suggestions". These are detailed in Table 3.

Table 3. Emerging themes from comments.

Frequency	Category	Definitions	Examples
28 (58.3%)	Thankful	Comments that expressed gratitude or a positive enthusiasm for the session.	• "Thank you so much for your time!" • "Need more lessons like this." • "Good job!"
26 (54.2%)	Helpful	Comments which directly expressed the session "helped" or was "helpful"; included comments that expressed an improvement in knowledge or comments that pointed out a specific reason they found the session beneficial.	• "This was sooooo helpful!" • "I learned so much." • "I like that this was shortly into rotation (not during orientation week)."
17 (35.4%)	Suggestions	Comments that provided constructive criticism or feedback as to how the sessions can be improved; included comments that "wish"; included comments that suggest a new program.	• "It would be nice to have a brief description of what will be covered during the session beforehand." • "...wish I'd had this experience during my first two years of medical school." • "...I feel that we could have another similar session like this toward the oral board, if people are available."

DISCUSSION

Findings from this study demonstrated the benefits to third-year medical students of a near-peer clinical anatomy review session taught during the surgery clerkship. There was a statistically significant improvement in student confidence level identifying structures in the operating room, as well as statistically significant improvement in anatomy test scores. Student post-session comments supported these quantitative results and contained sentiments of thankfulness for the session, session helpfulness, and suggestions for session improvement.

Upon literature review, no studies detailed similar anatomy review programs within the third-year surgery clerkship. However, two studies detailed the use of cadavers in resident training. The first by Gordinier et al.[13] explored whether a course in cadaver dissection could increase resident knowledge of pelvic anatomy significantly beyond that of current educational practices. Obstetrics and gynecology residents were assigned to a dissection group versus a control group and both groups completed a pre- and post-study examination. Both groups had statistically significant improvement on the post-test compared to the pre-test, but the dissection group scored nearly 50% higher on the test than did the controls. In their evaluation of the course, participants from the dissection group emphasized its educational value and urged that it be offered to residents as a regular part of their training. Though the evaluation of our review session did not include a control group, the pre- and post-session results and comments by third-year medical students were like those reported by Gordinier et al.[13]

Another anatomy program detailed in a study by Lewis et al.[14] described the development of a cadaver-based educational program for general surgery residents. Overall, residents held a positive view of the cadaver sessions and believed them to be useful for learning anatomy (94% agree or strongly agree). They also reported that compared with other learning modalities, cadaver sessions were ranked first by respondents for learning surgical anatomy. Our results aligned with those of Lewis et al.[14] in that third-year medical students found our institution's anatomy review sessions helpful.

While there was a statistically significant increase in student confidence level in post-session surveys compared to pre-session, this increase was small despite student comments containing sentiments of thankfulness and session helpfulness. This smaller than anticipated increase in confidence level may be the result of asking questions that were too general whereas our intervention included specific surgery cases. Perhaps student confidence level would have increased more if participants were asked more specific questions, such as to "Rate your confidence level identifying inguinal hernia anatomy in the operating room".

Upon review of the student comments containing sentiments coded as "helpful", most included a general comment such as "This session was helpful". However, four comments included mention of the clinical context being helpful.

Specific sentiments within this theme included: "I really found this helpful within the context of surgeries to understand the procedures that I'm seeing." "Felt this was very helpful, I liked how it was case based as well." "Very helpful, especially in the context of questions commonly asked during procedures." "It was good to go over some of the more common cases that we'll see on this rotation."

Upon review of the student comments containing sentiments coded as "suggestions", a few themes emerged. First, 10 comments included suggestions regarding timing of the review session within the eight-week surgery clerkship. All suggestions were for the review session to be held during the first half of the clerkship (weeks 1 to 4), but within that the suggestions were split between the first week of the clerkship as an orientation to surgery and weeks 3 to 4 after students have seen several cases in the operating room and have a clinical context for the review session material. This year, scheduling was dependent on the fourth-year near-peer teachers' availability, and the review session was held within weeks 1 to 5 of the surgery clerkship. Since completion of the academic year, anecdotal feedback has been provided by the third-year medical students during their mid-clerkship review with the surgery clerkship director that supported the suggestion for the review session to be held during the first week of the clerkship as part of orientation. In this coming academic year, the review session will be held during the

first week of the surgery clerkship.

