VOLUME 14 • 2021

WHAT'S INSIDE: ORIGINAL RESEARCH • CASE REPORT • COMMENTARY

KANSAS JOURNAL of MEDICINE

TABLE OF CONTENTS

KANSAS JOURNAL of MEDICINE

Bariatric Metabolic Surgery Reduced Liver Enzyme Levels in Patients with Non-Alcohol Fatty Liver Disease

Kennedy Kirkpatrick, MBA[1], Bobbie Paull-Forney, R.N., MPH[2], Hayrettin Okut, Ph.D.[1,3], Tiffany Schwasinger-Schmidt, M.D., Ph.D.[1,3,4]
[1]University of Kansas School of Medicine-Wichita, Wichita, KS
[2]Ascension Via Christi Weight Management Clinic, Wichita, KS
University of Kansas School of Medicine-Wichita, Wichita, KS
[3]Office of Research
[4]Department of Internal Medicine

Received Dec. 8, 2020; Accepted for publication April 22, 2021; Published online Sept. 1, 2021
https://doi.org/10.17161/kjm.vol1414984

ABSTRACT

Introduction. Approximately 93.3 million Americans are obese (BMI > 30 kg/m^2) and 51% have non-alcoholic fatty liver disease (NAFLD). Progression of NAFLD can lead to non-alcoholic steatohepatitis (NASH), which is the leading cause of liver transplant in the United States. This study analyzed liver enzyme levels following bariatric metabolic surgery in NAFLD patients up to one-year post-surgical intervention.

Methods. A retrospective analysis of adults with NAFLD who underwent bariatric metabolic surgery from 2009 to 2016 was conducted. The primary outcomes were transaminase levels following surgery. Secondary outcomes included levels of blood glucose and lipids.

Results. A total of 130 participants consisting of 80% Caucasian females with an average BMI of 47.5 kg/m^2 participated in the study. Reductions were noted in ALT (57.6% decrease) and AST (47.7% decrease) at one-year post-surgical intervention. Significant reductions also were noted in levels of blood glucose (22.34%; $p < 0.0001$), HbA1c (1.11% change; $p < 0.0001$), LDL (19.75%; $p = 0.0046$), total cholesterol (10.12%; $p = 0.0153$), and triglycerides (37.21%; $p < 0.0001$) with an increase in HDL levels (17.22%; $p = 0.0007$). Significant correlations were noted at six months between levels of alkaline phosphatase and both ALT ($p = 0.0101$) and AST ($p = 0.0009$), as well as an additional correlation trending toward significance between ALT and alkaline phosphatase at one year ($p = 0.0547$). When separated by obesity class, participants with class II obesity experienced improved outcomes compared to participants with class III obesity.

Conclusions. Bariatric metabolic surgery was associated with a reduction in liver enzyme levels in NAFLD. These findings suggested that bariatric metabolic surgery is a viable treatment option for participants with NAFLD. ***Kans J Med 2021;14:209-214***

INTRODUCTION

The prevalence of obesity in the United States has increased to 93.3 million, with 85% of individuals with class III obesity (Body Mass Index [BMI] 40-59.9 kg/m^2) estimated to have hepatic steatosis, 40% of whom also have steatohepatitis.[1] Bariatric metabolic surgery is associated with reduced obesity related morbidity and mortality and improvements in metabolic markers of disease; yet, its impact as a treatment option for patients with Non-Alcoholic Fatty Liver Disease (NAFLD) has not been well defined.[2,3]

Patients with NAFLD are at a significantly increased risk of cardiovascular disease, type 2 diabetes mellitus, and chronic kidney disease.[2,4,5] Patients with NAFLD may progress to Non-Alcoholic Steatohepatitis (NASH), which results in a three-fold increased risk of cardiovascular mortality; a seven-fold increased risk of developing hepatocellular carcinoma (HCC); and a six-fold increased risk of liver associated mortality. NASH has surpassed viral hepatitis as the second leading indication for liver transplant in the United States, with only 10% of transplant candidates with NAFLD or NASH receiving liver transplants yearly.[6]

Despite the success of bariatric metabolic surgery in obesity treatment, and the significant association between obesity and NAFLD, weight loss using diet and exercise remains the standard of care. Total body weight loss of 3 - 5% may reduce hepatic steatosis, but losses greater than 10% are necessary to prevent liver fibrosis. Unfortunately, only 10% of patients who attempt weight loss using diet and exercise alone achieve this goal.[7,8] Furthermore, randomized clinical trials for patients with NAFLD using weight loss alone has not decreased mortality, nor has it reduced cardiovascular events, which remain the number one cause of death for patients with NAFLD.[9] Additionally, use of pharmacologic therapy for weight loss in NAFLD is not superior to surgical intervention and there are currently no Food and Drug Administration (FDA) approved medications specifically used to treat NAFLD in the United States.[10]

Bariatric metabolic surgery can improve management of comorbid medical conditions. A single-center randomized control trial comparing remission of type II diabetes mellitus in patients with obesity, with diabetes mellitus defined by fasting glucose less than 100 mg/dL and HbA1c lower than 6.5% in the absence of pharmacotherapy at two years, using treatment with medical therapy versus bariatric metabolic surgery found that none of the patients treated with medical therapy alone achieved remission after two years, while 75% in the gastric-bypass group and 95% in the biliopancreatic-diversion group achieved remission.[11] Surgical patients not only experienced greater weight reduction when compared to patients using diet and exercise alone, but also had decreased rates of complications from diabetes including myocardial infarction (7%), retinopathy (7%), nephropathy (7%), and neuropathy (13%) when compared to patients using diet and exercise for weight loss.

A mortality benefit has been observed in patients undergoing bariatric metabolic surgery, with a reduced mortality rate of 2.51 per one thousand person-years in surgical candidates versus nonsurgical candidates.[12] A 0.76 decrease in overall mortality and 0.46 reduction in cardiovascular morality at 16 years was observed post-intervention in patients with NAFLD who underwent bariatric metabolic surgery compared to control groups, along with an increased likelihood of resolution of type II diabetes, hypertension, and reduction in the use of anti-hypertensive medications.[13,14] Additionally, 60.4% of gastric bypass patients and 22.7% with gastric banding experienced remission of hyperlipidemia following bariatric metabolic surgery in a three-year study focusing specifically on hyperlipidemia treatment.[14] Bariatric metabolic surgery for NAFLD patients specifically showed promising

effects in liver-related pathologic changes. A review of the current literature showed that a 9.75% to 36.5% reduction in BMI was associated with complete resolution of hepatic steatosis, ballooning, and fibrosis in 66% of patients across multiple studies.[15]

The objective of this study was to evaluate the effect of bariatric metabolic surgery on liver enzyme levels in participants with diagnosed NAFLD prior to bariatric metabolic surgery. Secondary analysis included the association of bariatric metabolic surgery with type II diabetes mellitus and hyperlipidemia. The effects of bariatric metabolic surgery were separated by obesity class to determine the impact of the intervention at all stages of obesity progression. Lastly, adverse effects on bone health and cholestatic disease were analyzed, as these markers have not been studied extensively in patients with NAFLD.

METHODS

Research Participants. Study participants included individuals ages 18 years and older who completed bariatric metabolic surgery from January 1, 2009 through April 1, 2016 at a Midwest hospital. Participants were included in the study if they had a diagnosis of NAFLD with elevations in transaminase levels at baseline, an absence of known chronic liver disease, no significant alcohol consumption, and demonstration of hepatic steatosis by imaging or liver biopsy. Participants were excluded if they were diagnosed previously with hepatitis B, hepatitis C, hepatocellular carcinoma, liver cirrhosis, alcohol abuse, substance abuse, pregnancy, any eating disorder or aberrant eating behavior, or severe liver disease defined by those awaiting liver transplant, renal failure defined by patients on dialysis or awaiting kidney transplant, active malignancy, Cushing's syndrome, bacterial endocarditis, osteomyelitis, or tuberculosis. All participants enrolled met the inclusion and exclusion criteria and were followed clinically for eight weeks prior to surgery and up to one-year post-surgical intervention. The study was approved by the local Institutional Review Board and by the university's Human Subjects Committee.

Data Collection. This study was a retrospective chart review of patients with a clinical diagnosis of NAFLD prior to completion of bariatric metabolic surgery. Data abstracted included the following demographics: age, race, ethnicity, gender, height, weight, date of birth, BMI, and date of surgery. Biometric variables included serum levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT), systolic and diastolic blood pressures, levels of hemoglobin A1c (HbA1c), fasting plasma glucose, lipids including total cholesterol, triglycerides, low density lipoprotein (LDL), and high density lipoprotein (HDL), alkaline phosphatase, total bilirubin, albumin, total protein, and creatinine. Other variables included medication use (anti-hypertensive, anti-diabetic, and cholesterol lowering medications) and associated comorbidities (obstructive sleep apnea, dyslipidemia, hypertension, hyperlipidemia, and diabetes mellitus). All biometric variables were collected at four discrete time points: at the time of bariatric metabolic surgery, and three months, six months, and one-year post-surgical intervention. Blood pressures were measured to the nearest 2 mmHg using an aneroid sphygmomanometer. Heights were measured without shoes to the nearest 0.125 inch. Verified body weights were measured to the nearest 0.1 pound (0.045 kg) with clothing and no shoes at baseline. BMI was calculated by kilograms divided by current height in meters squared. All patient data were deidentified and entered into a secure data processing website, REDCap®.[16]

Statistical Analysis. Data were analyzed using SAS version 9.4 (SAS Int. Inc., Cary, NC). Frequencies, proportions, means, and standard deviations were generated. Shapiro-Wilks tests were conducted to check variables for their distribution. As normality assumptions for variables and differences in time point measurements (between baseline and three months, three months and six months, and six months and twelve months) were rejected, the natural logarithm transformation was applied to the outcome variables.

For longitudinal data and to characterize the trajectories for individual units, random coefficient multilevel models were conducted to analyze the data and model parameters. Schwarz's Bayesian information criterion was considered for selecting the appropriate covariance structure between repeated measurements. Bonferroni adjusted least squared means of groups were used for pairwise comparisons.

Independent t-tests were applied to compare the mean difference between participants with diabetes and hypertension, and one-way ANOVA was used to compare the mean difference between BMI. A Tukey test was carried out for the pairwise comparisons of BMI. Moreover, linear single and multiple regression models and correlation analyses were conducted to reveal further associations between dependent and independent variables. All statistical tests at $p \leq 0.05$ were considered significant.

RESULTS

A total of 130 participants met the inclusion and exclusion criteria for the study. The majority were Caucasian (80%, n = 104) and female (79.2%, n = 103; Table 1). Additionally, 9.2% (n = 10) of participants were Hispanic or Latino. Average baseline BMI was 47.50 kg/m^2 ± 7.71 with 18.2% (n = 23) having class II obesity (BMI 35.0-39.9 kg/m^2) and 82.3% (n = 107) having class III obesity (Table 1). Average age was 49.37 ± 12.17 years (range 24 to 75; Table 1).

Table 1. Baseline demographic data from study participants.

Gender	**Percentage**
Male	20.8
Female	79.2
Ethnicity	
Caucasian	80
Hispanic	9.2
American Indian or Alaska Native	1.5
Asian or Pacific Islander	0.8
Other	8.5
Obesity class	
Class II	18.2
Class III	82.3

At baseline, participants were diagnosed with the following comorbidities: hypertension (81%, n = 106), type II diabetes mellitus (45%, n = 59), and hyperlipidemia (83%, n = 108). A total of 71% (n = 93) were taking at least one antihypertensive medication and 45% (n = 59) used at least one medication to treat type II diabetes mellitus.

Average liver enzyme levels were reduced markedly at one-year post-surgical intervention. ALT was reduced by 57% (28.58) and AST was reduced by 47% (24.21) at one-year post-intervention (Figure 1). Negative correlations were noted between both ALT and AST levels with alkaline phosphatase levels at six months (correlation coefficient of 0.35, p = 0.0101 with AST; correlation coefficient of 0.27, p = 0.0009 with ALT) and at one year between alkaline phosphatase and ALT (correlation coefficient of 0.21, p = 0.0547).

Statistically significant correlations were noted at one-year post-intervention between levels of ALT and total cholesterol (correlation coefficient of 0.30, p = 0.0311), triglycerides (correlation coefficient of 0.34, p = 0.0108), and LDL (correlation coefficient of 0.35, p = 0.0126).

Secondary outcome measures, including fasting blood sugar, HbA1c, total cholesterol, triglycerides, LDL, HDL, cholesterol, and systolic and diastolic blood pressures also showed improvement (Table 2). Fasting plasma glucose decreased on average by 36.09 mg/dL at one year (p < 0.0001) and HbA1c decreased from 6.59% at baseline to 5.49% at one year (p < 0.0001) following surgery (100-125 mg/dL fasting glucose; HbA1c 6.5% mmol/L; Table 2). Lipid levels improved at one-year post surgery, with cholesterol decreasing on average by 17 mg/dL (p = 0.0153), LDL decreasing by 24 mg/dL (p = 0.0046), and triglycerides decreasing by 68 mg/dL (p < 0.0001). The HDL level increased by 9 mg/dL at one year (p = 0.0007).

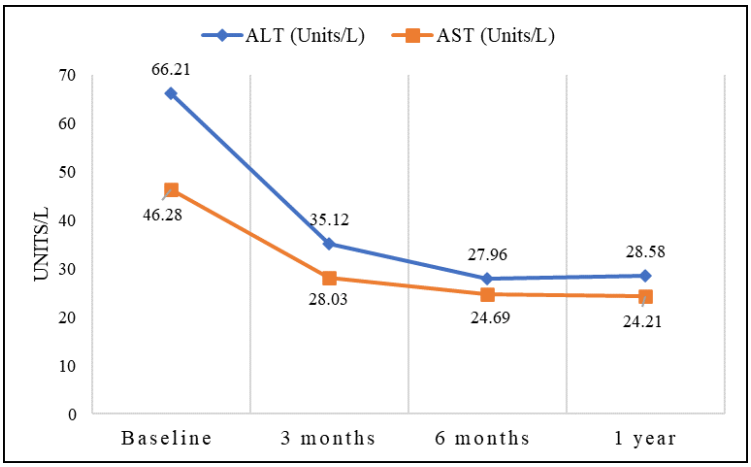


Figure 1. Transaminase level averages one-year post-surgical intervention.

Table 2. Laboratory values were measured at four different time points.

Survey item	Baseline*	3 months	6 months	1 year
ALT (0-35 units/L)	66.21	35.12	27.96	28.58
AST (0-35 units/L)	46.28	28.03	24.69	24.21
Glucose, fasting (70-100 mg/dL)	131.81	102.09	99.8	94.82
HbA1c	6.59%	5.93%	5.62%	5.49%
Total cholesterol (<239 mg/dL)	187.89	167.89	164.79	170.94
Triglycerides (< 199 mg/dL)	182.9	145.44	120.5	114.86
HDL (<40 mg/dL)	44.46	39.98	43.92	53
LDL (<129 mg/dL)	120.2			96.47
Alkaline phosphatase (26-104 units/L)	83.2	84.8	87.16	86.73
Total bilirubin (0.2-1.2 mg/dL)	0.51	0.57	0.61	0.61

*Baseline corresponds with the laboratory values observed at time of bariatric metabolic surgery.

At one-year post-surgical intervention, significant differences were noted in the change in transaminase levels when comparing by obesity class (Figure 2). Patients with class II obesity had lower average transaminase levels at one year with ALT at 33.03 (u/L) and AST at 26.99 (u/L), in contrast with patients with class III obesity who had an average ALT of 67.64 (u/L) and AST of 47.36 (u/L; Table 3). Participants with class II obesity also had statistically significant positive correlations between levels of ALT and glucose (correlation coefficient of 0.13; p = 0.00332), HbA1c (correlation coefficient of 0.22; p = 0.0109), and triglycerides (correlation coefficient of 0.17; p = 0.0321). Additionally, in participants with class II obesity, both ALT (correlation coefficient of 0.17, p = 0.0011) and AST (correlation coefficient of 0.19, p = 0.0034) levels were correlated with a rise in alkaline phosphatase levels from 83.2 (u/L) at baseline to 86.73 (u/L) at one year.

All participants in this study, regardless of obesity class, experienced increases in alkaline phosphatase and total bilirubin levels at one-year post-surgical intervention (Table 3). The mean alkaline phosphatase level was increased by 3.53 mg/dL with a peak level of 87.16 mg/dL (Figure 3), and total bilirubin levels increased by 0.11 u/L at one year.

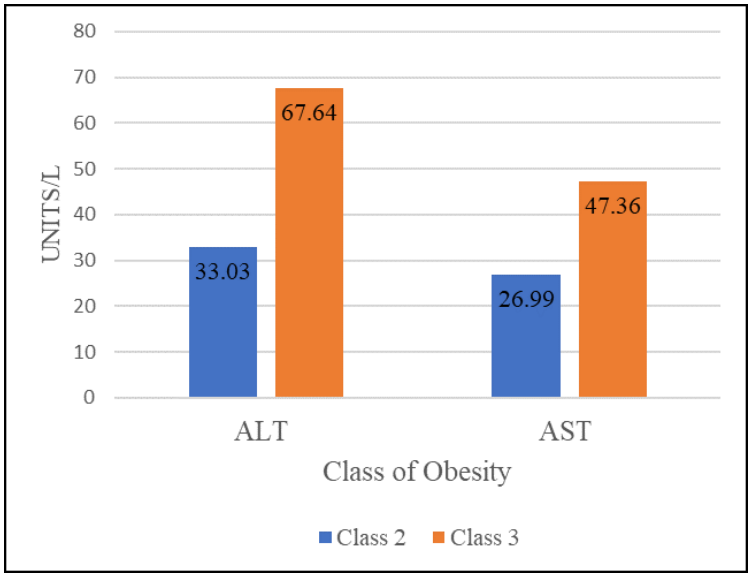


Figure 2. Transaminases based on obesity class.

Table 3. The average measurements for primary and secondary outcomes for patients with Class II and Class III obesity taken at one year.

Obesity class	Average
Class II	
ALT	33.03
AST	26.99
Glucose	100.76
HbA1c	5.80
Triglycerides	134.46
Total cholesterol	172.86
Alkaline phosphatase	86.39
Class III	
ALT	67.64
AST	47.36
Glucose	134.33
HbA1c	6.60
Triglycerides	182.16
Total cholesterol	184.47
Alkaline phosphatase	81.99

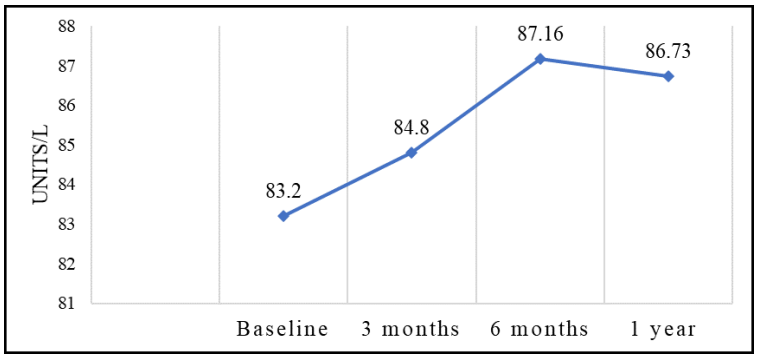


Figure 3. Alkaline phosphatase levels (units/L) were analyzed throughout this study.

DISCUSSION

Results obtained from this study showed that bariatric metabolic surgery was associated with significantly reduced liver enzyme levels in participants with NAFLD up to one-year post-surgical intervention with ALT reduced by 37.64 u/L and AST reduced by 22.08 u/L. A systematic review by Bower et al.[14] found similar results, with an average reduction in ALT of 11.63 u/L and AST of 3.91 u/L across all studies up to five years post-surgical intervention. Reducing transaminase levels is associated with a decreased risk of progression to NASH, hepatocellular carcinoma, and end-stage liver disease. A study evaluating elevated liver enzymes on all-cause mortality demonstrated patients with sustained elevations in AST had a 2.88 increased relative mortality rate (HR 1.93; aHR 1.54) and a 1.33 increased relative mortality rate (HR .72; aHR 1.38) when compared to patients with normal liver enzyme levels.[17]

Few prior studies have investigated reductions in liver enzyme levels based on obesity class in patients with NAFLD. The prevalence of NAFLD increases with increasing BMI, with non-obese individuals exhibiting 3% steatosis on average, individuals with class I or II obesity exhibiting 20% steatosis, and 40% steatosis exhibited by those diagnosed with class III obesity.[1] Our study found that participants with class II obesity showed 48% lower ALT levels and 57% lower AST levels at one-year post-surgical intervention compared to patients with class III obesity (Figure 2). Additionally, significant correlations were noted between ALT and levels of blood glucose, HbA1c, and triglycerides in class II obesity patients compared to participants with class III obesity who showed reductions in glucose alone. Current guidelines to qualify for bariatric metabolic surgery from the American Society for Metabolic and Bariatric Surgery include a BMI of ≥ 40 kg/m^2, being 100 pounds overweight, or a BMI of ≥ 35 kg/m^2 with significant comorbidities. However, findings from this study suggested that earlier surgical interventions may yield better results with regards to reductions in associated co-morbidities.

At one-year post-surgical intervention in this study, average levels of HbA1c and fasting blood glucose of all participants were within the normal range, alongside statistically significant positive correlations between AST and glucose in participants with class III obesity and ALT and glucose in patients with class II obesity. Simultaneous reductions in blood glucose and liver transaminase levels suggested bariatric metabolic surgery in patients with NAFLD can decrease comorbid disease burden and prevent irreversible end organ damage.

Numerous long-term studies on patients with NAFLD and type II diabetes mellitus demonstrated significant improvements in blood glucose and potential remission of type II diabetes mellitus following bariatric metabolic surgery.[2,3] Xourafas et al.[18] reported a significant positive correlation between ALT and HbA1c reduction at one-year post-surgical intervention with noted improvements in HbA1c from 8.3% to 6.1%, along with a 20% reduction in ALT among Roux-en-Y participants, and 17% reduction in laparoscopic adjustable gastric banding participants after three months post-surgical intervention. A meta-analysis by Panunzi et al.[19] demonstrated 71% of patients with type II diabetes mellitus with preoperative BMI < 35 kg/m^2 and 72% of patients with preoperative BMI > 35 kg/m^2 experienced diabetes remission. Our study also showed a reduction in HbA1c, with an average HbA1c of 5.5% at one-year post-surgical intervention. However, we cannot claim that participants in this study achieved remission of diabetes given that some participants were still taking anti-diabetic medications following surgical intervention.

Of all the benefits gained from patients in this study undergoing bariatric metabolic surgery, some alternate findings suggested potential risks from the procedure. Patients in this study had elevations in alkaline phosphatase and total bilirubin levels up to one-year post-surgical intervention. Although these elevations were within normal limits of the laboratory range, the pathogenesis of these findings are not understood fully given current literature review, and elevations in alkaline phosphatase and bilirubin values were unexpected.[20,21] Elevated bilirubin may be secondary to increased cholestatic liver patterns resulting in increased gallstone formation, primary biliary cholangitis, and potential development of cholangitis following bariatric metabolic surgery. The prevalence of gallstones in patients undergoing bariatric metabolic

surgery for obesity is estimated to be around 10% within 10 years after surgery.[22] One theory behind this association included decreased post-operative fat-soluble vitamin absorption resulting in reductions in active vitamin D and increased oxalate levels. This resulted in low calcium reabsorption in the intestines allowing for oxalate precipitation and stone formation. Hypocitraturia and hyperoxaluria has been exhibited in 29 - 74% of patients following bariatric metabolic surgery.[21] However, literature specific to patients with NAFLD who have undergone bariatric metabolic surgery to monitor cholestatic complications was sparse. This association will be important for future studies to target a potentially preventable adverse effect following surgical intervention.

Another potential adverse effect of bariatric metabolic surgery in this study is the observed elevation in alkaline phosphatase levels, indicating potential for early onset osteoporosis or osteomalacia from both bone demineralization and lack of fat-soluble vitamin absorption due to sequestration in adipose tissue among patients with NAFLD.[23] Risk of fracture seen in bariatric metabolic surgery is high, with an observed 10.2% decrease in femoral neck bone mineral density one-year post surgery.[24] However, these effects were not just short term; even when weight stabilizes, patients can experience an additional 2.7% decrease in bone density within the spine, radius, and tibia up to five years after surgery. Additional long-term studies regarding bone health in patients undergoing bariatric metabolic surgery among NAFLD patients specifically are needed to further characterize this observation and determine the best method to promote bone health in this at-risk population.

The strengths of this study included the observed reduction in transaminase levels among patients with NAFLD following bariatric metabolic surgery. In addition, this study was able to analyze the effects of bariatric metabolic surgery on comorbid conditions including type II diabetes mellitus and dyslipidemia. This study had an adequate sample size for a retrospective study allowing adequate correlations to be analyzed in the sample population. In addition, this study attained adequate follow up so that correlations up to one-year post-surgical intervention were able to be analyzed.

Limitations of this study included the retrospective design and absence of a control group for comparison of outcomes and management using the standard of care. Another limitation of this study was the lack of patients with class I obesity or overweight patients. Analysis of the effects of bariatric metabolic surgery on patients with NAFLD with concurrent class I obesity or being overweight may provide additional data to promote earlier surgical intervention. Another limitation of this study was the lack of diversity within the study with 80% of patients in this study being Caucasian and 79.2% being female. A larger, more diverse patient population would provide more generalizable results.

CONCLUSIONS

In conclusion, this study showed a significant improvement in liver enzyme levels following bariatric metabolic surgery in patients with NAFLD. This finding supported the use of bariatric metabolic surgery as a treatment modality for NAFLD to prevent increased liver fibrosis and progression to end stage liver disease. This study also demonstrated a reduction in the prevalence of comorbid conditions including type II diabetes mellitus and hyperlipidemia. Future controlled prospective studies should quantify the potential adverse effects of bariatric metabolic surgery on both bone and biliary function, as these are both theoretically preventable adverse events that could be addressed with a better understanding of the underlying pathogenesis.

ACKNOWLEDGEMENTS

The authors thank Dr. Elizabeth Ablah for her guidance through each stage of this process.

CONFLICTS OF INTEREST

Tiffany Schwasinger-Schmidt, M.D., Ph.D., has conducted clinical trials research as principal investigator for the following pharmaceutical companies over the last twelve months: Allergan, Eisai, Lundbeck, Janssen, SAGE pharmaceuticals, Sarepta, Corcept, Boehringer Ingelheim, and AstraZeneca. All clinical trial and study contracts were with and payments were made to the University of Kansas Medical Center Research Institute, which is a research institute affiliated with University of Kansas School of Medicine-Wichita.

REFERENCES

[1] Fabbrini E, Sullivan S, Klein S. Obesity and nonalcoholic fatty liver disease: biochemical, metabolic, and clinical implications. Hepatology 2010; 51(2):679-689. PMID: 20041406.
[2] Chavez-Tapia NC, Tellez-Avila FI, Barrientos-Gutierrez T, Mendez-Sanchez N, Lizardi-Cervera J, Uribe M. Bariatric surgery for non-alcoholic steatohepatitis in obese patients. Cochrane Database Syst Rev 2010; 2010(1):CD007340. PMID: 20091629.
[3] Lassailly G, Caiazzo R, Buob D, et al. Bariatric surgery reduces features of nonalcoholic steatohepatitis in morbidly obese patients. Gastroenterology 2015; 149(2):379-388. PMID: 25917783.
[4] Kim D, Kim WR, Kim HJ, Therneau TM. Association between noninvasive fibrosis markers and mortality among adults with nonalcoholic fatty liver disease in the United States. Hepatology 2013; 57(4):1357-1365. PMID: 23175136.
[5] Ekstedt M, Hagstrom H, Nasr P, et al. Fibrosis stage is the strongest predictor for disease-specific mortality in NAFLD after up to 33 years of follow-up. Hepatology 2015; 61(5):1547-1554. PMID: 25125077.
[6] Wong RJ, Singal AK. Trends in liver disease etiology among adults awaiting liver transplantation in the United States, 2014-2019. JAMA Netw Open 2020; 3(2):e1920294. PMID: 32022875.
[7] Alkhouri N, Poordad F, Lawitz E. Management of nonalcoholic fatty liver disease: Lessons learned from type 2 diabetes. Hepatol Commun 2018; 2(7):778-785. PMID: 30027137.
[8] Lassailly G, Caiazzo R, Pattou F, Mathurin P. Perspectives on treatment for nonalcoholic steatohepatitis. Gastroenterology 2016; 150(8):1835-1848. PMID: 26971824.
[9] Jenkins SS, Sowden N, Colquhoun D, Ferreira-Jardim A. Obesity is only a risk number for secondary prevention – Failure of randomised weight loss trials. [Abstract]. Heart Lung Circ 2019; 28(Suppl 4):S309.
[10] Oseini AM, Sanyal AJ. Therapies in non-alcoholic steatohepatitis (NASH). Liver Int 2017; 37(Suppl 1):97-103. PMID: 28052626.
[11] Mingrone G, Panunzi S, De Gaetano A, et al. Bariatric-metabolic surgery versus conventional medical treatment in obese patients with type 2 diabetes: 5 year follow-up of an open-label, single-centre, randomised controlled trial. Lancet 2015; 386(9997):964-973. PMID: 26369473.
[12] Reges O, Greenland P, Dicker D, et al. Association of bariatric surgery using laparoscopic banding, Roux-en-Y gastric bypass, or laparoscopic sleeve gastrectomy vs usual care obesity management with all-cause mortality. JAMA 2018; 319(3):279-290. PMID: 29340677.
[13] Aguilar-Olivos NE, Almeda-Valdes P, Aguilar-Salinas CA, Uribe M, Mendez-Sanchez N. The role of bariatric surgery in the management of nonalcoholic fatty liver disease and metabolic syndrome. Metabolism 2016; 65(8):1196-1207. PMID: 26435078.
[14] Bower G, Toma T, Harling L, et al. Bariatric surgery and non-alcoholic fatty liver disease: A systematic review of liver biochemistry and histology. Obes Surg 2015; 25(12):2280-2289. PMID: 25917981.

[15] Lee Y, Doumouras AG, Yu J, et al. Complete resolution of nonalcoholic fatty liver disease after bariatric surgery: A systematic review and meta-analysis. Clin Gastroenterol Hepatol 2019; 17(6):1040-1060.e11. PMID: 30326299.
[16] Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)--A metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009; 42(2):377-381. PMID: 18929686.
[17] Lee H., Shin DW, Lee TH, et al. Association between change in serum aminotransferase and mortality: A nationwide cohort study in Korea. Medicine (Baltimore) 2016; 95(12):e3158. PMID: 27015199.
[18] Xourafas D, Ardestani A, Ashley SW, Tavakkoli A. Impact of weight-loss surgery and diabetes status on serum ALT levels. Obes Surg 2012; 22(10):1540-1547. PMID: 22610995.
[19] Panunzi S, De Gaetano A, Carnicelli A, Mingrone G. Predictors of remission of diabetes mellitus in severely obese individuals undergoing bariatric surgery: Do BMI or procedure choice matter? A meta-analysis. Ann Surg 2015; 261(3):459-467. PMID: 25361217.
[20] Yu EW. Bone metabolism after bariatric surgery. J Bone Miner Res 2014; 29(7):1507-1518. PMID: 24677277.
[21] Froeder L, Arasaki CH, Malheiros CA, Baxmann AC, Heilberg IP. Response to dietary oxalate after bariatric surgery. Clin J Am Soc Nephrol 2012; 7(12):2033-2040. PMID: 23024163.
[22] Talha A, Abdelbaki T, Farouk A, Hasouna E, Azzam E, Shehata G. Cholelithiasis after bariatric surgery, incidence, and prophylaxis: Randomized controlled trial. Surg Endosc 2019; 34(12):5331-5337. PMID: 31858245.
[23] Melo TL, Froeder L, da Cunha Baia L, Heilberg IP. Bone turnover after bariatric surgery. Arch Endocrinol Metab 2017; 61(4):332-336. PMID: 28724055.
[24] Bruno C, Fulford AD, Potts JR, et al. Serum markers of bone turnover are increased at six and 18 months after Roux-en-Y bariatric surgery: Correlation with the reduction in leptin. J Clin Endocrinol Metab 2010; 95(1):159-166. PMID: 19858320.

Keywords: obesity, non-alcoholic steatohepatitis, NAFLD, liver steatosis, bariatric surgery

KANSAS JOURNAL of MEDICINE

Attitudes toward Rubella and Varicella Vaccination during Preconception Care

Elise Foley, MS-3[1], Shelby Breit, MS-3[1], Courtney Marsh, M.D.[2], Kevin Ault, M.D.[2], Michael Lydic, M.D.[2]
[1]University of Kansas School of Medicine-Salina, Salina, KS
[2]University of Kansas Medical Center, Kansas City, KS
Center for Advanced Reproductive Medicine

Received Feb. 16, 2021; Accepted for publication May 5, 2021; Published online Sept. 1, 2021
https://doi.org/10.17161/kjm.vol1415205

ABSTRACT

Introduction. Studies of anti-vaccine attitudes in the perinatal time period previously have not paid special attention to the MMR and varicella vaccines. Because both contain live attenuated virus, a contraindication during pregnancy, it is important to assess barriers to vaccination clinically during preconception to avoid the known fetal morbidity associated with congenital rubella or varicella infection.

Methods. The primary outcome of this study was to determine prevalence of patients with nonimmune status for rubella and varicella in the setting of advanced reproductive care. Secondary outcomes of interest included further understanding nonimmune reproductive-aged women's attitudes toward MMR and varicella vaccination during preconception. Patient records with laboratory orders for rubella or varicella immunoglobulin titers, placed at the KU Advanced Reproductive Care clinic between January 2017 and June 2020, were reviewed (n = 2,217). A cross-sectional survey was administered to patients with a laboratory reported negative titer result.

Results. Prevalence of nonimmunity to either rubella or varicella represented 6.0% (n = 134) and 3.8% (n = 85) of records, respectively; nineteen records (0.6%) demonstrated nonimmunity to both. The women who did not receive recommended vaccines following a nonimmune titer result (n = 19) most commonly cited their rationale was to not delay fertility treatment further (n = 8), a requirement when receiving live attenuated virus vaccines.

Conclusions. The prevalence of nonimmune persons in the study population fell within the range recognized to be sufficient for herd immunity. The majority of survey respondents indicated that CDC recommended vaccinations were of high personal importance, with strong congruence of thought among those who answered in favor of vaccines when posed with several true or false statements about personal beliefs and vaccine efficacy. The risk/benefit analysis of postponing fertility treatment to achieve adequate levels of immunity should be a focused discussion when establishing fertility treatment goals with patients in the setting of advanced reproductive care.

Kans J Med 2021;14:215-219

INTRODUCTION

Many components of prenatal care are endorsed by the literature of several physician organizations, one of which is routine screening for communicable disease.[1-4] The recommended tests for communicable disease screening are to be performed at the initial prenatal care visit and include documentation of immunity to rubella and varicella, serum tests for human immunodeficiency virus, syphilis, hepatitis B virus (HBV), and endocervix or vaginal swab for chlamydia. Hepatitis C virus (HCV) historically has been included as a selective testing option and remains as such according to guidelines from Society for Maternal-Fetal Medicine; however, the U.S. Centers for Disease Control and Prevention (CDC) recently revised its position and now suggests all pregnant women be screened for HCV except where prevalence of infection is less than 0.01%.[5,6] Importantly, screening is conducted because non-immune pregnant women and their fetuses who are exposed to these diseases experience higher morbidity than nonpregnant women.[7]

Of this panel, three diseases are preventable by vaccine: rubella, varicella, and HBV. An in-depth review of literature revealed that while there were several studies specifically regarding anti-influenza vaccine attitudes in women of childbearing age and pregnant women, measles, mumps, and rubella (MMR) and varicella largely have been ignored.[8,9] Both MMR and varicella vaccines contain live virus, thus are contraindicated during pregnancy, so the window of opportunity requires anticipating pregnancy, if at all possible, through preconception counseling.[10] Recommendations for non-immune pregnant women are to avoid exposure until postpartum, when live vaccines are no longer contraindicated. With increasing rates of nonimmunity due to anti-vaccine attitudes,[11] primarily held by parents for their young children, avoiding exposure may be a challenge in geographic locations where population disease burden is high.

As defined by The American Society of Reproductive Medicine, "The goal of prepregnancy care is to reduce the risk of adverse health effects for the woman, fetus, and neonate by working with the woman to... address modifiable risk factors".[4] Control of existing health conditions, limiting teratogen exposure, nutritional status, and treating or preventing infections are a few examples of risk factors that are considered modifiable, thus should be discussed during preconception counseling.

Preconception counseling around vaccines within the setting of an infertility clinic is a unique, understudied population. Since the timing of conception theoretically is controlled with treatment, providers have the opportunity to prevent the morbidity known to be associated with exposure to rubella and varicella. The primary outcome of this study was to assess the prevalence of nonimmunity within the patient population seeking fertility assistance. Secondary outcomes of interest included further understanding non-immune, reproductive aged women's attitudes toward MMR and varicella vaccination during the preconception timeline and assess how these attitudes may impact fertility treatment goals.