Second, three comments included requests for a brief description of the cases to be covered and/or preparatory materials to review before the review session. While students were not provided with information ahead of the session, they were provided with teaching outlines and case notes to review after the session. Next, two comments included suggestions to split the teaching cases more evenly between the two cadavers. The third-year medical students attending the session were split among the two cadavers and the groups switched halfway through the session to complete the remaining cases. During the first several teaching sessions early in the year, two cases were taught on a female cadaver (breast and carotid endarterectomy) and three cases on a male cadaver (exploratory laparotomy, inguinal hernia repair, and thyroidectomy). This original set up was uneven in length of time with the male cadaver cases taking longer than the female cadaver cases. To remedy this imbalance, the thyroidectomy and exploratory laparotomy cases were prepared and taught on the female cadaver. Finally, two comments included recommendation for future years and that the teaching session become an official component of the curriculum. With school and surgery department funding, this has been made possible.

Limitations of this study included lack of control group and the lack of long-term participant assessment. Future research questions include investigating the use of soft-embalmed cadavers for teaching, assessing long-term retention of participant knowledge at five to six months post-session, and studying outcomes of anatomy understanding and student confidence level for near-peer teachers.

CONCLUSIONS

Overall confidence score in identifying anatomical structures in the operating room in this study increased significantly from pre- to post-course. Additionally, students increased anatomy quiz correct responses for 9 of 10 anatomy questions with significant improvement in proportion of correct answers on quiz questions in 6 of 10 questions. Based upon these results, we can conclude that this review session designed at our institution was successful in improving anatomy test scores and confidence identifying structures in the operating room in third-year medical students during their surgery clerkship. This course could be modeled and included at other medical school settings to improve medical student confidence in identifying anatomic structures relevant to general surgery.

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Keywords: medical education, anatomy, clinical clerkship, dissection, general surgery

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THIRD-YEAR CLINICAL ANATOMY REVIEW SESSION
continued.

Pre/Post Session Survey & Anatomy Quiz

1. Create your own unique Study ID using the first two initials of your mother's maiden name followed by the two digits of your birth month. ___ ___ ___ ___

2. What week of your surgery clerkship is the cadaver teaching session being held? _____

For questions 3 through 15, circle the letter of the correct answer.

3. Is the teaching session held virtually or in person?
   a. Virtually b. In person

4. Is this the pre or post session survey?
   a. Pre-session survey b. Post-session survey

5. Rate your confidence level in identifying anatomical structures in the operating room.
   a. Poor b. Fair c. Okay d. Good e. Very Good

Answer the following anatomy quiz questions to best of your ability. This quiz is for research only and will not be a part of or influence your clerkship grade.

6. What is the first branch off the external carotid artery?
   a. Superior thyroid artery b. Facial artery
   c. Inferior thyroid artery d. Esophageal artery

7. What nerve at risk during a carotid endarterectomy, causes tongue deviation toward the side of the lesion if damaged?
   a. Vagus nerve b. Facial nerve
   c. Hypoglossal nerve d. Accessory nerve

8. To what layer depth is tissue removed during a simple mastectomy?
   a. External intercostal muscles b. Pectoralis minor
   c. Pectoralis major d. Rectus abdominus

9. What nerve at risk during axillary lymph node dissection, courses along the lateral chest wall in the midaxillary line and causes scapular winging if damaged?
   a. Medial pectoral nerve b. Lateral pectoral nerve
   c. Thoracodorsal nerve d. Long thoracic nerve

10. The inguinal ligament arises from which anterior abdominal wall structure?
    a. External oblique muscle aponeurosis b. Internal oblique muscle aponeurosis
    c. Transverse abdominus muscle aponeurosis d. Rectus abdominus muscle aponeurosis

11. Describe the relative location of the groin hernia that requires elective surgery because it has the highest risk of incarceration.
    a. Superior to the inguinal ligament, lateral to the femoral vein b. Inferior to the inguinal ligament, lateral to the femoral vein
    c. Superior to the inguinal ligament, medial to the femoral vein d. Inferior to the inguinal ligament, medial to the femoral vein

12. What are the three structures within the hepatoduodenal ligament?
    a. Hepatic vein, hepatic artery, cystic duct b. Hepatic artery, portal vein, common bile duct
    c. Hepatic vein, portal vein, cystic duct d. Hepatic artery, gastroduodenal vein, common bile duct

13. Which of the following structures is a primary branch off of the celiac trunk?
    a. Left gastric artery b. Right gastric artery
    c. Short gastrics d. Gastroduodenal artery

14. What is the indication for cricothyroidotomy? And through what structure is this procedure performed?
    a. Prolonged intubation; cricothyroid membrane b. Emergency airway; cricoid cartilage
    c. Emergency airway; cricothyroid membrane d. Prolonged intubation; 2nd and 3rd tracheal rings

15. What nerve is at risk during the ligation of the inferior thyroid artery?
    a. Inferior laryngeal nerve b. Superior laryngeal nerve
    c. Hypoglossal nerve d. Recurrent laryngeal nerve

16. If this is your post-session survey, then feel free to include any session feedback or additional comments below:

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Severe Hypertriglyceridemia as a Cause of Aortic Thrombus with Peripheral Embolic Complications

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INTRODUCTION

Hypertriglyceridemia is known to increase blood viscosity thus creating a hypercoagulable state. However, this predominantly has been associated with venous thrombosis.[1,2] Pro-thrombotic mechanisms mediated by triglycerides include: 1) increased platelet aggregation, decreased antithrombin III activity, interaction with coagulation factors, 2) increase in proinflammatory markers, and 3) endothelial dysfunction. However, while hypertriglyceridemia has been associated with an increased risk of venous thrombosis, its association with arterial thrombosis has not been described previously. We present a case of elevated triglycerides and isolated aortic atherothrombosis causing renal and splenic infarcts.

CASE REPORT

A 51-year-old white female with history of hypertension and type 2 diabetes presented with nausea, vomiting, and acute left-sided flank pain. A computed tomographic angiogram (CTA) demonstrated the presence of splenic and bilateral renal infarcts. No obvious risks for thrombosis were evident on history except for the use of combination oral contraceptives to control menorrhagia. There was also a family history of hypertriglyceridemia. Her physical exam was unremarkable with body mass index of 33 kg/m^2. A test for COVID-19 infection was negative. Her basic chemistries and complete blood count were normal. Fasting lipid profile revealed elevated triglycerides at 1,274 mg/dL (replicated on two separate occasions), directly measured low-density lipoprotein cholesterol was 39 mg/dL, lipoprotein(a) was 6 mg/dL, very low-density lipoprotein-cholesterol (VLDL) was 255 mg/dL, and non-high-density lipoprotein-cholesterol level was 214 mg/dL. Her fasting blood glucose and hemoglobin A1c were 170 mg/dL and 7.6%, respectively.

An extensive hypercoagulable and autoimmune work-up was unremarkable (Table 1). A CTA of the chest, abdomen, and pelvis revealed a focal protruding noncalcified atherothrombotic lesion in the mid to distal segment of the descending thoracic aorta (Figure 1A). No significant atherosclerotic lesions were visualized in the other segments of the aorta or vascular beds. No vascular calcification was seen. The lesion in the distal thoracic aorta was determined as a culprit for the visceral infarctions via embolic mechanisms. Treatment with low dose aspirin and therapeutic dose of low-molecular weight heparin was initiated followed by apixaban and aspirin on discharge. Over the course of the hospital stay, her abdominal pain gradually resolved. She was started on atorvastatin 40 mg, fenofibrate 145 mg, icosapent ethyl 4 g, resulting in a 70% reduction in the triglyceride levels on the follow-up testing (Table 2).

In three months, a repeat CTA showed almost complete resolution of the aortic lesion with a mild residual plaque on the adjacent aortic wall (Figure 1B). Further supporting that the etiology of the lesion was a bulky thrombus developing on a mild plaque. At the six month follow-up visit, she was switched to dual antiplatelet therapy and remained asymptomatic.

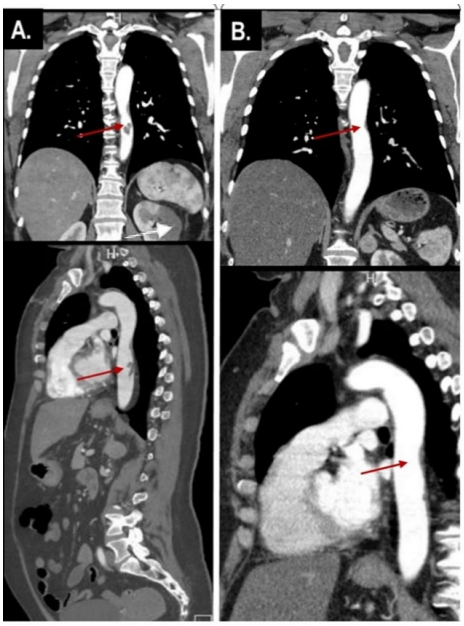

Figure 1. A) Admission CTA images show 8.3 x 2.7 cm left renal hypoattenuation consistent with infarction (white arrow). Normal caliber thoracic aorta with mural thickening in the mid thoracic aorta with associated mild atherosclerotic plaque and 10x6 mm posterior eccentric thrombus within caudal thoracic aorta (red arrow). Tiny right lower pole renal infarct. B) At three month follow-up: A significant improvement in irregular eccentric thrombus in the posterior descending thoracic aorta with nearly resolved endophytic portion extending into the aortic lumen.