METHODS

A cross-sectional survey was performed to assess prevalence of fertility clinic patients who were non-immune to rubella and varicella. The population of interest was identified through a report of all patients with a venipuncture order placed at the University of Kansas Center for Advanced Reproductive Medicine between January 2017 and June 2020 and was narrowed by laboratory draw orders that included rubella and varicella antibody titers. Using the electronic medical record, the

titer data were collected for the patients previously identified to have a laboratory order for rubella and varicella titer. The laboratory-reported qualitative value for each titer was used to determine each patient's status: immune, equivalent, or non-immune. To meet inclusion criteria, patients had to have a laboratory-reported qualitative value of non-immune for either rubella or varicella serology titers.

Patients within the equivalency range for IgG were considered to have positive immunity since the University of Kansas Center for Advanced Reproductive Care did not recommend further vaccinating patients within the equivalency range routinely; therefore, they would not have been advised to receive a vaccine and would not meet inclusion criteria for this study. Patients with unknown titer results for both rubella and varicella were excluded from analysis.

The survey was comprised of 27 questions and took an estimated 10 minutes to complete. Questions were posed in a variety of formats, including true/false, prepared answer multiple choice, and optional free-text response fields. Survey respondents supplied basic demographic information (gender, ethnicity, race, education, age, and annual household income as a function of federal poverty limits) followed by answering 15 questions about self-reported general attitudes toward vaccines, self-reported incidence of follow-up, recency of vaccine counseling, and knowledge of CDC vaccination recommendations.

In 2017, Reavis et al.[12] conducted a cross-sectional survey assessing parental attitudes toward MMR vaccination for children under 18, using a 5-point Likert scale to measure average support for or denial of statements regarding the vaccine. Similarly, conclusions in this study were drawn by making the assumption that personal affirmation of a statement is a surrogate marker for belief in effectiveness of the vaccine but hold no statistical significance. Respondents' attitudes toward the protective effects of vaccination were analyzed further by relationship to the respondent. This was measured using the following questions, with the relationship association in parentheses: personal feelings about the importance of receiving the influenza vaccine during pregnancy (Flu-self/fetus), plans to follow CDC recommended vaccination schedules for their children (CDC-children), and belief in the ability of the varicella vaccine to protect others who are immunocompromised (Varicella-others).

True knowledge regarding the vaccines of interest was measured by percent correctly answered questions based upon CDC "what everyone should know" criteria for the MMR and chickenpox (varicella) vaccines.[13,14] This percentage was compared to self-reported confidence in knowledge of each vaccine, rated as a sliding scale between 0 and 100. In an attempt to control for the influence of recency bias on true knowledge, respondents were asked to provide the time frame in which they were last counseled on the MMR or varicella vaccines.

Study data were collected and managed using REDCap® electronic data capture tools hosted at University of Kansas Health System. Patients received an explanatory email with an informed consent form and a self-administered survey. In an attempt to maximize the response rate, reminder emails were sent twice after which the study team made one phone call per non-respondent.

Data were summarized using frequencies and percentages for categorical data and mean and standard deviations for continuous data. Basic descriptive statistics were calculated for demographic data, and all quantitative variables regarding vaccine beliefs, history, and knowledge. Answers from open-ended questions were grouped into common themes, with consideration for similarity and pervasiveness, and analyzed qualitatively. This study was approved by the Human Subjects Committee at the University of Kansas School of Medicine.

RESULTS

A total of 2,217 records were identified to have lab orders for rubella and varicella titers with 89.3% (n = 1,979) of patients' demonstrating immunity to both. Non-immune status to rubella and varicella represented 6.0% (n = 134) and 3.8% (n = 85) of records, respectively. Non-immune status to both rubella and varicella was nominal (0.6%, n = 19) and had no underlying factors identified that would delineate this group from the larger study population.

There was a small discrepancy between the number of non-immune patients (n = 238) and number of surveys administered (n = 244). Surveys were administered to 238 non-immune patients with a valid/current email address or phone number on file. Some non-immune patients were identified by providers on the same day as their lab titer resulted and subsequently were administered a survey without being included in the REDCap® report totals. In addition, a select few patients represented two survey invitations since they provided a valid email address after the initial survey link was sent. There were 73 completed surveys, making the response rate per all administered surveys equal to 29.9%.

Self-reported demographics are shown in Figure 1 and Table 1. The minimum and maximum participant ages were 21 and 43 years, respectively, and the average age was 31.8 years. Eight of the 73 survey respondents did not provide age data.

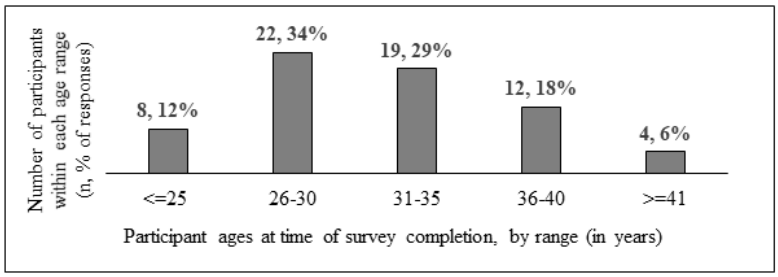


Figure 1. Survey participant age in years at time of survey completion. Ages are presented by number that fell within each age range, and the percentage each range represents of all respondents who provided a value for this metric (n = 65).

Table 1. Survey participant demographics including race, ethnicity, highest level of education, and annual income by household (n = 73).

Race	Number of responses n (% of total)
White	62 (84.9%)
Black or African American	6 (8.2%)
Asian	3 (4.1%)
More than one	2 (2.7%)
Ethnicity	
Hispanic or Latino	3 (4.1%)
Not Hispanic or Latino	70 (95.9%)
Highest level of education	
High school or equivalent	4 (5.5%)
Post-secondary non-degree award	2 (2.7%)
Some college, no degree	7 (9.6%)
Associate degree	7 (9.6%)
Bachelor's degree	26 (35.6%)
Master's degree	22 (30.1%)
Doctoral or professional degree	5 (6.8%)
Annual income by household	
< $16,910	1 (1.4%)
$16,911 - $33,820	3 (4.1%)
$33,821 - $50,730	5 (6.8%)
$50,731 - $67,640	9 (12.3%)
$67,641 - $84,550	6 (8.2%)
$84,551 - $101,460	16 (21.9%)
$101,461 - $118,370	5 (6.8%)
> $118,370	28 (38.4%)

Of respondents, 73.6% elected to receive recommended vaccines (n = 54). The highest selected rationale as to why they elected to receive the recommended vaccinations was that "It was recommended by my provider" (n = 50). Several respondents also selected, "I understand the potential severity of rubella and/or varicella symptoms" (n = 35).

The desire not to postpone attempts to conceive was the most selected option among the 19 participants that opted not to receive the recommended vaccines (n = 8, Table 2). "Other" open-ended rationale included the following comments: "I've just been lazy. I need to do it", "I was not offered vaccine", "I was immune", "Already pregnant when notified of titer results...would have gotten vaccination and delayed attempts to conceive".

Participants' answers to questions regarding vaccine attitudes, as they related to CDC-children and Varicella-others, indicated that they placed an overall high importance on recommended vaccinations. Sixty-seven (91.7%) of respondents anticipated following CDC guidelines for childhood vaccines for current and future children and acknowledged the statement, "Healthy people who get vaccinated against varicella can protect immunocompromised people from being exposed to the disease" as true. Participants were less likely to recognize the protective effects of vaccines in relationship to Flu-self/fetus, with 56 (76.7%) indicating that they personally felt it was important to receive the flu vaccine during pregnancy. Respondents provided rationale as to why the flu vaccine was not important during pregnancy included, "never received flu vaccine prior in life" and "rarely effective at predicting what viruses to protect against in upcoming flu season".

Table 2. Participant prepared multiple choice survey results regarding why they did or did not elect to receive the recommended vaccines, and the timeframe in which they last spoke with their health care provider about these vaccines.

From the following list, please select any that align with why you elected to receive the MMR (measles, mumps, rubella) and/or varicella (chickenpox) vaccines upon a negative immunity titer. (N = 54)	Number of responses n (% of total)
It was recommended by my provider	50 (92.6%)
Personal or religious beliefs	10 (18.5%)
I understand the potential severity of rubella and/or varicella symptoms	35 (64.8%)
Other	4 (7.4%)
Of the following, please select all that may be true as to why you did not elect to receive the MMR (measles, mumps, rubella) and/or varicella (chickenpox) vaccines. (N = 19)	**Number of responses n (% of total)**
I did not wish to postpone my attempts to conceive	8 (42.1%)
Personal or religious beliefs	-
I have already received the vaccination series once and did not want to proceed with receiving a second series	6 (31.6%)
I have already received the vaccination series twice and did not continue with a third series upon the recommendation from my provider	3 (15.8%)
Effectiveness has not been proven	-
These diseases have been eradicated	-
Preference for natural way of living	-
Fear of needles	-
Fear of adverse reactions	-
Too many vaccines given at once can compromise the immune system	-
Other	6 (31.6%)
Select the time frame in which you last recall speaking with a health care provider about either the MMR (measles, mumps, rubella) or varicella (chickenpox) vaccines. (N = 73)	**Number of responses n (% of total)**
< 6 months	34 (46.6%)
6 months - 1 year	17 (23.3%)
> 1 year	13 (17.8%)
I do not recall	9 (12.3%)

The time frame in which women reported they last spoke with their providers about MMR or varicella vaccines was evaluated in six-month intervals. Most survey participants reported having discussed the vaccines with their providers within the previous six months (n = 34, Table 2).

The study population's average self-reported confidence in knowledge of MMR and varicella CDC recommendations was 66.0% and 61.0%, while their calculated true knowledge of CDC recommendations for specific populations, scheduling, and effectiveness of MMR and varicella vaccines were 72.7% and 79.0%, respectively.

To analyze differences between thought and action, self-reported follow-up immunizations for rubella and/or varicella were compared with the vaccine attitudes (Flu-self/fetus, CDC-children, Varicella-others). Forty-four of the 54 women who elected to receive the necessary vaccine(s) after a negative titer result affirmed protective effects for Flu-self/fetus. Seven of the 19 women who did not elect to receive the necessary vaccine(s) after a negative titer result denied protective effects for Flu-self/fetus.

Higher rates of concordant thought were observed in those who acknowledged some protective effects compared to those who denied some or all of the above-mentioned questions. Fifty-four women affirmed protective effects for all Flu-self/fetus, CDC-children, and Varicella-others (96.4%, total n = 56), compared to five women who denied protective effects for both Flu-self/fetus and Varicella-others (29.4%, total n = 17), two of which also denied protective effects for CDC-children.

By percent, calculated true knowledge of vaccines was generally greater than self-reported confidence. Since participants were more likely to have discussed vaccines with their provider within the past six months to one year, recency may have influenced retention of knowledge about each vaccine (Table 2). All participants demonstrated a fairly high level of understanding regarding the vaccine specific CDC recommendations, with an average of 79% correct for varicella recommendations and 72.5% for MMR recommendations. Further analysis demonstrated that there was no difference in true knowledge or self-reported confidence between the individuals who were or were not open to further education regarding MMR and varicella vaccines (Table 3).

Table 3. Survey participant self-reported confidence in knowledge of MMR and varicella vaccines, broken down by openness to receiving further education on the topic.

	Indicated openness to further vaccine education	Average self-reported confidence in knowledge of CDC recommendations	Average answer accuracy regarding vaccine specific CDC recommendations
MMR	Yes, n = 52	66.4%	73.0%
	No, n = 21	66.2%	72.0%
Varicella	Yes, n = 52	61.3%	79.0%
	No, n = 21	61.0%	79.0%

DISCUSSION

At 6.0% prevalence of non-immunity to rubella, the study population was well within the 15% non-immune population threshold value accepted by the World Health Organization (WHO) to be protected by herd immunity.[15] Plans-Rubió[16] suggested that the rubella R_0 requires a threshold of 83 - 94% prevalence of protected individuals to achieve herd immunity, notably much higher than that recognized by the WHO. The same analysis found that the varicella R_0 requires 86 - 91% prevalence of protected individuals for herd immunity. Based on these suggested thresholds, the 3.8% prevalence of non-immunity to varicella found in this study population is protected by herd immunity. Non-immunity rate within the study population would theoretically have decreased even further if the 73.6% (n = 54) survey respondents who reported receiving the recommended vaccines achieved adequate immunity; however, record of receiving the vaccine was not requested nor were any subsequent titers reviewed.

Those who did not continue to receive the recommended vaccinations most commonly cited their rationale as "not wishing to delay treatment". The American Society for Reproductive Medicine and the American College of Obstetricians and Gynecologists committee opinions uphold that pregnancy is contraindicated for four weeks after vaccination with a live attenuated virus.[17,18] In contrast, Keller-Stanislawski et al.[19] conducted a review over the risks of disease compared to the risk of vaccinating during pregnancy and determined that the wait time prior to conception following MMR is "purely precautionary". Further research regarding the necessity of a wait period prior to conception may be valuable for managing expectations in women who would forgo vaccination in this scenario.

Survey respondent demographics were not depictive of all women who seek preconception care. The study population was remarkable for being highly educated, wealthy, and non-Hispanic Whites. Fujimoto et al.[20] conducted a retrospective cohort study across several assisted reproduction technology (ART) centers and reported demographic findings similar to this study population in regard to age, racial, and ethnic distributions. This comparison supported external validity within the setting of ART, while validity to other preconception/prenatal care settings remains unknown without comparison to demographic data, although unlikely.

One respondent stated that they were a healthcare worker and required to have immunity to these diseases. The results of the study could have been clearer if occupation demographic data were collected to isolate for healthcare workers, a population expected to have increased knowledge about vaccines compared to the general public. Without controlling for this variable, it was possible that this data set represented a higher-than-average true knowledge, as well as higher confidence, than the general population. Level of education was collected but not quantified, therefore cannot be correlated with confidence. Some responses could be quantified, but to do so would compromise the validity of any positive or negative correlation.

CONCLUSIONS

The purpose of this study was to determine the prevalence of non-immunity within the patient population at the University of Kansas Center for Advanced Reproductive Medicine. Rubella and varicella

immunity titer results showed that this population falls well within the parameters recognized to be protected by herd immunity. Upon receipt of a non-immune titer result, most study participants continued to receive the recommended vaccination. The number of participants with negative and mixed attitudes of MMR, varicella, influenza, and general childhood vaccines was lower than the number who held positive attitudes and recognized the beneficial effects of vaccines. Additionally, many patients expressed they would feel open to further vaccine education from their provider. In light of the increased literature demonstrating maternal anti-vaccine attitudes, these results are reassuring for providers who wish to initiate such conversations with their patients.[8,11,14]

Additional retrospective analyses need to be performed that evaluate the necessity of a 28-day wait time until treatment, following the administration of a live attenuated virus vaccine. Based on the attitudes presented in the results of this survey, the risk/benefit analysis of postponing fertility treatment to achieve adequate levels of immunity should be a focused discussion when establishing fertility treatment goals with patients in the setting of ART clinics.

Potential areas for further investigation include comparing prevalence of non-immunity within this study population to local immunity rates via state vaccine records, and how the two compare demographically to determine generalizability. Other ideas to be explored could include analysis of data from generalist obstetrics and gynecology or primary care offices to evaluate the number of patients screened for preventable disease prior to conception as compared to the first prenatal visit, screening results, and surveys to assess the rate of follow-up if results show non-immunity.

REFERENCES

[1] No authors listed. ACOG Committee Opinion No. 741: Maternal immunization. Obstet Gynecol 2018; 131(6):e214-e217. PMID: 29794683.
[2] Coonrod DV, Jack BW, Boggess KA, et al. The clinical content of preconception care: Immunizations as part of preconception care. Am J Obstet Gynecol 2008; 199(6 Suppl 2):S290-s295. PMID: 19081423.
[3] Zolotor AJ, Carlough MC. Update on prenatal care. Am Fam Physician 2014; 89(3):199-208. PMID: 24506122.
[4] American Society for Reproductive Medicine, American College of Obstetricians and Gynecologists' Committee on Gynecologic Practice. Prepregnancy counseling: Committee Opinion No. 762. Fertil Steril 2019; 111(1):32-42. PMID: 30611411.
[5] Society for Maternal-Fetal Medicine, Hughes BL, Page CM, Kuller JA. Hepatitis C in pregnancy: Screening, treatment, and management. Am J Obstet Gynecol 2017; 217(5):B2-B12. PMID: 28782502.
[6] Schillie S, Wester C, Osborne M, Wesolowski L, Ryerson AB. CDC recommendations for hepatitis C screening among adults-United States, 2020. MMWR Recomm Rep 2020; 69(2):1-17. PMID: 32271723.
[7] Kourtis AP, Read JS, Jamieson DJ. Pregnancy and infection. N Engl J Med 2014; 370(23):2211-2218. PMID: 24897084.
[8] Danchin MH, Costa-Pinto J, Attwell K, et al. Vaccine decision-making begins in pregnancy: Correlation between vaccine concerns, intentions and maternal vaccination with subsequent childhood vaccine uptake. Vaccine 2018; 36(44):6473-6479. PMID: 28811050.
[9] Scheminske M, Henninger M, Irving SA, et al. The association between influenza vaccination and other preventative health behaviors in a cohort of pregnant women. Health Educ Behav 2015; 42(3):402-408. PMID: 25504630.
[10] Marin M, Marlow M, Moore KL, Patel M. Recommendation of the Advisory Committee on Immunization Practices for use of a third dose of mumps virus-Containing vaccine in persons at increased risk for mumps during an outbreak. MMWR Morb Mortal Wkly Rep 2018; 67(1):33-38. PMID: 29324728.
[11] Hussain A, Ali S, Ahmed M, Hussain S. The anti-vaccination movement: A regression in modern medicine. Cureus 2018; 10(7):e2919. PMID: 30186724.
[12] Reavis RD, Ebbs JB, Onunkwo AK, Sage LM. A self-affirmation exercise does not improve intentions to vaccinate among parents with negative vaccine attitudes (and may decrease intentions to vaccinate). PLoS One 2017; 12(7):e0181368. PMID: 28704520.
[13] U.S. Centers for Disease Control and Prevention. Measles, Mumps, and Rubella (MMR) Vaccination: What Everyone Should Know. January 26, 2021. https://www.cdc.gov/vaccines/vpd/mmr/public/index.html. Accessed March 2, 2021.
[14] U.S. Centers for Disease Control and Prevention. Chickenpox Vaccination: What Everyone Should Know. August 7, 2019. https://www.cdc.gov/vaccines/vpd/varicella/public/index.html. Accessed March 2, 2021.
[15] World Health Organization. Manual for the Laboratory-based Surveillance of Measles, Rubella, and Congenital Rubella Syndrome. Immunization, Vaccines and Biologicals. Third Edition. June 2018. https://www.who.int/immunization/monitoring_surveillance/burden/laboratory/manual/en/.
[16] Plans-Rubió P. Evaluation of the establishment of herd immunity in the population by means of serological surveys and vaccination coverage. Hum Vaccin Immunother 2012; 8(2):184-188. PMID: 22426372.
[17] American College of Obstetricians and Gynecologists. Management of pregnant and reproductive aged women during a measles outbreak. April 2019. https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2019/04/management-of-pregnant-and-reproductive-aged-women-during-a-measles-outbreak. Accessed August 9, 2020.
[18] Practice Committee of the American Society for Reproductive Medicine. Current recommendations for vaccines for female infertility patients: A committee opinion. Fertil Steril 2018; 110(5):838-841. PMID: 30316421.
[19] Keller-Stanislawski B, Englund JA, Kang G, et al. Safety of immunization during pregnancy: A review of the evidence of selected inactivated and live attenuated vaccines. Vaccine 2014; 32(52):7057-7064. PMID: 25285883.
[20] Fujimoto VY, Luke B, Brown MB, et al. Racial and ethnic disparities in assisted reproductive technology outcomes in the United States. Fertil Steril 2010; 93(2):382-390. PMID: 19081561.