DISCUSSION

Insights from biology, epidemiology, and genetics strongly suggested that elevated triglyceride-rich lipoproteins (TRL) represent causal risk factors for atherosclerosis, inflammation, and all-cause mortality.[3-7] However, there were limited clinical data on association of hypertriglyceridemia with arterial thrombosis. We reported a clinical case of a woman who developed embolic complications from an aortic wall atherothrombotic lesion in the setting of familial hypertriglyceridemia. Contributing risk factors included type 2 diabetes, hypertension, and contraceptive use. Almost complete resolution of the thrombus was observed with conservative management including an antiplatelet agent, anticoagulant, and aggressive triglyceride-lowering regimen. Oral contraceptive use has been linked to an increased risk of stroke, myocardial infarction, and deep venous thrombosis.[8-10] However, arterial thrombosis was less likely to occur with the use of oral contraceptive pills in the absence of cardiovascular risk factors. This clinical observation highlighted importance of optimization of lipid control in patients taking contraceptives.

Table 1. Results of the autoimmune, coagulation, and systemic work-up prior to initiation of anticoagulation.

Autoimmune Work-Up		Coagulation Work-Up		Systemic/Infectious Work-Up	
ANA	< 80 titer/ Negative	**Prothrombin F2 G20210A PCR**	Negative	**Tuberculosis testing**	Negative
Myeloperoxidase antibodies	< 0.2/ Negative	**INR**	1.1	**Hepatitis panel**	Negative
Serine Protease3 antibodies	< 0.2/ Negative	**aPTT**	29	**Syphilis antibodies (rapid plasma reagin)**	Negative
Immunoglobin G with normal subclasses	915 mg/dL	**F5 Leiden Screen (activated protein C resistance)**	3.2 (> 2.5)/Negative	**1,25-dihyroxyvitamin D**	78 pg/mL
Beta-2 glycoprotein 1 antibodies for IgG	< 1.4 U/mL/ Negative	**Homocysteine**	7.9 Umol/L (5-15)	**Serum electrophoresis**	No paraprotein
Beta-2 glycoprotein 1 antibodies for IgM	0.8 U/mL/ Negative	**Protein S**	108% (55-124%)	**Angiotensin Converting Enzyme**	6 U/L (16-85)
Cardiolipin antibodies for IgM	0.8 gpl/mL/ Negative	**Protein C activity**	150% (70-130)		
Cardiolipin antibodies for IgG	< 1.6 gpl/mL/ Negative	**Serum cryoglobulin**	Trace cryoprecipitate		
Hexagonal phase phospholipid test (confirmatory test for lupus anticoagulant)	0 sec/Negative	**Dilute Russell's viper venom time (dRVVT)**	1.4		

Table 2. Fasting lipid profile on admission and following three months of lipid-modifying therapy (all in mg/dL).

	Admission	Three Month Follow-Up
Total cholesterol	253	227
Triglycerides	1,274	306
LDL-C	39	55
VLDL-C	255	-
HDL-C	90	111
Non-HDL-C	214	-
Lp(a)	6	-

LDL-C = low-density lipoprotein cholesterol; Lp(a) = lipoprotein(a); VLDL = very low-density lipoprotein; HDL-C = high-density lipoprotein cholesterol

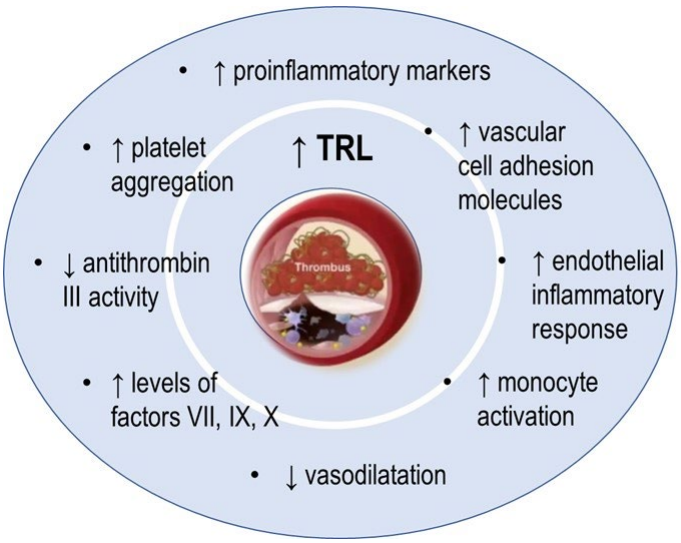

Figure 2. Summary of reported pro-thrombotic mechanisms mediated by triglyceride-rich lipoproteins and remnants.

As a hypothesis-generating finding, we speculated that the driving force in the formation of the arterial thrombosis was aggregation of TRL in the subintimal space leading to accumulation of lipid-laden macrophages, inflammation, platelet aggregation and activation of the coagulation cascade in the setting of high shear stress (Figure 2). TRL comprise chylomicrons and VLDL and serve as transporters of triglycerides and cholesterol in circulation. Alteration of the rheological properties, including redistribution of the wall shear stress, endothelial lining damage, disorganization of the fibroelastic microstructure, platelet activation, intima-media remodeling, are implicated in thrombogenesis.

TRL enter the arterial intima at a slower speed than the LDL particles due to a larger particle size; however, once trapped, reentry into arterial lumen against blood pressure gradient is more difficult.[11,12] TRL can be taken up by peripheral macrophages via the VLDL and apolipoprotein B48 receptors without modification or downregulation by intracellular lipoproteins, along with lipoprotein lipase.[13-17] TRL have shown to cause low grade inflammation at a whole-body level, including arterial intimal inflammation.[18,19] TRL retain in the subendothelial space and contribute to the atherosclerotic lesion initiation and progression. Through apolipoprotein E-mediated uptake of TRL,[20] activation of metalloprotease expression prompted by atherogenic macrophage modification was shown to result in a vulnerable, thin fibrous cap atheroma phenotype.

Meta-analyses including 57,277 individuals demonstrated that an 89 mg/dL elevation in triglycerides was associated with a 14% to 37% higher incidence of cardiovascular disease independent of other risk factors in men and women, respectively.[21,22] Although multivariable Mendelian randomization analyses have suggested a deleterious causal effect of increased triglycerides on coronary heart disease risk,[23,24] there was heterogeneity amongst different TRL. In 29,039 individuals with no history of myocardial infarction from the Copenhagen General Population Study, during a mean follow-up of 10 years, the hazard ratio for myocardial infarction was 3.5-fold for VLDL and 1.3-fold for intermediate-density lipoproteins and LDL combined for the same number of apoB-containing particles measured using nuclear magnetic resonance spectroscopy.[25]

Prothrombotic properties of TRL are thought to be driven by direct and indirect mechanisms. A redox-sensitive mechanism has been implicated in upregulation of endothelial expression intercellular adhesion molecule-1, vascular cell adhesion molecule-1, tissue factor in cultured human endothelial cells by TRL remnants.[26] Platelet activation was shown to be increased in patients with hypertriglyceridemia.[27] Low antithrombin III activity and increased platelet aggregation have been observed in individuals with triglyceride levels above 200 mg/dL.[28] Heparin has been shown to activate lipoprotein and hepatic lipases; therefore, heparin-containing therapies might be considered as a preferred initial strategy in individuals with hypertriglyceridemia.

In animal models, intravenous infusion of long chain saturated fatty acids caused thrombosis and resulted in significant reduction of cardiac output.[29] Properties of triglyceride-containing particles affect the activity of vitamin K dependent coagulation factors. For instance, coagulation factors VII and X are transported by TRL and show a strong fixation to chylomicrons and VLDL fractions.[30] Increased levels of factor VII were observed in individuals with elevated triglyceride levels.[31]

CONCLUSIONS

The atherothrombogenic potential of TRL composition is an area of active investigation. This case suggested that elevated triglycerides can be considered as a risk factor for arterial thrombosis, supporting further research of the role of targeted triglyceride-lowering therapies on atherothrombotic outcomes. Further studies on impact of genetic architecture of hypertriglyceridemia on clinical outcomes in cohorts with diverse ethnic/racial backgrounds are warranted.

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Keywords: coronary thrombosis, triglycerides, blood viscosity, high density lipoproteins, prevention.

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Injection Site Reaction to Extended-Release Buprenorphine (Sublocade®) for Opioid Use Disorder Fourteen Days after Administration

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INTRODUCTION

In recent years, treatment options for Opioid Use Disorder (OUD) have grown to encompass a host of medications with various treatment formulations. Buprenorphine, a mainstay of treatment of OUD since approval from the U.S. Food and Drug Administration (FDA) in 2002, has benefited from a variety of treatment formulations including sublingual, buccal formulations and long-acting subcutaneous injection.[1] In recent years, buprenorphine extended-release injections have grown popular, providing patients and clinicians with another tool to treat the debilitating symptoms of addiction.

Buprenorphine, while generally well tolerated in its older formulations, has had less research in its newer extended-release form.[2] The novelty of the extended-release formulation of buprenorphine explains the dearth of research on adverse events specifically related to its subcutaneous route. In this case study, a particular case of post-injection cellulitis is discussed and briefly potential causes explored. As extended-release formulations of buprenorphine continue to increase in use, cases studies like these will help identify more uncommon adverse events and help broaden practitioners' differentials.