Keywords: vaccine-preventable diseases, preconception care, measles-mumps-rubella vaccine

KANSAS JOURNAL of MEDICINE

Patient Perspectives of Rural Kansas Maternity Care

Meghan Blythe, M.D.[1], Kathryn Istas, MPH[2], Shane Johnston, MPA[3], Jasmine Estrada, M.D.[1], Maci Hicks, M.D.[1], Michael Kennedy, M.D.[4]

[1]University of Kansas School of Medicine, Kansas City, KS
[2]American Academy of Family Physicians, Leawood, KS
University of Kansas School of Medicine, Kansas City, KS
[3]Office of Medical Education
[4]Office of Rural Medical Education

Received Oct. 11, 2020; Accepted for publication May 5, 2021; Published online Sept. 1, 2021
https://doi.org/10.17161/kjm.vol14414752

ABSTRACT

Introduction. Pregnant women in rural areas face a unique set of challenges due to geographic maldistribution of obstetric services. The perspectives of rural Kansas women were sought regarding experience of birth and satisfaction with maternity care.

Methods. Medical student research assistants facilitated discussion groups and structured interviews in rural Kansas communities distributed throughout the state with women who had an uncomplicated delivery in the last 24 months. Participants were recruited via convenience sampling from clinic medical records and appointments over a two-to-three-week period. Guiding questions were used to facilitate discussion. Survey instruments were used to gather information about satisfaction with maternity care. Data for qualitative and quantitative analysis was aggregated using Rural Urban Commuting Area (RUCA) codes.

Results. Fourteen groups with 47 total participants completed the survey and discussion. Participants came from large rural, small rural, and isolated areas in Kansas as described by RUCA Code Four Category Classification. Survey results indicated that satisfaction with maternity care in participants' home county was significantly higher in small rural and isolated compared to large Rural RUCAs. Qualitative analysis results showed positive experiences related to doctor characteristics, relationship with doctor, doctor's involvement with care, alternative labor options, and distance convenience. Negative experiences were related to doctor bedside manner, doctor not there until delivery, and staff related complaints.

Conclusions. Kansas women in small rural and isolated RUCA codes appeared to be more satisfied with care. ***Kans J Med 2021;14:220-226***

INTRODUCTION

Women's satisfaction with maternity services is an important measure of quality and is integral to any assessment of quality or plans for improvement of maternity care.[1] Studies have suggested that quality of care is a complex concept.[2-7] Many factors contributed to women's satisfaction including organization of care, resources, facilities, perceived physician concern, communication with physician and staff, perception of shared decision-making, perceived safety, and the technical competence of the practitioner.

Women in rural areas face a unique set of challenges due to a geographic maldistribution of obstetric services.[8] In 2012, half of U.S. counties lacked a single obstetrician-gynecologist. Overall, the density of obstetrician-gynecologists declined from metropolitan to micropolitan to rural counties.[9] Family physicians play an important role in providing maternity care services in U.S. rural hospitals, including cesarean deliveries.[10] While small rural hospitals providing maternity care services by family physicians showed no evidence of difference in perinatal outcome,[11] the challenges of decreased access and increased distance to travel for maternity care have been correlated with an increase in adverse birth outcomes.[12,13] The impact of rurality on maternal satisfaction has been studied previously; however, the correlations vary and there is a lack of research on rural care in America. Studies in Australia,[14] New Zealand,[15] and Northwest Ethiopia[16] showed a negative correlation between rurality and maternity care satisfaction; whereas a study from Nepal[17] showed a positive correlation, and a Scottish study[18] showed no correlation. Additionally, two Canadian qualitative studies reported that birth experience was influenced by geographic realities, the availability of local health services resources, and relational care characterized by time spent with the patient, continuity, and personalization.[19-20]

No assessment of satisfaction of maternity care has been conducted in rural Kansas, though variation in population density and population to physician ratio would suggest that differences might be found.[21] We hypothesized that geographical area and access to maternity care in rural and remote areas in Kansas impact the maternal birth experience and satisfaction with care.

METHODS

Study Design. Rural-Urban Commuting Areas (RUCA) were used to stratify the rurality of the maternal care experiences. The University of Washington published a four-category classification scheme using a division of the RUCA codes into urban, large rural, small rural, and isolated areas.[22] Using the ERS 2010 RUCA code database[22] and the University of Washington four-category classification scheme,[23] 14 family medicine clinics in 12 Kansas communities representing large rural, small rural, and isolated RUCAs were identified as medical student clinical rotation sites that offered maternity care with labor and delivery. Thirteen second-year medical students placed in these communities conducted the patient recruitment, informed consent, discussion, and survey facilitation at their respective site according to a standardized protocol. The family medicine clinics were a combination of private and hospital associated clinics.

Inclusion criteria included women 18 years old or older who had given birth without significant complications in the past 24 months. Patients with birth complications were excluded as it was a project goal to explain satisfaction with a typical birth experience and complications were expected to occur rarely. Patients meeting the inclusion criteria were recruited via convenience sampling and were identified from the clinic medical records and were invited via phone call using a standardized script or while in clinic for an appointment to participate in the study. No incentive was provided for participation.

This investigation employed a cross-sectional study design using a

combination of discussion groups/structured interviews and a single administration of a survey instrument. Groups utilized the same set of questions (Table 1), protocol, and informed consent. These guiding questions were developed from a similar focus group study assessing maternity care,[20] the input of the Kansas Rural Obstetrics Access Taskforce patient and community workgroup,[24] and utilized the approach to conducting a focus group described by the Mobilizing for Action through Planning and Partnerships (MAPP) Network developed by the National Association of County & City Health Officials.[25] Discussions and interviews were led according to a standardized protocol by a trained medical student research assistant and were audio recorded. Transcription was completed by a third-party and transcripts were used for qualitative analysis. Participant identifying information was not tied to the discussion comments for the purpose of anonymity.

Table 1. Guiding questions for all discussion groups.

1. Tell us about your experience of birth.
2. What maternity care services did you have access to in your community?
3. How satisfied were you with the services available?
4. Did you go to another community for maternity care, and if so, why?
5. What items are important in choosing where you get maternity care?
6. If you could change things to promote better maternity care in your community, what would they be?

In addition to facilitated group discussion, participants completed a paper survey. Survey responses were recorded by research assistants. Study data were managed using the REDCap® electronic data capture tools hosted at the University of Kansas Medical Center. REDCap® is a secure, web-based software platform designed to support data capture for research studies providing: 1) an intuitive interface for validated data capture; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for data integration and interoperability with external sources.[26,27]

The survey obtained participant zip code of residence (which was used to look up the RUCA code), age, ethnicity, average annual household income, level of education, number of deliveries, miles traveled to most recent delivery, and satisfaction of maternity care in home county. These survey questions were developed from the input of the Kansas Rural Obstetrics Access Taskforce patient and community workgroup,[24] and were based on bypass behavior, distance to delivery options, number of deliveries, ethnicity, age, and income.[28] Participant identifying survey information was not linked to patient discussion group comments for anonymity. The University of Kansas Medical Center Institutional Review Board approved this study protocol.

Data Analysis. The primary outcome of interest was patient satisfaction of rural maternity care. This outcome was investigated using a mixed methods approach with qualitative analysis of discussion group transcriptions and quantitative analysis of survey results. The qualitative analysis began with development of the codebook of words, phrases, and patterns by two principal investigators. Each of the 14 transcripts was coded using the codebook by three team members, including two medical student research assistants previously involved in discussion group facilitation and one principal investigator. Any disagreements between the three coders were resolved by discussion. To ensure consistency, quality, and accuracy, each of the completed coded transcripts was reviewed and discussed by the entire team. Codes were added and/or combined as needed based on team consensus.

An inductive analysis of the transcripts was conducted to capture richness beyond the language constraints built into the codebook. The team discussed each transcript and compiled emerging ideas into thematic categories. Team members then pulled quotes from corresponding transcript segments to support the themes.

Quantitative analysis of survey data used Spearman correlation to measure the association between satisfaction and the following socio-demographic characteristics: RUCA code, average household income, education level, ethnicity, age, multiple pregnancies vs. first time, and miles travelled for prenatal care. Self-reported satisfaction was measured by a single item asking participants to express their level of agreement with the following statement: "I am satisfied with maternity care services in my home county". Responses were collected on a 5-point Likert scale ranging from "strongly agree" to "strongly disagree". Variables were recoded from ordered categories to numeric levels, with level 1 corresponding to the level lowest in magnitude (i.e., smallest RUCA category, least frequent, least satisfied, lowest education level, least time or distance travelled). Partial correlation measured the association between RUCA and satisfaction, controlling for distance travelled. Statistical analysis was conducted using R version 4.0.5. All analyses were based on two-tailed tests with alpha = 0.05.

Variables for hospital in zip code, hospital with labor and delivery in zip code, hospital in county, and hospital with labor and delivery in county were derived via internet search from patient reported zip code. Patients also reported the hospital location of their most recent delivery. This was compared to the search results for hospital in county with labor and delivery and hospital in zip code with labor and delivery to derive the variables for most recent delivery in hospital with labor and delivery in county and most recent delivery in hospital with labor and delivery in zip code. Variables for county and zip code were derived and reported as zip code correlates with RUCA designation; however, many rural hospital resources were designated by county.

RESULTS

Participants. Fourteen groups with 47 total participants completed the survey and discussion. Average group size was three participants. The 14 discussion groups were held in 12 Kansas counties distributed throughout the state as shown in Figure 1. The participants were an average of 28.3 years old (range 20 - 37 years), Caucasian (96%), and had a mean annual household income greater than $50,000 (68%). Participants were distributed by RUCA codes per four-category classification as follows: 17/47 (36%) large rural, 13/47 (28%) small rural, and 17/47 (36%) isolated. Subject demographics are shown in Table 2.

Table 2. Participant descriptive statistics and demographics.*

Variables	Total (N = 47)
Age**	28.3
20 - 24	11 (23%)
25 - 29	18 (38%)
30 - 34	13 (28%)
35 - 49	5 (11%)
Ethnicity	
White/Caucasian	45 (96%)
Other	2 (4%)
Education level	
Some high school, no diploma	1 (2%)
High school graduate	2 (4%)
Some college credit, no degree	9 (19%)
Trade/technical training	1 (2%)
Associate degree	13 (28%)
Bachelor's degree	18 (38%)
Master's degree	3 (6%)
Annual household income	
Less than $10,000	1 (2%)
$10,000 - $14,999	0 (0%)
$15,000 - $24,999	4 (9%)
$25,000 - $49,999	13 (28%)
$50,000 - $99,999	24 (53%)
$100,000 - $149,999	4 (9%)
Number of births (including the birth within last 24 months)	
1	22 (47%)
2	16 (34%)
3	5 (11%)
4	3 (6%)
5 or more	1 (2%)
Distance traveled for most recent delivery	
0 - 20 miles	37 (79%)
20 - 40 miles	8 (17%)
40 - 60 miles	2 (4%)
Four-category RUCA codes	
Large rural	17 (36%)
Small rural	13 (28%)
Isolated	17 (36%)
Hospital in zip code	32 (68%)
Hospital with labor and delivery in zip code	30 (64%)
Hospital in county	46 (98%)
Hospital with labor and delivery in county	42 (89%)
Delivery at hospital with labor and delivery in zip code	28 (60%)
Delivery at hospital with labor and delivery in county	37 (79%)

*Data are given as number of participants (percent of total N=47) unless otherwise indicated.
**Data are given as the mean.

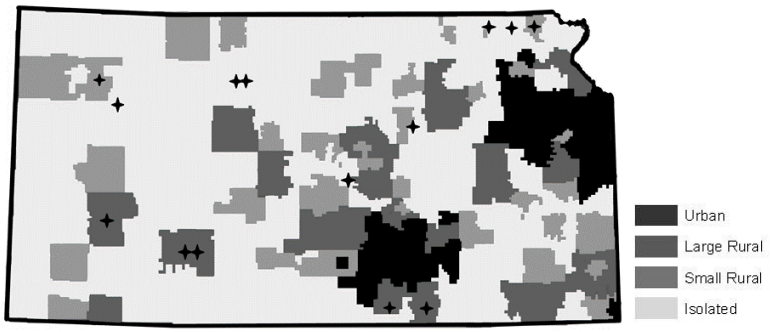


Figure 1. RUCA map of Kansas using a four-code description showing locations of discussion groups with a four-point star.[23]

Of the 47 participants, 32 (68%) had a hospital in their zip code, 30 (64%) had a hospital with labor and delivery in their zip code, 46 (98%) had a hospital in their county, 42 (89%) had a hospital with labor and delivery in their county, 28 (60%) reported delivery at a hospital with labor and delivery in their zip code, and 37 (79%) reported delivery at a hospital with labor and delivery in their county.

Quantitative Analysis. Satisfaction survey responses grouped by RUCA levels are shown in Figure 2. Higher satisfaction was associated with more rural RUCA levels ($r = -0.52$, $p < 0.001$) and with shorter distance travelled for prenatal care ($r = -0.31$, $p < 0.05$). Higher satisfaction also was associated with more positive responses across other survey questions. For example, higher levels of satisfaction were associated with greater likelihood of delivering future children at the same place ($r = 0.50$, $p < 0.001$) and greater likelihood of recommending the same place to another person ($r = 0.36$, $p < 0.05$).

Partial correlations were used to examine the relationship between RUCA level and satisfaction after accounting for the relationship between proximity to a hospital and satisfaction. The partial correlation between RUCA level and satisfaction was $r = -0.48$ ($p < 0.001$) after adjusting for whether respondents had a hospital offering obstetrical services in their county or zip code. The partial correlation between RUCA level and satisfaction was $r = -0.36$ ($p < 0.05$) when further adjusting for level of agreement with the statement, "I will go for obstetrical services wherever I have the most confidence in the hospital and facilities whether this is in my county or not".

Qualitative Analysis. A range of one to six participants was included per discussion group/structured interview with an average of three participants per discussion group. Using the codebook, discussion group participants' stories of their birth experiences (responses to Question 1) were coded as positive or negative and responses to Questions 2 - 6 were categorized accordingly.

The mention of themes during the participant discussion groups/structured interviews, shown in Table 3, provided insight into the difference of participant satisfaction by rurality. The codes were binary and counted if the theme was mentioned during the discussion/interview. This avoided a group of more participants having more cumulative codes.

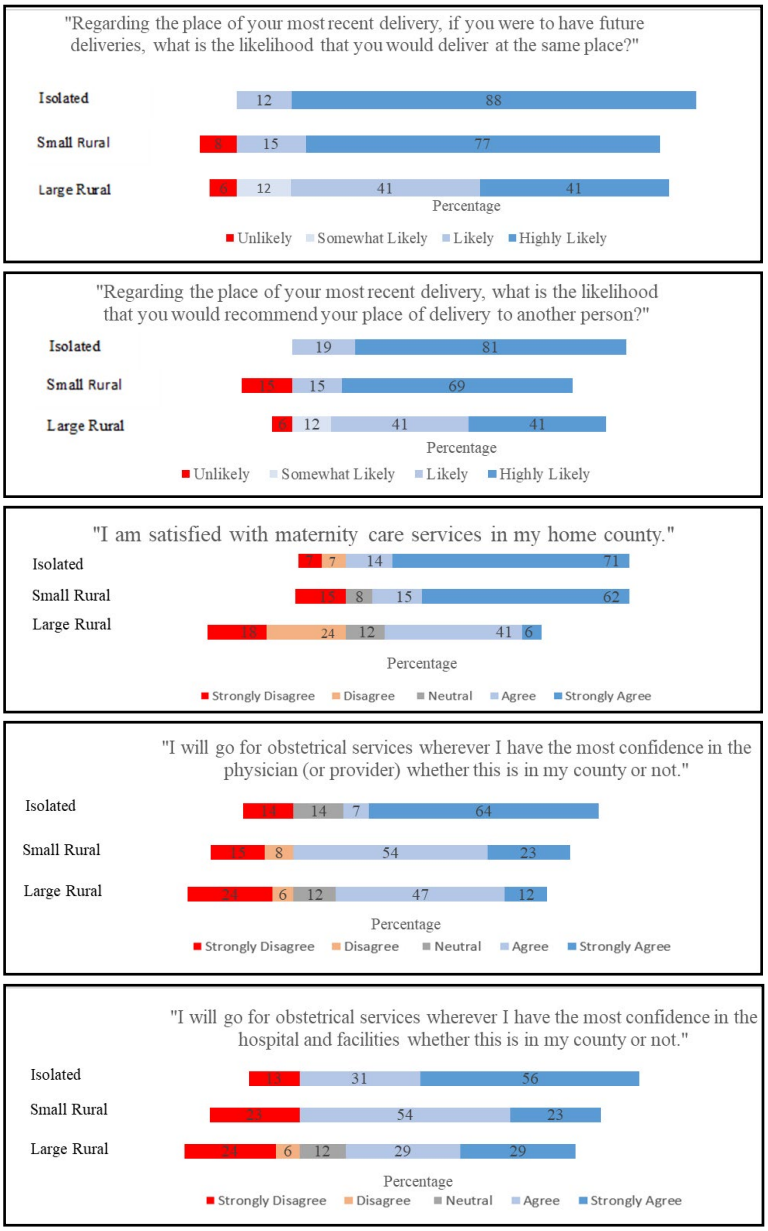


Figure 2. Satisfaction survey responses grouped by RUCA Code (n = 47).