CASE REPORT

A 35-year-old female with severe opioid use disorder on buprenorphine injection (Sublocade®) therapy presented to the addiction psychiatry treatment center with reported injection site pain, erythema, swelling, and a rash of two days duration. Fourteen days prior to presentation, she had received her second buprenorphine injection in the right lower quadrant of her abdomen. She initially did not develop redness or pain, but while reporting withdrawal symptoms eleven days post-injection, she mentioned unintentionally scratching the site with an acrylic nail the previous day. She denied bleeding but experienced slight pain when this occurred. Of note, she had tolerated her initial injection well with only slight soreness and redness lasting two days. Between her first and second subcutaneous doses, supplemental sublingual buprenorphine/naloxone 8-2 mg daily had been prescribed to ease irritability and cravings.

On evaluation, she emphasized the scratch was unintentional. The pain was significant enough that she needed to wear loose clothing over the area. She denied fevers, chills, or expression of material from the site. Vitals were stable with a temperature of 36.4 degrees Celsius, blood pressure of 136/93 mmHg, heart rate of 85 beats/minute, respiratory rate of 17 breaths/minute, and blood oxygen saturation of 100%. Physical exam demonstrated a 3 x 5 cm indurated injection site with slight protuberance from her abdomen. Erythema extended into the surrounding skin involving a total area of 10 x 15 cm, including her striae gravidarum (Figure 1). The site was tender and warm to the touch, but no disruptions in the skin barrier were noted. The induration and surrounding erythema were outlined with a marking pen, and due to concern for cellulitis, the patient was escorted directly to the emergency department. After a seven-day course of cephalexin and trimethoprim-sulfamethoxazole, the cellulitis successfully resolved (Figure 2).

This patient's history was significant for buprenorphine/naloxone diversion, which served as the indication for her treatment to be converted to the injectable formulation. While accepting her history of diversion and its implications on her treatment options, she initially desired to discontinue the injections and resume sublingual treatment on follow-up. She was given the option of converting to methadone treatment, but she ultimately chose to continue the injections due to the significant functional benefit that this treatment modality awarded her. Although guidelines recommended subcutaneous buprenorphine to be dosed at 300 mg for the first two injections and 100 mg thereafter,[3] this patient likely will continue to receive doses of 300 mg due to continued cravings and withdrawal symptoms.

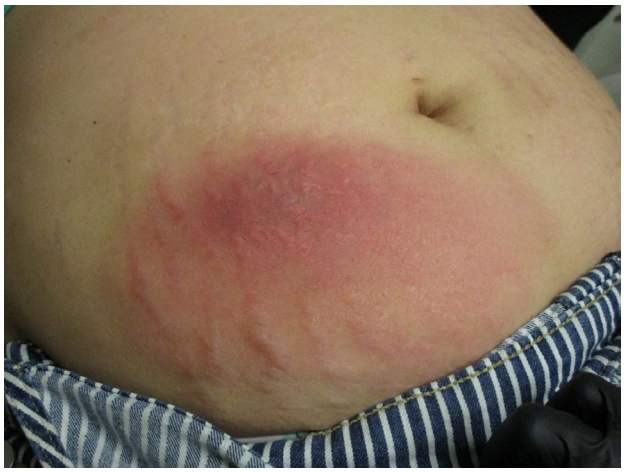

Figure 1. Injection site cellulitis at the time of presentation.

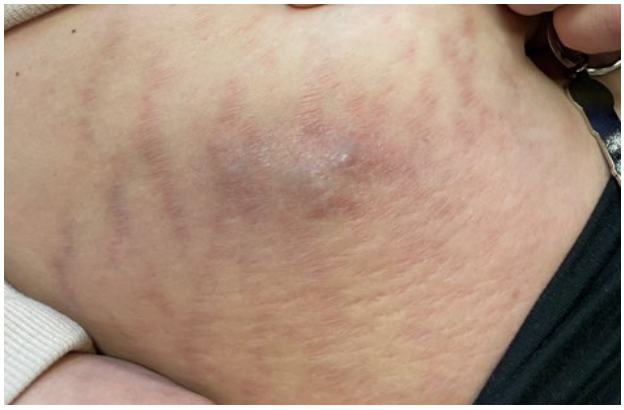

Figure 2. Resolved cellulitis seven days post-treatment.