More isolated discussion groups mentioned positive birth experiences related to their doctor being family medicine trained, details about their hospital room, and other positive birth experiences that included personal attention from staff and immediate skin to skin contact with the baby. Participant quotes from isolated discussion groups supporting these themes included:

- "[The doctor] is my general practitioner as well so they knew [my past medical history]. So they took care of me the whole time and would monitor my pregnancy and other conditions; that really did help."
- "I like the really big windows in my room. The natural light made such a big difference because I was exhausted but wasn't disoriented."
- "The personal attention really helped; I was the only person delivering in the hospital."

More small rural and isolated discussion groups mentioned positive birth experiences related to convenience. Participant quotes from isolated and small rural discussion groups supporting the theme of convenience included:

- "[The hospital location] was very convenient. My doctor told me that if my water was to break naturally, then I would have time to shower and get something to eat. I had plenty of time for all of that. Had I not lived in the same town [as the hospital] I'm not sure if I would have taken the time to shower and eat something before I left. I probably would have been a little bit more freaked out of having to drive 30 minutes to the nearest hospital."
- "I was very glad that we were only 10 minutes away [from the hospital] because I think I had 4 contractions in the car and I don't think I could have done too many more because my baby was born soon after got to the hospital."

Additionally, more large rural discussion groups mentioned negative birth experiences related to their doctor. Poor bedside manner, doctor not there until delivery, and delivery with a different doctor were sub-themes identified. Participant quotes from large rural discussion groups supporting the theme of doctor related negative birth experiences included:

- "[The doctor] had really bad bedside manners and the whole experience was just miserable."
- "I thought the doctor should have been checking on me the whole time I was in the hospital, but she didn't come until the very last minute."
- "I had my baby on a weekend, and my doctor wasn't there. So I had a different doctor who I did not care for at all."

Themes identified as being "Factors Important in Choosing Care" are shown in Table 4. Across discussion groups/structured interviews held in large rural, small rural, and isolated Kansas RUCAs, more isolated discussion groups mentioned family medicine trained and doctor characteristics as factors that were important to their choice of care. Participant quotes from isolated discussion groups supporting these themes included:

- "I preferred a family doctor. [The doctor] can be your OB, your doctor, and your kid's doctor. So everything."
- "[The doctor] is relatable and understands my lifestyle and religious beliefs."

More small rural and isolated discussion groups mentioned convenience as being important to choosing maternity care. Participant quotes supporting the theme of convenience included:

- "I work full time and didn't want to take off half a day to doctor in the neighboring county."
- "My husband is a farmer and busy certain times of year; that puts me on my own if I need to come in fast so I wanted to deliver somewhere close."

Table 3. Mention of themes by four-category RUCA in response to Question 1 (Tell us about your experience of birth).

		Four-category RUCA by zip code of discussion group location	Large rural	Small rural	Isolated
	Theme	**Sub-theme (examples)**	**n = 4**	**n = 5**	**n = 5**
Positive experience	Doctor related	Doctor characteristics (*available, open, makes me laugh, supportive, communication/bedside manner, trust/confidence, trust/respect of other doctors, parent/doctor has kids too*)	4	3	5
		Family medicine trained/"general practitioner"	2	-	3
	Staff related (*OB nurse, nurse, midwife, lactation consultant*)		4	3	5
	Resource related	Room related (*own room, natural light*)	1	1	3
	Distance related	Convenience	1	3	4
	Medical related (*VBAC, epidural*)		-	2	1
	Other (*personal attention, immediate skin to skin*)		-	-	3
Negative experience	Doctor related		4	1	1
	Staff related		2	2	3
	Distance related		-	1	1
	Medical related (*Gestational Diabetes, nausea, epidural, induction*)		1	1	3
	Other (*billing confusion, lack of communication with referral center*)		-	2	1

Table 4. Mention of themes by four-category RUCA in response to Question 5 (What items are important in choosing where you get maternity care?).

		Four-category RUCA by zip code of discussion group location	Large rural	Small rural	Isolated
	Theme	**Sub-theme (examples)**	**n = 4**	**n = 5**	**n = 5**
Factors important in choosing care	Doctor related	Doctor characteristics (*comfortable with doctor, bedside manner, character, personality, credibility, trust, relatable*)	1	2	4
		Family medicine trained	1	1	3
		Female provider	1	1	1
		Personal relationship with doctor	-	1	1
	Distance related	Doctor response time	-	2	1
		Convenience	1	5	5
	Resource related factor (labor options, doula, birthing class, VBAC, lactation consultation)		-	1	1
	Recommendation from others/reputation		2	2	1
	Patient works at hospital/clinic		1	3	1

DISCUSSION

Key Findings. The quantitative analysis of survey results suggested that rurality influences satisfaction of maternity care, specifically that women in small rural and isolated Kansas RUCA codes appeared to be more satisfied with care. From qualitative analysis of the discussions/interviews, these results seemed to be a factor of convenience of having a local maternity care option, as well as influenced by doctor characteristics and family medicine training.

As many rural counties rely on maternity care provided by family physicians,[10] we expected mention of family medicine trained doctors during the discussions/interviews. For isolated discussion groups, the theme of family physicians was identified as a doctor related positive experience, as well as a factor important to choosing care. Additional comments linked to mention of care by a family physician include "relationship with doctor", "delivery with my doctor", and "prior experience with doctor". These results highlighted the broad scope of practice including maternity care offered by family physicians.

Female provider was identified from the discussions as a factor influencing maternity care decisions. This theme was not mentioned in previous studies regarding satisfaction of rural care, nor was it captured in the survey results. The influence of this theme in rural Kansas warrants further investigation.

The derived variables of hospital in zip code, hospital with labor and delivery in zip code, hospital in county, and hospital with labor and delivery in county suggested a disproportion of facilities that did not offer labor and delivery. This disproportion has been described as "obstetrical deserts".[24] Despite the existence of this disproportion in our study, the majority of participants were satisfied with their maternity care.

When compared to the derived variables of hospital with labor and delivery in zip code and hospital with labor and delivery in county, the derived variables of delivery at hospital with labor and delivery in zip code and delivery at hospital with labor and delivery in county showed a difference of 2 (4%) and 5 (11%), respectively. Further investigation is needed to explain these differences, but it may represent "bypass behavior" or a patient's choice to seek services other than those offered in their home county.[28]

Implications and Application of Findings. The identified themes and codebook will inform future research questions and projects, including a clinic survey of women in rural areas regarding satisfaction of care and distance traveled.

Study Limitations. The number of participants was not reflective of the more than 9,853 births in rural Kansas counties during the time of the study; there were a total of 36,264 live births statewide.[29] The selection of study participants was through general solicitation and participants were not selected randomly. However, there was no specific selective process to get participants. Overall, the convenient sampling method made the results subject to general bias. Participant recruitment was not bilingual and may have contributed to under sampling of Hispanic populations in rural Kansas. Additional bias is acknowledged as some participants reported working for or having worked at the local clinic and/or hospital. There was, however, good representation across the state by region and RUCA code.

CONCLUSIONS

Women in small rural and isolated RUCA codes in Kansas appeared to be more satisfied with their maternity care. From the discussions/interviews, these results seemed to be a factor of the convenience of a local maternity care option as well as doctor characteristics and family medicine training.

ACKNOWLEDGEMENTS

The authors acknowledge and thank the participating patients in rural Kansas communities and the medical student research assistants who collected data for this project. Abstracts of these results were presented at the KUMC Student Research Forum on April 1, 2019 (Kansas City, KS), the National Rural Health Association Annual Conference May 7-9, 2019 (Atlanta, GA), and the Kansas Academy of Family Physicians Annual Conference on June 8, 2019 (Wichita, KS). This project was supported in part by a KUMC Auxiliary grant. There was also general funding for the STORM program from the Hansen Foundation, Sutton Fund, KAFP-Foundation, and the Baker Trust.

REFERENCES

[1] Perriman N, Davis D. Measuring maternal satisfaction with maternity care: A systematic integrative review: What is the most appropriate, reliable and valid tool that can be used to measure maternal satisfaction with continuity of maternity care? Women Birth 2016; 29(3): 293-299. PMID: 26782087.
[2] Lewis L, Hauck YL, Ronchi F, Crichton C, Waller L. Gaining insight into how women conceptualize satisfaction: Western Australian women's perception of their maternity care experiences. BMC Pregnancy Childbirth 2016; 16:29. PMID: 26846257.
[3] Zweig S, Kruse J, LeFevre M. Patient satisfaction with obstetric care. J Fam Pract 1986; 23(2):131-136. PMID: 3734717.
[4] Attanasio L, McPherson ME, Kozhimannil KB. Positive childbirth experiences in US hospitals: A mixed methods analysis. Matern Child Health J 2014; 18(5):1280-1290. PMID: 24072597.
[5] Goberna-Tricas J, Banús-Giménez MR, Palacio-Tauste A, Linares-Sancho S. Satisfaction with pregnancy and birth services: The quality of maternity care services as experienced by women. Midwifery 2011; 27(6):e231-237. PMID: 21145632.
[6] Séguin L, Therrien R, Champagne F, Larouche D. The components of women's satisfaction with maternity care. Birth 1989; 16(3):109-113. PMID: 2789558.
[7] Handler A, Raube K, Kelley MA, Giachello A. Women's satisfaction with prenatal care settings: A focus group study. Birth 1996 ;23(1):31-37. PMID: 8703255.
[8] Rayburn WF, Richards ME, Elwell EC. Drive times to hospitals with perinatal care in the United States. Obstet Gynecol 2012; 119(3):611-616. PMID: 22353960.
[9] Rayburn WF, Klagholz JC, Murray-Krezan C, Dowell LE, Strunk AL. Distribution of American Congress of Obstetricians and Gynecologists fellows and junior fellows in practice in the United States. Obstet Gynecol 2012; 119(5):1017-1022. PMID: 22525913.
[10] Young R. Maternity care services provided by family physicians in rural hospitals. J Am Board Fam Med 2017; 30(1): 71-77. PMID: 28062819.
[11] Chaska BW, Mellstrom MS, Grambsch PM, Nesse RE. Influence of site of obstetric care and delivery on pregnancy management and outcome. J Am Board Fam Pract 1988; 1(3):152-163. PMID: 3177013.
[12] Grzybowski S, Stoll K, Kornelsen J. Distance matters: A population based study examining access to maternity services for rural women. BMC Health Serv Res 2011; 11(1):147-155. PMID: 21663676.
[13] Larimore WL, Davis A. Relation of infant mortality to the availability of maternity care in rural Florida. J Am Board Fam Pract 1995; 8(5):392-399. PMID: 7484227.
[14] Brown S, Lumley J. Satisfaction with care in labor and birth: A survey of 790 Australian women. Birth 1994; 21(1):4-13. PMID: 8155224.

[15] Dawson P, Hay-Smith J, Jaye C, Gauld R, Auvray B. Do maternity services in New Zealand's public healthcare system deliver on equity? Findings from structural equation modelling on national maternal satisfaction survey data. Midwifery 2021; 95:102936. PMID: 33592369.
[16] Gashaye KT, Tsegaye AT, Shiferaw G, Worku AG, Abebe SM. Client satisfaction with existing labor and delivery care and associated factors among mothers who gave birth in university of Gondar teaching hospital; Northwest Ethiopia: Institution based cross-sectional study. PLoS One 2019; 14(2):e0210693. PMID: 30726297.
[17] Mehata S, Paudel YR, Dariang M, et al. Factors determining satisfaction among facility-based maternity clients in Nepal. BMC Pregnancy Childbirth 2017; 17(1):319. PMID: 28946851.
[18] Cheyne H, Elders A, Hill D, Milburn E. Is maternity care in Scotland equitable? Results of a national maternity care survey. BMJ Open 2019; 9(2):e023282. PMID: 30804027.
[19] Sutherns R. Adding women's voices to the call for sustainable rural maternity care. Can J Rural Med 2004; 9(4):239-244. PMID: 15603695.
[20] Kornelsen J, Grzybowski S. The reality of resistance: The experiences of rural parturient women. J Midwifery Womens Health 2006; 51(4):260-265. PMID: 16814220.
[21] County Health Rankings. 2020 County Health Rankings. State Reports. http://www.countyhealthrankings.org. Accessed March 20, 2018.
[22] USDA Economic Research Service. Rural-Urban Commuting Area Codes. https://www.ers.usda.gov/data-products/rural-urban-commuting-area-codes.aspx. Accessed March 8, 2018.
[23] WWAMI Rural Health Research Center. RUCA Four category classification, Census Division. https://depts.washington.edu/uwruca/ruca-maps.php. Accessed March 8, 2018.
[24] Kansas Rural Obstetric Access Task Force. Kansas Rural Obstetrics Access Task Force Report and Recommendations, 2017. Unpublished document, 2017.
[25] National Association of County and City Health Officials. Mobilizing for Action through Planning and Partnerships (MAPP). https://www.naccho.org/programs/public-health-infrastructure/performance-improvement/community-health-assessment/mapp. Accessed March 20, 2018.
[26] Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009; 42(2):377-381. PMID: 18929686.
[27] Harris PA, Taylor R, Minor BL, et al. The REDCap consortium: Building an international community of software platform partners. J Biomed Inform 2019; 95:103208. PMID: 31078660.
[28] Liu JJ, Bellamy GR, McCormick M. Patient bypass behavior and critical access hospitals: Implications for patient retention. J Rural Health 2007; 23(1):17-24. PMID: 17300474.
[29] Mosier S. Annual Summary of Kansas Vital Statistics, 2016. Kansas Department of Health and Environment. September 2017. http://www.kdheks.gov/phi/as/2016/Annual_Summary_2016.pdf. Accessed March 8, 2018.

Keywords: obstetrics, rural health services, patient satisfaction, Kansas

KANSAS JOURNAL of MEDICINE

A Case of Actinomycosis Presenting as Purulent Pericarditis with Cardiac Tamponade

Nicholas Tuck, M.D.[1,2], Jo Leatherman, MS-3[1], Maha Assi, M.D.[1,2,3], K. James Kallail, Ph.D.[1,2]

[1]University of Kansas School of Medicine-Wichita, Wichita, KS

[2]Department of Internal Medicine

[3]Infectious Disease Consultants, Wichita, KS

Received March 15, 2021; Accepted for publication April 28, 2021; Published online Sept. 1, 2021
https://doi.org/10.17161/kjm.vol1415262

INTRODUCTION

Purulent pericarditis (PP), a neutrophilic effusion in the pericardial space, is relatively uncommon and frequently identified only post-mortem.[1] When presented, prompt diagnosis and intervention is a necessity, as the mortality rate ranges from 20 - 30% and can be as high as 80% if left untreated.[1,2] It also may result in cardiac tamponade which is a rare yet life-threatening complication reported in patients of all ages and levels of immunocompetency.[3] The antibiotic era has changed the landscape of PP incidence, with pneumonia being the most common risk factor, along with cardiothoracic procedures, and immunocompromised states.[4] The most common organisms isolated from such infections are usually gram positive bacteria including *Staphylococcus* and *Streptococcus*. While other organisms are uncommon due to effective antibiotics and antifungals in the post-antibiotic era, their incidence may be increasing, likely from increased use of percutaneous procedures.[5] The following case highlighted *Actinomyces* as a cause of PP and cardiac tamponade in a patient initially misdiagnosed with sarcoidosis.

CASE REPORT

A 22-year-old male presented to the emergency department (ED) with intermittent, non-specific shortness of breath. In the ED, his vitals and physical exam were unremarkable and overall, he appeared well. Laboratory studies, including basic chemistry and blood counts, were also unremarkable. No cultures were done. Initial x-ray showed enlarged hila and lymphadenopathy (Figure 1). Computed tomography (CT) of the chest revealed mediastinal lymphadenopathy, multiple solid and subsolid nodules, most notably in the right upper and middle lobes.

The patient was discharged from the ED with a referral to pulmonology for suspected lymphoma versus sarcoidosis given imaging findings. He underwent an endobronchial ultrasound with the biopsy of station 4R and 7 lymph nodes. Pathology revealed necrotizing granulomas with a negative stain for fungal or mycobacterial organisms. Further workup for *Histoplasma capsulatum* was negative. Given the unremarkable findings on physical exam and in the laboratory studies, the patient tentatively was diagnosed with sarcoidosis and started on prednisone.

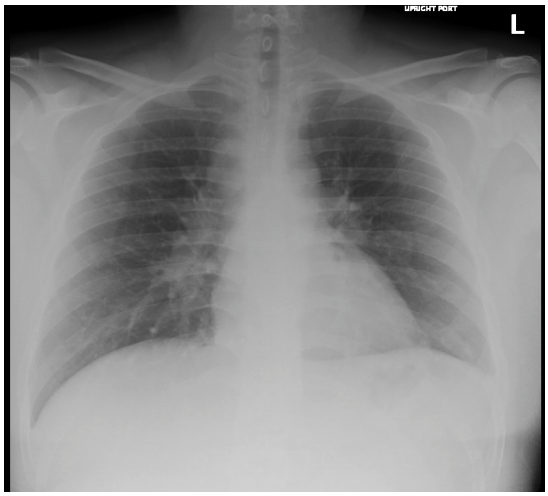


Figure 1. Chest x-ray showed enlarged hila and lymphadenopathy.

Approximately three weeks later, the patient presented to the ED with progressive, non-specific chest pain of two to three weeks duration. Vitals and physical exam were pertinent for tachycardia, and the patient appeared generally anxious. His electrocardiogram (EKG) showed diffuse ST segment elevation (Figure 2). Repeat imaging was unable to rule out pulmonary embolism definitively, but chest x-ray and CT were unchanged. The patient was diagnosed with acute pericarditis and his two-day hospital course was unremarkable. At this time, 2-D echocardiogram (echo), blood cultures, basic chemistries, and troponin levels were unremarkable. The patient's pain significantly improved with limited intervention, and he was given a prescription for colchicine 0.6 mg twice a day upon discharge.

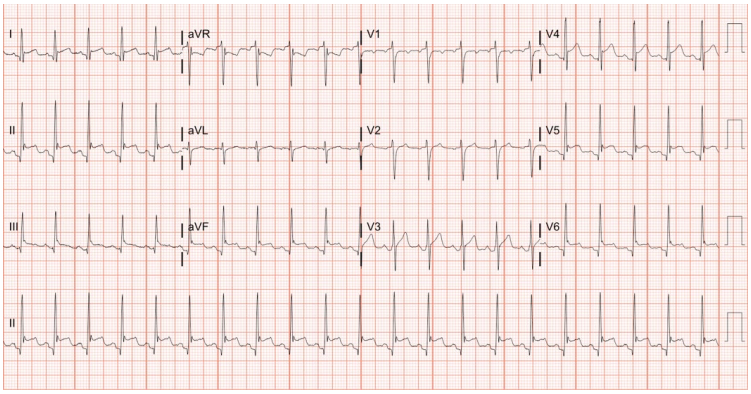


Figure 2. Electrocardiogram showed diffuse ST segment elevation.

Two days following this discharge, the patient presented to the ED with severe dyspnea, diaphoresis, and chest pain. Pertinent physical exam findings included distant heart sounds, shallow breathing, and obvious distress. Labs were pertinent for white blood cell count of 45 x 10^3/µL, troponin of 0.62 ng/ml, and overall metabolic acidosis. EKG again showed diffuse ST elevations, and bedside echo showed large pericardial effusion with suspected tamponade. He subsequently underwent subxiphoid pericardiotomy (pericardial window) with drainage of grossly purulent fluid with cultures collected and sent to the lab. Empiric antibiotics, vancomycin and piperacillin-tazobactam, were started.

Although blood cultures were not recollected on this admission, specimen cultures grew *Parvimonas micra*, *Prevotella* (undifferentiated), *Actinomyces odontolyticus*, and *Peptostreptococcus* (undifferentiated). Targeted therapy with ampicillin-sulbactam was started. Echo obtained four days following admission showed near complete resolution of pericardial effusion, but had residual fluid with fibrous appearance. Given organisms cultured, further investigation into the oral cavity was done. Panorex imaging of the mandible showed one dental caries, and physical exam of the oral cavity was unremarkable. He was discharged home with plan to receive four to six weeks of intravenous antibiotics before changing to oral maintenance for several months, pending clinical picture.

DISCUSSION

The most common organism isolated in PP infections is *Staphylococcus aureus*, accounting for approximately 31% of cases, followed by *Streptococcus pneumoniae*.[1] Fungal infections have increased in incidence recently. Anaerobic causes of PP are uncommon, although increasing;[5] multi-organism anerobic infections are rarer.[6] *Actinomyces* isolated from PP is rare, fastidious, and multi-factorial in nature. Patients can have subclinical presentations that delay diagnosis. *Actinomyces* as a cause of PP dates as far back as 1950.[6] A majority of cases are related to either significant cardiothoracic surgery, periodontal infection, alcohol abuse, or a previous diagnosis of pneumonia or disseminated *Actinomyces* infection. The four organisms isolated in this case were far higher than the average of 1.4 per specimen.[7] While it is suspected that *Actinomyces* is the predominate infectious organism present, the other organisms may increase virulence or provide other unknown contributions.[8] This requires further investigation.

The pathogenesis of PP is well-documented and includes hematogenous spread, intrathoracic trauma, subdiaphragmatic spread, or from an intrathoracic site such as pneumonia or suppurative mediastinal lymphadenitis.[6] *Actinomyces* causing PP is usually secondary to intrathoracic spread.[9] In this patient, it was suspected that his initial symptoms were from pulmonary actinomycosis and the diagnosis of sarcoidosis was inaccurate.

Actinomyces is usually spread from the oropharynx or upper gastrointestinal track via aspiration or inhalation and is related to poor oral and dental hygiene.[8] Unfortunately, the biopsy tissue was sent for pathology and not for culture, thus *Actinomyces* could not be identified. It is likely that the transbronchial lymph node biopsies of station 4R and 7 may have allowed the infection to spread from the respiratory track into the pericardium given the anatomical proximity.

Antimicrobial agents, proper source control, and drainage are the mainstay of treatment in patients with PP.[9] Prior to culture results, the patient was started on empiric antibiotics, vancomycin and piperacillin-tazobactam. *Actinomyces* is classically sensitive to penicillin, but given the presence of other anaerobic organisms on culture, the treatment was broadened to ampicillin-sulbactam. Most patients require at least four to six weeks of intravenous antibiotics followed by oral suppression to clear the infection.[10]

CONCLUSIONS

Sarcoidosis is a diagnosis of exclusion and should be made only after infection has been ruled out by tissue culture. Purulent pericarditis caused by *Actinomyces* and other anaerobic organisms is uncommon. Both the indolent and acute presentations of PP should be recognized, as well as how the clinical course impacts the management, treatment, and outcome of the infection.

REFERENCES

1 Sagristà-Sauleda J, Barrabés JA, Permanyer-Miralda G, Soler-Soler J. Purulent pericarditis: Review of a 20-year experience in a general hospital. J Am Coll Cardiol 1993; 22(6):1661-1665. PMID: 8227835.
2 Rubin RH, Moellering RC Jr. Clinical, microbiologic and therapeutic aspects of purulent pericarditis. Am J Med 1975; 59(1):68-78. PMID: 1138554.
3 Könönen E, Wade WG. Actinomyces and related organisms in human infections. Clin Microbiol Rev 2015; 28(2):419-442. PMID: 25788515.
4 Augustin P, Desmard M, Mordant P, et al. Clinical review: Intrapericardial fibrinolysis in management of purulent pericarditis. Crit Care 2011; 15(2):220. PMID: 21575282.
5 Parikh SV, Memon N, Echols M, Shah J, McGuire DK, Keeley EC. Purulent pericarditis: Report of 2 cases and review of the literature. Medicine (Baltimore) 2009; 88(1):52-65. PMID: 19352300.
6 Brook I. Pericarditis caused by anaerobic bacteria. Int J Antimicrob Agents 2009; 33(4):297-300. PMID: 18789852.
7 Brook I, Frazier EH. Microbiology of acute purulent pericarditis. A 12-year experience in a military hospital. Arch Intern Med 1996; 156(16):1857-1860. PMID: 8790081.
8 Mabeza GF, Macfarlane J. Pulmonary actinomycosis. Eur Respir J 2003; 21(3):545-551. PMID: 12662015.
9 Han JY, Lee KN, Lee JK, et al. An overview of thoracic actinomycosis: CT features. Insights Imaging 2013; 4(2):245-252. PMID: 23242581.
10 Valour F, Sénéchal A, Dupieux C, et al. Actinomycosis: Etiology, clinical features, diagnosis, treatment, and management. Infect Drug Resist 2014; 7:183-197. PMID: 25045274.

Keywords: actinomyces, actinomycosis, pericarditis, cardiac tamponade

KANSAS JOURNAL of MEDICINE

Electrocardiographic Limb Leads Placement and Its Clinical Implication: Two Cases of Electrocardiographic Illustrations

Robert T. Tung, M.D., FACC
Department of Veterans Affairs, Eastern Kansas HealthCare System, Cardiology Section, Topeka, KS

Received March 14, 2021; Accepted for publication May 3, 2021; Published online Sept. 1, 2021
https://doi.org/10.17161/kjm.vol14152359

INTRODUCTION

Since its introduction, the electrocardiography (ECG) has become the most commonly performed cardiac diagnostic procedure and a fundamental tool of clinical practice.[1,2] It is indispensable for the diagnosis and prompt treatment of patients with acute coronary syndromes and is an accurate, noninvasive tool for diagnosing cardiac conduction disturbances and arrhythmias. Proper, standard ECG leads placement is essential in providing accurate information from the recordings. Modified limb leads placement on the torso has the important advantages of ease and speed of application, particularly in emergent situations and has become commonplace. However, modified limb placement was reported to have unwanted abnormal ECG findings.[3] Clinically significant abnormal ECG findings due to this modified, non-standard limb placement are illustrated by two cases.

CASE REPORT

ECG Illustration 1. A 74-year-old patient with known severe ischemic cardiomyopathy was admitted for congestive heart failure and atrial fibrillation with type 2 myocardial ischemia. The initial 12-lead ECG (Figure 1A) was obtained with limb leads placed on the torso position and reported as "ST elevation and possible acute inferior wall myocardial infarction (MI)". Repeat ECG with limb leads placed in standard, distal limb positions showed resolution of "ST elevation" in the inferior leads (Figure 1B).

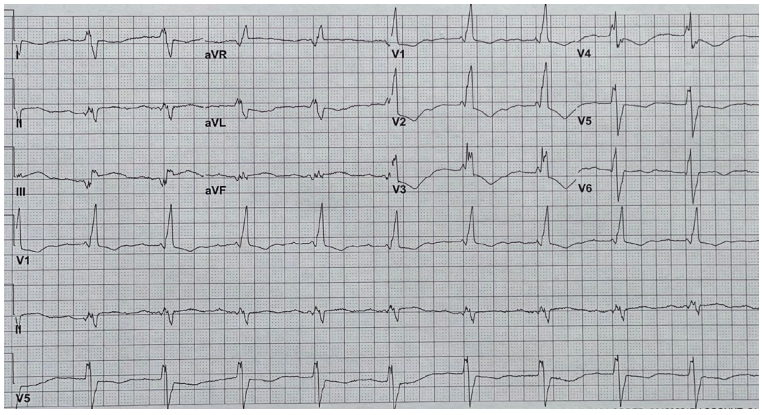


Figure 1A. ECG Illustration 1 with torso limb leads placement showed ST elevation in leads III, mimicking acute MI.

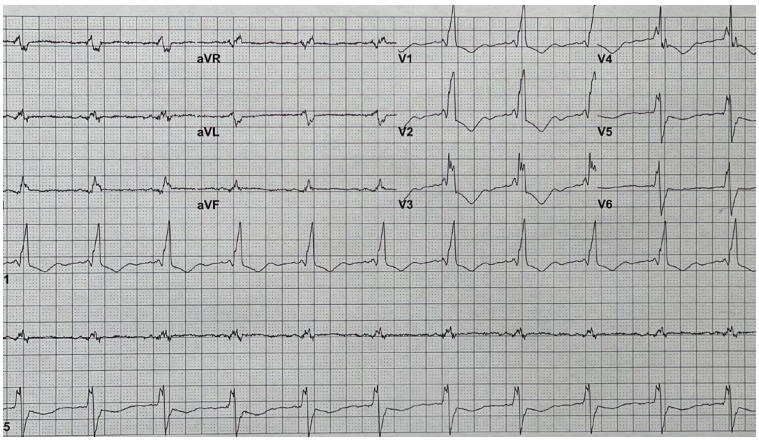


Figure 1B. ECG Illustration 1 with standard limb leads placement showed no ST elevation in lead III.

ECG Illustration 2. This ECG (Figure 2A) with torso limb leads placement was obtained in a 76-year-old patient which showed the presence of a Q wave in lead aVL suggestive of an old lateral wall MI. When the limb leads were moved from torso position to standard distal limb positions, a repeat ECG (Figure 2B) showed resolution of Q waves in lead aVL.

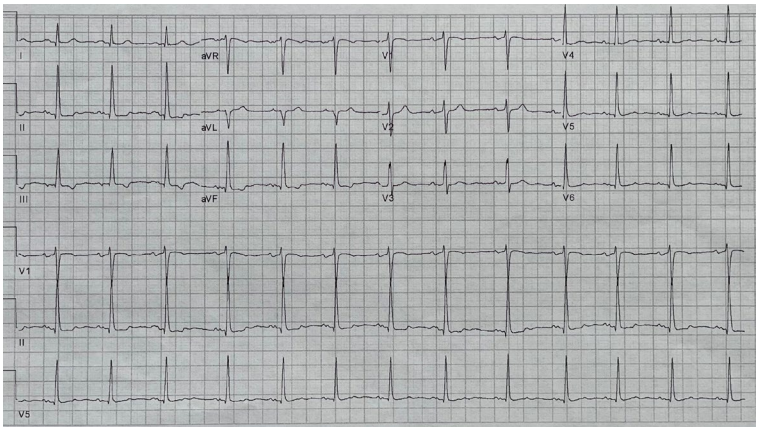


Figure 2A. ECG Illustration 2 with torso limb leads placement showed Q waves in lead aVL, suggestive of prior lateral MI.

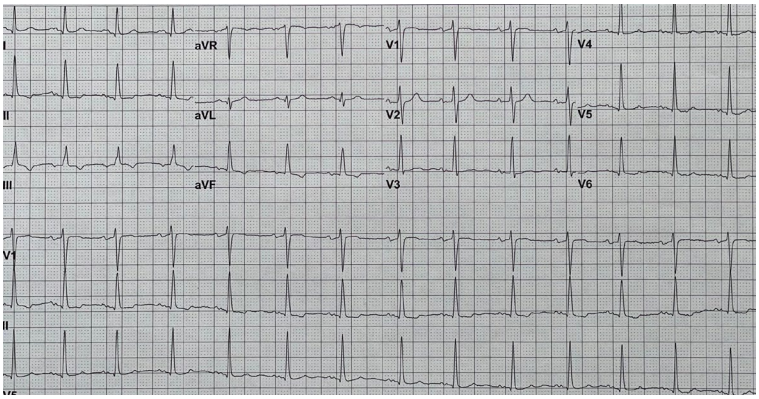


Figure 2B. ECG Illustration 2 with standard limb leads placement showed normal QRS morphology in lead aVL.

DISCUSSION

Because of its broad applicability, the accurate recording and precise interpretation of the ECG is critical. The establishment of, and adherence to, professionally developed and endorsed evidence-based standards for all phases of the ECG procedure is an important step in ensuring the high level of precision required and expected by clinicians and their patients.[4,5] The standard 12-lead ECG consists of three limb leads (leads I, II, and III), three augmented limb leads (leads aVR, aVL, and aVF), and six precordial leads (V1 through V6).[4]

Historically, limb lead electrodes have been attached at the wrists and the ankles with the patient in the supine position. For routine 12-lead recording, the American Heart Association (AHA) statement of 1975 recommended placement of the four limb lead electrodes on the arms and legs distal to the shoulder and hips,[4] and not necessarily on the wrists and ankles. Different placement of lead electrodes on the limbs can alter the ECG.[6] Clinically, recording of the ECG from the upper arm rather than from the wrist to reduce motion artifact has become popular and is facilitated by the development of disposable tab electrodes. However, it affects ECG voltages and durations, most importantly in the limb leads.

Noise from motion of the arms and legs during ambulatory and exercise ECG can be reduced by placement of the limb leads on the torso position. This is described as the Mason-Likar lead position, in which the arm electrodes are placed in the infraclavicular fossae medial to the deltoid insertions and the left leg electrode is placed midway between the costal margin and iliac crest in the left anterior axillary line.[7] Torso limb leads placement sometimes is used to reduce motion artifact during recording in infants. This modified lead placement may affect QRS morphology more than repolarization compared with standard ECG, including false-negative and false-positive infarct criteria.[3,6,8]

The torso limb leads placement is a very common practice. This nonstandard modification has the important advantages of ease and speed of application, especially in an emergency. The limb movement artifact also is reduced. This application was promoted by ECG manufacturers with diagram of such limb lead positions posted on their ECG machines (Figure 3). Present ECG illustrations showed that clinically significant ECG findings could be observed with the modified leads placement. Such abnormalities could lead to unnecessary investigations, procedures, and worries for the patients. Thus, ECGs recorded with torso placement of the extremity electrodes cannot be considered equivalent to standard ECG for all purposes and should not be used interchangeably with standard ECGs for serial comparison, according to guideline recommendations,[4,5] with exception for situations that torso limb lead placement may be appropriate. In the latter situation, these ECGs should be marked with "torso limb leads position" to alert the clinician to its limitations and repeat ECG with standard lead position is warranted for confirmation when abnormal findings are encountered.

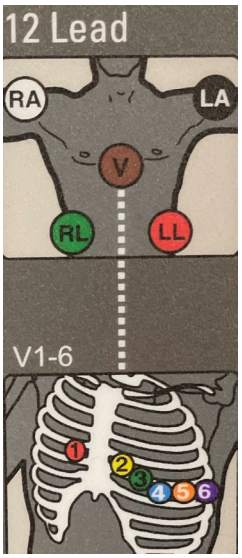


Figure 3. Diagram of ECG leads placement posted on a commercial ECG machine.

CONCLUSIONS

In summary, the ECG is the most widely used cardiac diagnostic tool in the clinical practice. Standard lead electrode placement according to guideline recommendations[5] should be observed closely to avoid abnormal findings which might lead to further, unnecessary testing, or procedures and worries for patients. All ECG with torso limb lead placement during exercise testing, urgent acquisition, or in other appropriate situations should be marked as such to alert clinician of its limitation. When abnormal findings are encountered, ECG with standard lead placement should be repeated for confirmation.

REFERENCES

1 Kligfield P. The centennial of the Einthoven electrocardiogram. J Electrocardiol 2002; 35 (Suppl):123-129. PMID: 12539109.
2 Fye WB. A history of the origin, evolution, and impact of electrocardiography. Am J Cardiol 1994; 73(13):937-949. PMID: 8184849.
3 Pipberger HV, Arzbaecher RC, Berson AS, et al. Recommendations for standardization of leads and of specifications for instruments in electrocardiography and vectorcardiography: Report of the Committee on Electrocardiography. Circulation 1975; 52:11-31.
4 Jowett NI, Turner AM, Cole A, Jones PA. Modified electrode placement must be recorded when performing 12-lead electrocardiogram. Postgrad Med J 2005; 81(952):122-125. PMID: 15701746.
5 Klighfield P, Gettes LS, Bailey JJ, et al. Recommendations for the standardization and interpretation of the electrocardiogram: Part I: The electrocardiogram and its technology – A scientific statement from the American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology; the American College of Cardiology Foundation; and the Heart Rhythm Society. J Am Coll Cardiol 2007; 49(10):1109-1127. PMID: 17349896.
6 Pahlm O, Haisty WK, Edenbrandt L, et al. Evaluation of changes in standard electrocardiographic QRS waveforms recorded from activity-compatible proximal limb lead positions. Am J Cardiol 1992; 69(3):253-257. PMID: 1731468.
7 Mason RE, Likar I. A new system of multiple-lead exercise electrocardiography. Am Heart J 1966; 71(2):196-205. PMID: 5902099.
8 Sevilla DC, Dohrmann ML, Somelofski CA, Wawrzynski RP, Wagner NB, Wagner GS. Invalidation of the resting electrocardiogram obtained via exercise electrode sites as a standard 12-lead recording. Am J Cardiol 1989; 63(1):35-39. PMID: 2909158.