DISCUSSION

Opioid use disorder is a public health emergency that has become a serious epidemic in the United States, specifically the high risk of overdose with opioids such as heroin, prescription opioids, and illicit fentanyl.[4] Moderate to severe forms of OUD requires continuing sustained care for effective treatment and achieving long-term opioid abstinence. There are three medications currently approved by FDA used for OUD treatment that targets opioid receptors: methadone, buprenorphine, and long-acting naltrexone. These medications have been shown to reduce relapse to opioid use, overdose, and HIV and HCV transmission, as well as improve other health outcomes.[4-7]

Buprenorphine is a partial μ-opioid agonist used for the maintenance treatment of opioid use disorder.[2] Buprenorphine has potential merits, including a lower overdose risk and "low ceiling effect" for respiratory depression, fewer pharmaceutical interactions, and less risk of QTc-prolongation when compared to methadone.[8] Buprenorphine is available in three formulations: sublingual films and tabs and buprenorphine extended-release injection (Sublocade®).[4,6,7,9] The extended-release injectable formulation was approved by FDA in November 2017. This formulation is a monthly subcutaneous injection administered only by a healthcare provider. It is available in two doses of 300 mg/1.5 ml and 100/0.5 ml. Per current guidelines, the first two doses recommended are 300 mg each with the following monthly maintenance dose of 100 mg each.[4,6,7] The monthly formulation of extended-release buprenorphine produces a sufficient steady-state blood level and may be more favorable for persons who have difficulty adhering to daily sublingual forms.[4,5,10]

The most common adverse drug reactions of extended-release buprenorphine injection are injection site pain, injection site pruritus, constipation, sweating, nausea, vomiting, headache, fatigue, and sedation (more than 5%).[3,4,11-14] The majority of injection-site adverse reactions are mild to moderate in severity and include pain, hives, and erythema.[3,4,12-13] These side effects are usually temporary and appear most commonly with the first injection and decrease in frequency with subsequent injections.[4,15]

Our case report was unique as an injection site reaction appeared in a patient 14 days after her second injection of extended-release buprenorphine, following unintentional scratching of the injection site with an acrylic nail while in the shower. Looking specifically at the Phase 3 trial data, only 1 of the 201 patients in the initial trial experienced injection site cellulitis, and 2 others of a total of 412 participants have experienced injection site cellulitis in the ongoing open-label long-term safety study.[15] Possible explanations that may have predisposed our patient to an injection site reaction may have included improper injection of the medication, as adverse reactions are more likely to occur with intradermal or intramuscular injection.[3] Both of these considerations were difficult to reconcile given the delayed onset from the injection. Our patients' acrylic nails may have acted as a nidus that seeded an infection over time as well.

It is important to consider that the cellulitis could have resulted from the patient attempting to remove the Sublocade® dose in an attempt to divert depot buprenorphine. The manufacturer suggested providers continue to monitor injection sites for evidence of tampering or attempts to remove the depot.[3] In a clinical setting, removal of the depot can be performed through surgical excision under anesthesia within 14 days of injection. Given that the depot formulation is meant to decrease the risk of diversion,[10] this finding would be of considerable interest. However, the patient denied intentional tampering and it cannot be confirmed if this patient actually attempted to remove the medication.

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The patient has given written consent for publication of the figures and the details of the case in the literature.

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Keywords: sublocade, opioid use disorder, buprenorphine, drug side effects, cellulitis

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Ureteral Inguinal Herniation

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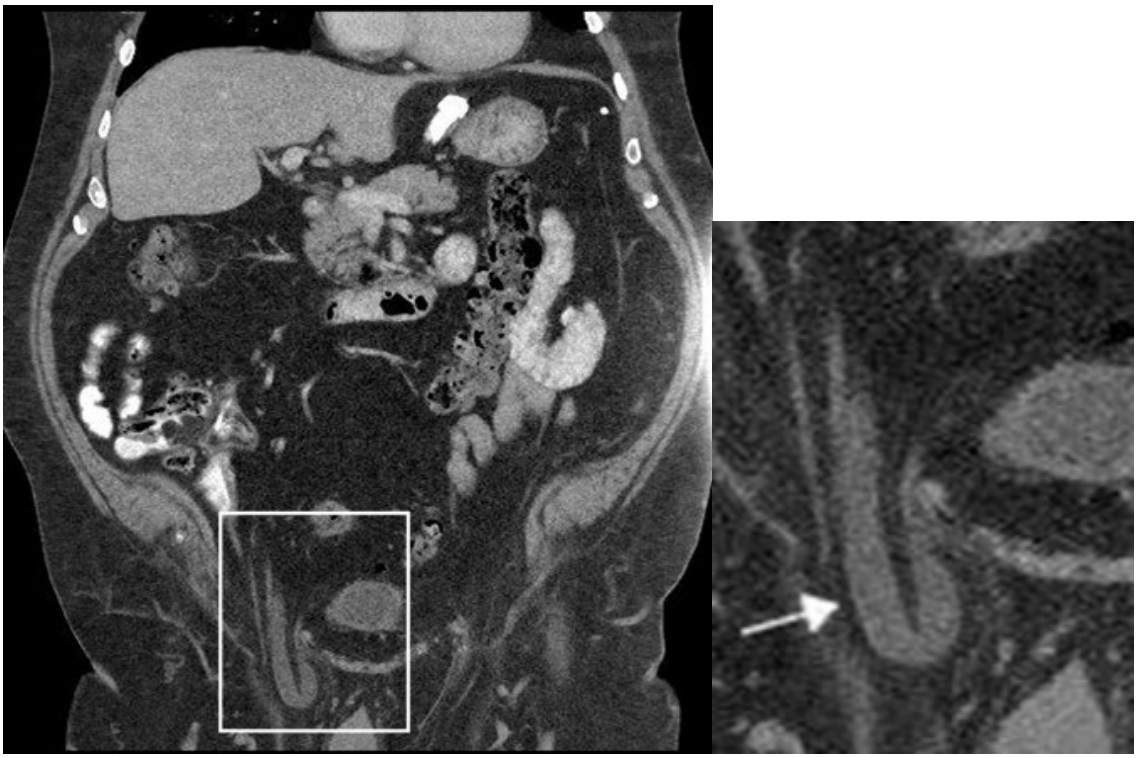