Keywords: ECG, myocardial infarction, cardiac electrophysiologic technique

KANSAS JOURNAL of MEDICINE

Traumatic Hypopharyngeal Perforation from Football Helmet Chinstrap

Sue M. Nyberg, MHS, PA-C[1], Donald G. Vasquez, D.O., MPH[2,3], Eric M. Brown, PA-S[1], Jimmy Ntelekos, PA-S[1], Marcella R. Stanley, MPA, PA-C[1], Matthew A. Williams, MPA, PA-C[1]
[1]Wichita State University, Wichita, KS
Department of Physician Assistant
[2]Wesley Medical Center, Wichita, KS
Department of Trauma Services
[3]University of Kansas School of Medicine-Wichita, Wichita, KS
Department of Surgery

Received March 23, 2021; Accepted for publication May 5, 2021; Published online Sept. 1, 2021
https://doi.org/10.17161/kjm.vol14152900

INTRODUCTION

Hypopharyngeal perforation is a rare but potentially serious injury typically resulting from instrumentation or external penetrating trauma.[1-3] Perforation following blunt trauma is even more rare.[1] Due to the nature of this injury and the serious complications that can arise, prompt and proper diagnosis is key for a good patient outcome and prognosis. This case report describes an unusual case of a hypopharyngeal perforation believed to have been caused by a dislodged chinstrap of a football helmet.

CASE REPORT

An 18-year-old male presented to a local emergency department following a high school football game. He complained of hoarseness and difficult, painful swallowing. During the game, he was running with the ball when he was hit in the facemask of his helmet twice during the same play. After the first hit, the chinstrap of his helmet became dislodged posteriorly and rotated under his chin. With the second hit to his facemask, he felt the chinstrap tighten, forcing him to swallow. He continued to play a majority of the game but began to notice anterior neck pain, shortness of breath, odynophagia, sore throat, and hoarseness.

On initial examination, the patient's voice was raspy and he complained of anterior neck pain with odynophagia. The decision was made to transfer the patient to the nearest Level I trauma center for further evaluation of suspected blunt neck trauma.

Upon arriving at the trauma center approximately one hour later, the physical exam revealed a small (1 cm) midline mandibular laceration, stable vital signs, and clear breath sounds bilaterally. Mild soft tissue swelling of the neck suggesting possible subcutaneous emphysema was found, however, no crepitus was noted. A chest radiograph was within normal limits. The patient's cervical spine was non-tender to palpation along the spinous processes with full range of motion.

Cervical radiographs revealed air in the prevertebral soft tissues, posterior to the hypopharynx (Figure 1). A computed tomography (CT) scan of the neck was performed, revealing an irregularity of the posterior hypopharyngeal wall and extensive air in the soft tissues of the neck extending from the nasopharynx to the mediastinum (Figures 2 and 3). An esophagram confirmed the diagnosis of a small posterior hypopharyngeal perforation (Figure 4).

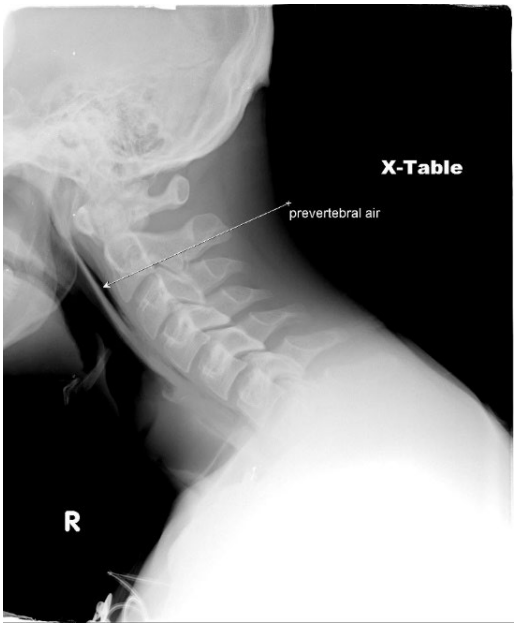
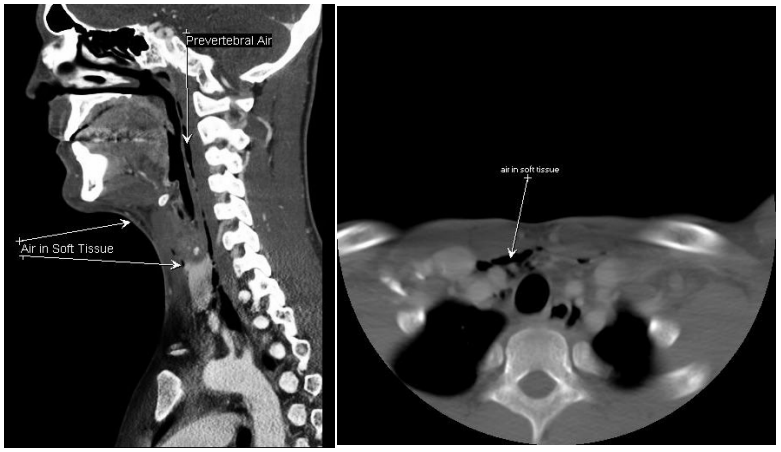


Figure 1. Lateral cervical radiograph displaying air in the prevertebral soft tissues, posterior to the hypopharynx.



Figures 2 and 3. CT scan exhibiting irregularity of the posterior hypopharyngeal wall and extensive air in the soft tissues of the neck extending from the nasopharynx to the mediastinum.

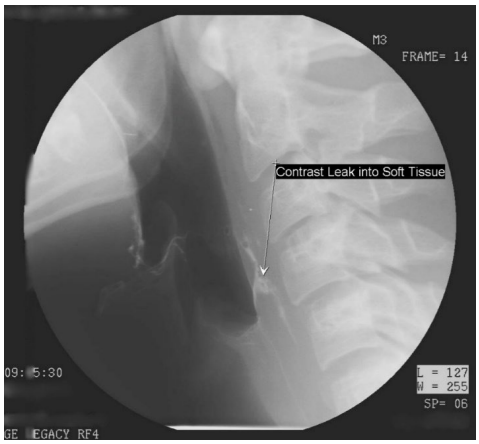


Figure 4. Esophagram confirming a hypopharyngeal perforation due to contrast leak into soft tissue.

The patient initially was admitted to the Intensive Care Unit for close observation. He was kept nil per os (NPO) and treated conservatively with cefotetan 1 gram every 12 hours and metronidazole 500 milligrams every 12 hours intravenously. Esophagrams were repeated every two days and showed gradual improvement with no extravasation noted by the sixth day of hospitalization. At that time, the patient was afebrile with a normal white blood cell count and differential. His initial symptoms of anterior neck pain, shortness of breath, and odynophagia were resolved. The patient was dismissed on a clear liquid diet with close outpatient follow-up. An esophagram three weeks after the initial injury confirmed a healed lesion.

DISCUSSION

Pharyngoesophageal injury leading to hypopharyngeal perforation is a rare clinical condition.[4] The majority of hypopharyngeal perforations presented to trauma centers are after iatrogenic, penetrating, or blunt trauma to the neck.[1-6] Blunt trauma is responsible for less than 2% of hypopharyngeal perforations with most following a fall, blunt assault, motor vehicle or motorcycle collisions, or direct impact during sports activities.[3,6-10]

Perforations are most likely to occur at the hypopharyngeal-esophageal junction. This area, known as Killian's dehiscence, lacks the longitudinal muscle fibers of the inferior pharyngeal constrictor and consists solely of mucosa and serosa.[7,11-13] The most commonly postulated mechanism of perforation from blunt trauma is shearing force after cervical hyperextension with concurrent compression of the larynx against the vertebral bodies.[7,14,15] Various other blunt trauma mechanisms have been thought to contribute to these injuries, such as barometric perforation (hyperextension of the neck with a closed airway combined with forced exhalation), forced compression of soft tissues against hypertrophic anterior cervical osteophytes, and displaced hyoid fracture resulting in pharyngeal perforation.[7,14,15] Based on the physical and diagnostic findings, the likely mechanism of injury of this patient occurred as a result of compression of the larynx against the vertebral bodies by the chinstrap during the initial hit, followed by a shearing force during the second hit.

Aerodigestive tract injury (ATI) can cause serious morbidity and may result in increased mortality if not diagnosed and treated expeditiously.[6,8,16] In a patient with a history of instrumentation or blunt trauma, common symptoms that should prompt suspicion of hypopharyngeal injury include subcutaneous emphysema, chest or neck pain, odynophagia, dysphagia, dysphonia, and hemoptysis.[8,11] In addition, it has been suggested that "the presence of hoarseness or stridor is an important indicator of potential upper ATI when concomitant emphysema is present".[8] Extent and location are critical in determining management of this injury; thus, appropriate use of diagnostic studies is crucial in the identifying hypopharyngeal perforations.[11]

There is no consensus regarding the best diagnostic study for a suspected hypopharyngeal perforation, but some combination of plain radiographs, CT scans, fluoroscopy, and nasopharyngolaryngoscopy have been recommended in evaluating patients for this injury.[11,17-19] Radiographs of the chest and lateral cervical spine are reasonable initial studies and may demonstrate cervical emphysema suggesting hypopharyngeal peroration. CT scans with water-soluble contrast can be utilized to rule out other injuries and determine the precise location of a perforation.[10,16,18-20] Fluoroscopic swallow studies are highly sensitive and can confirm a hypopharyngeal perforation.[8,18,19] Ultimately, direct visualization through endoscopy is the diagnostic gold standard, however, this may not be necessary in all cases.[21]

The absence of management guidelines for a pharyngoesophageal injury, particularly for optimal operative management, probably results from the infrequent incidence of these injuries. Most recommendations are extrapolated from penetrating neck trauma experiences.[16] Historically, surgical treatment has been the preferred management of hypopharyngeal perforation secondary to blunt trauma.[19,21] Recently, a trend toward nonoperative treatment has been emerging which includes broad spectrum antibiotics, NPO status, parenteral nutrition, and follow-up imaging studies.[3,18,22]

Criteria to select patients for nonoperative management are not well defined. Some have recommended this approach for perforations under 2 centimeters in length, presentation within 24 hours, no oral intake in the interval between injury and presentation to the hospital, and no signs of systemic infection or injury superior to the arytenoid cartliage.[2,4,16] Overall, the management and treatment of hypopharyngeal perforation varies depending on the severity of the injury, as numerous factors influence treatment decisions: time of clinical presentation, physical signs and symptoms, degree of extravasation of contrast media, and the location and size of the perforation.[1-3,6,10,15,18,19,22]

CONCLUSIONS

Hypopharyngeal perforation secondary to blunt trauma is uncommon. The unique mechanism of injury seen in this case demonstrated the need for heightened level of suspicion when assessing a patient with pertinent symptoms. Hypopharyngeal perforations are associated with high morbidity and even mortality if not recognized early and treated properly and promptly.

REFERENCES

1 Demetriades D, Velmahos GG, Asensio JA. Cervical pharyngoesophageal and laryngotracheal injuries. World J Surg 2001; 25(8):1044-1048. PMID: 11571970.
2 Stanley RB, Armstrong WB, Fetterman BL, Shindo ML. Management of external penetrating injuries into the hypopharyngeal-cervical esophageal funnel. J Trauma 1997; 42(4):675-679. PMID: 9137257.
3 Barmparas G, Navsaria PH, Serna-Gallegos D, et al. Blunt pharyngoesophageal injuries: Current management strategies. Scand J Surg 2018; 107(4):336-344. PMID: 29628012.
4 Niezgoda JA, McMenamin P, Graeber GM. Pharyngoesophageal perforation after blunt neck trauma. Ann Thorac Surg 1990; 50(4):615-617. PMID: 2222052.
5 Graeber GM, Niezgoda JA, Albus RA, et al. A comparison of patients with endoscopic esophageal perforations and patients with Boerhaave's syndrome. Chest 1987; 92(6):995-998. PMID: 3677845.
6 Hagr A, Kamal D, Tabah R. Pharyngeal perforation caused by blunt trauma to the neck. Can J Surg 2003; 46(1):57-58. PMID: 12585799.
7 Hagan WE. Pharyngoesophageal perforations after blunt trauma to the neck. Otolaryng Head Neck Surg 1983; 91(6):620-626. PMID: 6420742.
8 Goudy SL, Miller FB, Bumpous JM. Neck crepitance: Evaluation and management of suspected upper aerodigestive tract injury. Laryngoscope 2002; 112(5):791-795. PMID: 12150608.
9 Berry BE, Ochsner JL. Perforation of the esophagus: A 30 year review. J Thorac Cardiov Sur 1973; 65(1):1-7. PMID: 4682465.

[10] Salemis NS, Georgiou C, Alogdianakis E, Gourgiotis S, Karalis G. Hypopharyngeal perforation because of blunt neck trauma. Emerg Radiol 2009; 16(1):71-74. PMID: 18188618.
[11] Smith D, Woolley S. Hypopharyngeal perforation following minor trauma: A case report and literature review. Emerg Med J 2006; 23(1):e7. PMID: 16373792.
[12] Cross KJ, Koomalsingh KJ, Fahey TJ, Sample J. Hypopharyngeal rupture secondary to blunt trauma: Presentation, evaluation, and management. J Trauma 2007; 62(1):243-246. PMID: 17215764.
[13] Miracle AC, Uzelac A. Imaging blunt and penetrating trauma to the neck: Clinical relevance and management. Appl Radiol 2016; 45(7):14-19.
[14] Gulbrandson RN, Gaspard DJ. Steering wheel rupture of the pharyngoesophagus. A solitary injury. J Truama 1977; 17(1):74-76. PMID: 833910.
[15] Elleson DA, Rowley SD. Esophageal perforation: Its early diagnosis and treatment. Laryngoscope 1982; 92(6):678-680. PMID: 7087630.
[16] Zenga J, Kreisel D, Kushnir VM, Rich JT. Management of cervical esophageal and hypopharyngeal perforations. Am J Otolaryngol 2015; 36(5):678-685. PMID: 26122742.
[17] Català J, Puig J, Muñoz JM, Vivancos J, Llopart JR. Perforation of the pharynx caused by blunt external trauma. Eur Radiol 1998; 8(1):137-140. PMID: 9442146.
[18] Søreide J, Viste A. Esophageal perforation: Diagnostic work-up and clinical decision-making in the first 24 hours. Scand J Trauma Resusc Emerg Med 2011; 19:66. PMID: 22035338.
[19] Onat S, Ulku R, Cigdem KM, Avci A, Ozcelik C. Factors affecting the outcome of surgically treated non-iatrogenic traumatic cervical esophageal perforation: 28 years experience at a single center. J Cardiothoracic Surg 2010; 5(1):1-5. PMID: 20509978.
[20] Dolgin SR, Kumar NR, Wykoff TW, Maniglia AJ. Conservative medical management of traumatic pharyngoesophageal perforations. Ann Otol Rhinol Laryngol 1992; 101(3):209-215. PMID: 1543329.
[21] Pathak B, Yu DC, Linden BC. Transoral closure of a perforation of the hypopharynx from blunt trauma. J Pediatr Surg 2009; 44(12):2402-2405. PMID: 20006037.
[22] Ho KF, Soo G, Abdullah VJ, van Hasselt CA. Hypopharyngeal perforation after blunt neck trauma. J Otolaryngol 2004; 33(3):200-202. PMID: 15872003.

Keywords: hypopharynx, blunt injuries, neck injuries, esophageal perforation

KANSAS JOURNAL of MEDICINE

Reimbursement Policies for Diabetes Prevention Program (DPP): Implications for Racial and Ethnic Health Disparities

Taynara Formagini, M.Sc.[1], Joanna V. Brooks, MBE, Ph.D.[1,2], Lisette T. Jacobson, MPA, Ph.D.[3], Andrew W. Roberts, Pharm.D., Ph.D.[1,2,4]

[1]University of Kansas School of Medicine, Kansas City, KS Department of Population Health

[2]University of Kansas Cancer Center, Kansas City, KS

[3]University of Kansas School of Medicine-Wichita, Wichita, KS Department of Population Health

[4]University of Kansas School of Medicine, Kansas City, KS Department of Anesthesiology

Received Jan. 26, 2021; Accepted for publication April 30, 2021; Published online Sept. 1, 2021
https://doi.org/10.17161/kjm.vol14.15125

INTRODUCTION

Black and Latinx individuals face many diabetes-related disparities compared to non-Hispanic Whites.[1-3] In 2002, The Diabetes Prevention Program (DPP) clinical trial demonstrated a 58% reduction in diabetes incidence among adults with prediabetes who reduced their body weight by 5 - 7%.[4] In 2018, Medicare started offering reimbursement to healthcare and community organizations delivering the DPP, using a performance-based payment methodology that does not account for racial and ethnic disparities.[5] Blacks and Latinxs are less likely than non-Hispanic Whites to achieve the performance benchmark required for full DPP reimbursement,[6] which can discourage providers from delivering DPP to these groups.[7] We discuss how the Medicare DPP reimbursement model and the dismissal of racial and ethnic disparities associated with diabetes are problematic and provide alternative approaches to adapt Medicare reimbursement for DPP to mitigate disparities in diabetes prevention efforts.

Diabetes Prevention and the Medicare Reimbursement Program

Blacks and Latinxs face striking injustices and disparities in health outcomes and healthcare services in the United States.[1] Type 2 diabetes (hereafter referred to as diabetes) is one disease where these disparities are clear.[3] Compared to non-Hispanic Whites, Blacks and Latinxs face higher rates of diabetes prevalence, worse diabetes control, and higher rates of diabetes-related complications and mortality.[2] These diabetes-related health disparities are projected to worsen through 2030.[8] Therefore, delivering effective preventive interventions for Black and Latinx individuals with prediabetes can reduce diabetes-related disparities for these groups while also reducing the burden of diabetes nationwide, and reducing the high costs associated with the disease.[1]

To date, the best evidence for guiding strategies to prevent diabetes at the individual level comes from randomized clinical trials of lifestyle interventions (i.e., adherence to a healthy diet and physical activity), such as the Diabetes Prevention Program (DPP).[4] The DPP clinical trial published in 2002 demonstrated that a mean body weight loss of 5 - 7% among adults with impaired glucose tolerance or impaired fasting glucose (known as prediabetes) led to a 58% reduction in diabetes incidence after three years.[4] Blacks and Latinxs represented 35.6% of the sample and the incidence of diabetes was similar among non-Hispanic Whites, Blacks, and Latinxs, which gives support to the claim that the DPP is effective for these two minority groups under experimental conditions. The original findings, followed by a 10-year follow-up study that reaffirmed positive benefits on diabetes incidence outcomes,[9] led to implementation of the National Diabetes Prevention Program (National DPP) in 2012.