CASE DESCRIPTION

Abdominal computed tomography (CT) was obtained in a patient for evaluation of a colon mass. The CT showed a slight dilatation of the right renal pelvis with no hydronephrosis, but inguinal herniation of the right ureter, which was dilated to 7 mm and looped inside the inguinal hernia with enlarged insert on the left (highlighted in the Figure within the white box and shown to the right). The arrow in the Figure insert points to the herniated and dilated right ureter.

DISCUSSION

A hernia is defined as a protrusion or bulge of an organ or a part of an organ through the body wall that normally contains it. Groin hernias include inguinal and femoral hernias with a prevalence of 5-10% in the U.S.,[1] among them 96% are inguinal and 4% femoral hernia.[2]

The inguinal canal is lined by the aponeuroses of the abdominal oblique musculature, running from the deep (internal) inguinal ring to the superficial (external) ring. The internal ring is formed by an opening in the transversalis fascia while the superficial ring is formed by a gap in the external oblique aponeurosis. The canal contains the ilioinguinal nerve as well as the spermatic cord in males and round ligament in females.

The groin hernias can be classified according to the anatomic location of the abdominal wall defect into indirect inguinal, direct inguinal, and femoral hernias.[3,4]

- Indirect inguinal hernia is the most common type of groin hernia in both males and females.[5] It protrudes through the deep inguinal ring and inguinal canal.
- Direct inguinal hernia accounts for 30-40% of groin hernias in the male and 14-21% in the female.[5] It protrudes through an area of weakness in the transversalis fascia, the Hesselbach's triangle (defined laterally to rectus abdominis, medially to the inferior epigastric vessels and above the inguinal ligament).
- Femoral hernia represents less than 10% of all groin hernias.[6] They are located inferior to the inguinal ligament and protrude through the femoral ring, which is medial to the femoral vein and lateral to the lacunar ligament. The femoral ring can widen and become patulous with aging and following injury.

Groin hernias have a variety of clinical presentations from a benign finding of a bulge in groin region on routine physical examination to serious complications including acute intestinal obstruction as the result of incarcerated hernias. Inguinal herniation of the ureters is a rare phenomenon. It was first described by Leroux in 1880 as an autopsy finding.[7] The first preoperative diagnosis was achieved in 1937 using intravenous pyelography.[8] Since then, only isolated cases or small series have been reported in the literature.[9,10] Ureteral inguinal hernias are predominantly indirect rather than direct (80% vs. 20%). It is classified in two anatomical variants. The para-peritoneal type (80%) is defined by a loop of ureter that slides with a peritoneal sac into the hernia. This usually is acquired and has been associated with kidney transplants. The less common type (20%) is extra-peritoneal herniation of the ureter, which is thought to be congenital and caused by failure of ureter to separate from the mesonephric duct during development, resulting in the ureter being pulled along with testis as it descends into the scrotum.[11]

Ureteral herniation is usually an asymptomatic urological finding, often diagnosed incidentally by imaging evaluation of unrelated medical condition as in this case or by direct observation intraoperatively during surgical inguinal hernia repair.[11] Complications associated are uncommon, including ureteral obstruction/uropathy or inadvertent damage to the ureter during inguinal hernia repair.[12]

Awareness of this uncommon condition is important in evaluation of patients with obstructive uropathy and during surgical repair of inguinal hernia to prevent inadvertent damage to the ureter.

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Keywords: ureteral diseases, inguinal hernia, computed tomography

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