The National DPP is a year-long lifestyle change program administered through healthcare and community organizations that partner with the U.S. Centers for Disease Control and Prevention (CDC). Key features of the program include a 16-session core curriculum focused on a healthy diet and physical activity, and regular engagement with a certified lifestyle coach and group support sessions over the course of a year. The primary measure of the DPP's effectiveness is participants' percentage change in body weight from the beginning to end of the intervention.[6]

A report from the National DPP released by the CDC showed that between 2012 and 2016, 14,747 adults with prediabetes participated in the program in healthcare and community settings, of which 13.8% were Blacks and 10% were Latinxs.[6] Following the findings of the original clinical trial,[4,9] a minimum of a 5% reduction of body weight was set as a benchmark for success for all participants in the program. However, only 35.5% of all participants, compared with 70% in the clinical trial, achieved the goal of at least a 5% body weight reduction.[6] Compared to non-Hispanic Whites, Blacks and Latinxs who participated in the National DPP were half as likely to achieve a 5% weight loss. Similarly, multiple implementation studies have shown that compared to non-Hispanic Whites, Blacks and Latinxs are less likely to enroll in the DPP and to lose body weight.[10-14] In general, studies have discussed lower engagement to the intervention (i.e., adherence to a healthy diet and physical activity) and other non-intervention related factors, such as social, economic, and environmental factors, as the main reasons for low enrollment and low effectiveness among these groups.[10-14]

In 2018, Medicare started offering reimbursement to healthcare and community organizations delivering the DPP to incentivize broader adoption of this intervention among the 24 million seniors with prediabetes in the U.S. (the equivalent of 46% of the U.S. population with 65 years or older).[15] Of note, Black and Latinx Medicare beneficiaries have a higher prevalence of diabetes compared to non-Hispanic Whites (38%, 38%, versus 23%, respectively). Implementing Medicare reimbursement for the DPP provides an important policy conduit for potentially addressing these high rates of diabetes prevalence among both Blacks and Latinxs.

Medicare reimbursement for DPP services is contingent on a performance-based payment methodology. Full Medicare reimbursement for delivering the DPP requires that participants achieve the 5% weight loss benchmark established by the earlier clinical trial.[4,9] DPP reimbursement is reduced significantly starting with month six of the program if individual participants have not achieved the required weight loss. For example, from months 7 - 12, providers can receive up to $124 per participant if the required weight loss is achieved, but only

$30 per participant who does not achieve the required weight loss (Table 1). Payment is not risk-adjusted for economic, social, and environmental factors and does not account for findings from the National DPP[6] and from other studies[10-14] that show Black and Latinx participants are less likely to achieve the 5% weight loss benchmark.

Limitations of Medicare DPP Reimbursement: Disadvantages for Blacks and Latinxs

When Medicare reimbursement for the DPP was first announced, it received immediate criticism based on concerns that the structure of the reimbursement would discourage broad dissemination of the program and widen health disparities. Ritchie et al.[16] offered an analysis on critical limitations of this reimbursement model, calling attention to the fact that tying payment to a 5% weight loss outcome was likely to discourage providers serving minority populations to offer the program, since these populations are less likely to achieve the 5% benchmark due to economic, social, and environmental factors. Later, at least two analyses projected that Medicare reimbursement might be insufficient to cover the DPP's costs, particularly for healthcare systems serving a majority of Black and Latinx participants.[7,17] Unsurprisingly, a recent analysis shows 9 of the 10 states with the largest population of Blacks and Latinxs have severe shortages of Medicare DPP providers.[18]

Greater DPP uptake among non-Hispanic Whites and less access among Blacks and Latinxs have the potential to exacerbate the previously discussed diabetes-related health disparities by increasing the gap in the prevalence of diabetes between these two minority groups and non-Hispanic Whites. Yet, no changes have been made to the Medicare DPP reimbursement model to date to address the fact that Blacks and Latinxs experience systemic barriers to achieving the 5% weight loss benchmark required by the Medicare DPP reimbursement model, and simultaneously have higher rates of diabetes. Moreover, other large payers, including Medicaid, have started to follow the same model to reimburse for the DPP.[5,19]

Dismissal of Racial and Ethnic Disparities in DPP Reimbursement

By not adjusting payment for economic, social, and environmental factors influencing weight loss success, Medicare reimbursement for the DPP maintains the predominant biomedical model approach used in the U.S. healthcare system. This approach views diabetes prevention solely as an individual effort and responsibility, feasible through adherence to a healthy diet and physical activity. This model of reimbursement disregards that Black and Latinx populations are less likely to achieve the required weight loss due to structural and systemic barriers outside of individual behaviors. In other words, this approach fails to account for economic, social, and environmental factors that influence behavior change and are particularly important to individuals attempting to prevent diabetes.

First, Blacks and Latinxs face challenges related to economic factors. Blacks and Latinxs have the lowest household income in the U.S.[20] Among Medicare beneficiaries, a total of 19% of Blacks and 18% of Latinxs are below 100% of the Federal Poverty Level compared to 8% of non-Hispanic Whites.[15] Limited economic resources generally are linked to higher consumption of a poor diet quality and less engagement in recreational physical activity, which in turn, are associated with obesity.[21,22]

Social and environmental factors, such as where a person lives and works, have an important impact on diet quality and physical activity as well. Neighborhoods with a large concentration of Blacks and Latinxs tend to have less access to healthy food options; Blacks and Latinxs also experience fewer opportunities to exercise and lower quality resources.[23,24] Additionally, they are more likely to have low-paying jobs with worse working conditions, more work hours, and fewer benefits.[25] Taken together, these factors may be associated with less available time to exercise and to buy and cook healthy foods. Moreover, Blacks and Latinxs are less likely to try to lose weight.[26] Among middle-aged and older adults (the majority of DPP participants), Blacks and Latinxs are significantly less likely than non-Hispanic Whites to engage in physical activity and healthy dietary behaviors for weight loss.[27]

These realities help to explain why Blacks and Latinxs have been less likely to achieve the expected 5% body weight reduction compared to non-Hispanic Whites. However, the current 5% weight loss benchmark for Medicare DPP reimbursement ignores these systemic economic, social, and environmental barriers that disadvantage these two minority groups. Assuring that reimbursement for the DPP is equitable for different populations is imperative, as it can help to mitigate racial and ethnic disparities in the burden of diabetes for millions of individuals in the country.

Accounting for Racial and Ethnic Disparities in the DPP Reimbursement Model

Medicare and other payers should consider alternative reimbursement approaches for the DPP. Particularly, to improve DPP outcomes for Blacks and Latinxs and reduce the harmful consequences of racial and ethnic disparities in disease burden of diabetes, payers and health systems considering reimbursement models could improve upon the current Medicare DPP model to address disparities in at least three different ways.

First, as others have recommended,[16] we suggest revising the 5% weight loss threshold for full reimbursement. While the 5% weight reduction should be encouraged, previous studies have shown a linear association between any body weight reduction and reduction of diabetes incidence,[28,29] suggesting that any reduction of body weight can be beneficial in attempting to prevent diabetes. Therefore, we recommend that sites receive full reimbursement if participants reduce and maintain some body weight. Revising this threshold has the potential to encourage providers to deliver the DPP intervention to more participants from racial and ethnic populations and increase the likelihood of Blacks and Latinxs to receive the intervention.

Second, reimbursement should be risk-adjusted based on beneficiaries' socioeconomic status and race/ethnicity, an approach that has been used previously by other Medicare efforts.[30,31] These are two measurable social risk factors that should be considered in DPP reimbursement. Sites providing care to low-income Blacks and Latinxs should receive an adjusted rate for each participant. These participants may require more intensive care and greater costs to overcome

Table 1. Medicare DPP payment structure.

	Core Sessions Months 0 - 6	Core maintenance sessions Months 7 - 12		Ongoing maintenance sessions Months 13 - 24			
	16 sessions	3 sessions	3 sessions	3 sessions	3 sessions	3 sessions	3 sessions
Attendance only	Attend 1 session total: $26 (G9873) Attend 4 sessions total: $52 (G9874) Attend 9 sessions total: $94 (G9875)	Attend 2 sessions (without at least 5% WL): $15 (G9876)	Attend 2 sessions (without at least 5% WL): $15 (G9877)	5% WL and attendance must be achieved to receive payment during ongoing maintenance sessions			
Attendance and weight loss	5% WL is not required to receive payment	Attend 2 sessions (with at least 5% WL): $63 (G9878)	Attend 2 sessions (with at least 5% WL): $63 (G9879)	Attend 2 sessions (with at least 5% WL): $52 (G9882)	Attend 2 sessions (with at least 5% WL): $52 (G9883)	Attend 2 sessions (with at least 5% WL): $52 (G9884)	Attend 2 sessions (with at least 5% WL): $52 (G9885)
Additional codes	5% WL achieved: $165 (G9880)						
	9% WL achieved: $26 (G9881)						
	Bridge payment: $26 (G9890)						
	Report attendance at sessions that are not associated with a performance goal. Non-payable codes should be listed on the same claim as the payable code with which they are associated: $0 (G9891)						

Maximum possible payment per eligible beneficiary: $689;
Table adapted from Medicare Diabetes Prevention Program (MDPP) Quick Reference Guide to Payment and Billing.

barriers they face to achieving the same outcomes as more advantaged participants.[31] Doing so may prevent underpayment and appropriately incentivize sites serving Blacks and Latinxs to provide the program for these groups.

Third, payers could consider providing supplemental financial support to low-income participants to offset the costs of healthy meals and access to physical activity-related facilities aiming to overcome some of the barriers faced by these individuals to engaging in behavior change. These two strategies were used on the original DPP clinical trial[4] and as others have shown, it can increase participants' likelihood of eating healthier food and exercising, and improve DPP attendance,[32,33] which in turn may improve weight loss outcomes.

CONCLUSIONS

In short, the DPP has been shown to prevent diabetes effectively among Blacks and Latinxs under ideal experimental conditions.[4] However, Medicare's current reimbursement model for the DPP overlooks the fact that Blacks and Latinxs are less likely to achieve the required weight loss under real world conditions. Medicare also is dismissing the data showing reimbursement is insufficient to cover the program's cost for these populations. This model appears to be insufficient for creating widespread adoption of the DPP among sites caring for Black and Latinx beneficiaries by discouraging providers serving these groups to pursue the DPP. Even though reimbursement for the DPP, as one policy, is unable to address all economic, social, and environmental factors or to eliminate health disparities fully, the current reimbursement model is poised to exacerbate disparities by further disadvantaging the quantity and quality of DPP services delivered to Blacks and Latinxs. A new risk adjusted DPP reimbursement model may pave the way to improved prevention of diabetes and mitigation of racial and ethnic disparities in the disease burden of diabetes. While we intended to provide initial evidence about the need to consider alternative approaches for reimbursement of the DPP, more robust evidence is needed to determine best practices and optimal reimbursement benefit designs for improving DPP uptake among racial and ethnic minority populations and improving diabetes prevention outcomes. Interventions addressing providers knowledge about delivering the DPP for Blacks and Latinxs also can be useful to improve access to the DPP for these groups.

ACKNOWLEDGMENTS

Taynara Formagini was supported by a scholarship from the Brazilian Coordination for the Improvement of Higher Education Personnel (CAPES) to pursue doctoral education. Dr. Andrew Roberts was supported by a career development grant from the National Center for Advancing Translational Science awarded to the Frontiers: University of Kansas Clinical and Translational Science Institute (#KL2TR002367).

REFERENCES

[1] Smedley BD, Stith AY, Nelson AR. Institute of Medicine, Committee on Understanding and Eliminating Racial and Ethnic Disparities in Health Care. Unequal treatment: Confronting racial and ethnic disparities in healthcare. Washington, DC: National Academies Press, 2003.
[2] Spanakis EK, Golden SH. Race/ethnic difference in diabetes and diabetic complications. Curr Diab Rep 2013; 13(6):814-823. PMID: 24037313.
[3] Hill-Briggs F, Adler NE, Berkowitz SA, et al. Social determinants of health and diabetes: A scientific review. Diabetes Care 2020; 44(1):258-279. PMID: 33139407.
[4] Diabetes Prevention Program Research Group, et al. 10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study. Lancet 2009; 374(9702):1677-1686. PMID: 19878986.
[5] National DPP Coverage Toolkit. National Diabetes Prevention Program Coverage Toolkit: Participating Payers and Employers. 2020. https://coveragetoolkit.org/participating-payers/. Accessed October 9, 2020.
[6] Ely EK, Gruss SM, Luman ET, et al. A national effort to prevent type 2 diabetes: participant-level evaluation of CDC's National Diabetes Prevention Program. Diabetes Care 2017; 40(10):1331-1341. PMID: 28500215.

[7] Ritchie ND, Gritz RM. New Medicare diabetes prevention coverage may limit beneficiary access and widen health disparities. Med Care 2018; 56(11):908-911. PMID: 30312286.
[8] Rowley WR, Bezold C, Arikan Y, Byrne E, Krohe S. Diabetes 2030: Insights from yesterday, today, and future trends. Popul Health Manag 2017; 20(1):6-12. PMID: 27124621.
[9] Diabetes Prevention Program Research Group, et al. 10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study. Lancet 2009; 374(9702):1677-1686. PMID: 19878986.
[10] Wadden TA, West DS, Neiberg RH, et al. One-year weight losses in the Look AHEAD study: Factors associated with success. Obesity (Silver Springs) 2009; 17(4):713-722. PMID: 19180071.
[11] Wing RR, Hamman RF, Bray GA, et al. Achieving weight and activity goals among diabetes prevention program lifestyle participants. Obes Res 2004; 12(9):1426-1434. PMID: 15483207.
[12] West DS, Prewitt TE, Bursac Z, Felix HC. Weight loss of black, white, and Hispanic men and women in the Diabetes Prevention Program. Obesity (Silver Spring) 2008; 16(6):1413-1420. PMID: 18421273.
[13] AuYoung M, Moin T, Richardson CR, Damschroder LJ. The Diabetes Prevention Program for underserved populations: A brief review of strategies in the real world. Diabetes Spectr 2019; 32(4):312-317. PMID: 31798288.
[14] Samuel-Hodge C, Johnson C, Braxton D, Lackey M. Effectiveness of Diabetes Prevention Program translations among African Americans. Obes Rev 2014; 15(Suppl 4):107-124. PMID: 25196409.
[15] Kaiser Family Foundation (KFF). Profile of Medicare Beneficiaries by Race and Ethnicity: A Chartpack. Washington, DC: Kaiser Family Foundation (KFF), 2016.
[16] Ritchie ND, Havranek EP, Moore SL, Pereira RI. Proposed Medicare coverage for diabetes prevention: Strengths, limitations, and recommendations for improvement. Am J Prev Med 2017; 53(2):260-263. PMID: 28336351.
[17] Parsons AS, Raman V, Starr B, Zezza M, Rehm CD. Medicare underpayment for Diabetes Prevention Program: Implications for DPP suppliers. Am J Manag Care 2018; 24(10):475-478. PMID: 30325189.
[18] Ritchie ND, Sauder KA, Gritz RM. Medicare Diabetes Prevention Program: Where are the suppliers? Am J Man Care 2020; 26(6):e198-e201. PMID: 32549070.
[19] Porterfield D, Jacobs S, Farrell K, et al. Evaluation of the Medicaid Coverage for the National Diabetes Prevention Program Demonstration Project. Final Report Research. Triangle Park, NC RTI International Research Institute, 2018.
[20] Wilson V, Williams J. Racial and ethnic income gaps persist amid uneven growth in household incomes. September 11, 2019. https://www.epi.org/blog/racial-and-ethnic-income-gaps-persist-amid-uneven-growth-in-household-incomes/. Accessed Nov 11, 2019.
[21] Darmon N, Drewnowski A. Does social class predict diet quality? Am J Clinical Nutr 2008; 87(5):1107-1117. PMID: 18469226.
[22] Stalsberg R, Pedersen AV. Are differences in physical activity across socioeconomic groups associated with choice of physical activity variables to report? Int J Environ Res Public Health 2018; 15(5):922. PMID: 29734745.
[23] Walker RE, Keane CR, Burke JG. Disparities and access to healthy food in the United States: A review of food deserts literature. Health Place 2010; 16(5):876-884. PMID: 20462784.
[24] Heinrich KM, Lee RE, Suminski RR, et al. Associations between the built environment and physical activity in public housing residents. Int J Behav Nutr Phys Act 2007; 4(1):56. PMID: 17997820.
[25] Carnevale A, Strohl J, Gulish A, Van Der Werf M, Peltier Campbell K. The Unequal Race for Good Jobs: How Whites Made Outsized Gains in Education and Good Jobs Compared to Blacks and Latinos. 2019. https://1gyhoq479ufd3yna29x7ubjn-wpengine.netdna-ssl.com/wp-content/uploads/Full_Report-The_Unequal_Race_for_Good_Jobs.pdf. Accessed February 3, 2021.
[26] Marquez B, Murillo R. Racial/ethnic differences in weight-loss strategies among US adults: National Health and Nutrition Examination Survey 2007-2012. J Acad Nutr Diet 2017; 117(6):923-928. PMID: 28330732.
[27] August KJ, Sorkin DH. Racial/ethnic disparities in exercise and dietary behaviors of middle-aged and older adults. J Gen Intern Med 2011; 26(3):245-250. PMID: 20865342.
[28] Kim ES, Jeong JS, Han K, et al. Impact of weight changes on the incidence of diabetes mellitus: A Korean nationwide cohort study. Sci Rep 2018; 8(1):3735. PMID: 29487293.
[29] Hamman RF, Wing RR, Edelstein SL, et al. Effect of weight loss with lifestyle intervention on risk of diabetes. Diabetes Care 2006; 29(9):2102-2107. PMID: 16936160.
[30] Durfey SNM, Kind AJH, Gutman R, et al. Impact of risk adjustment for socioeconomic status on Medicare Advantage plan quality rankings. Health Aff (Millwood) 2018; 37(7):1065-1072. PMID: 29985685.
[31] Steinwachs DM, Stratton KR, Kwan LY. Accounting for Social Risk Factors in Medicare payment. Washington, DC: National Academies Press, 2016. ISBN: 0-309-44801-8.
[32] Alva ML, Romaire M, Acquah J. Impact of financial incentives on diabetes prevention class attendance and program completion: Evidence from Minnesota, Montana, and New York. Am J Health Promot 2019; 33(4):601-605. PMID: 30122055.
[33] Desai JR, O'Connor PJ, Taylor GL, et al. 688-P: Factors associated with Diabetes Prevention Program (DPP) compliance and weight loss among low income participants. Diabetes 2019; 68(Suppl 1):688-P.

Keywords: minority health, Medicare, health insurance reimbursement, healthcare disparities, prediabetic state

KANSAS JOURNAL of MEDICINE

Letter to the Editor: Morphea, Gluten, and Autoimmunity: HLA Behind the Scenes?

Nada Boutrid, M.D.[1,2], Hakim Rahmoune, M.D.[1,2]
Ferhat Abbas Setif-1 University, Algeria
[1]Faculty of Medicine, LMCVGN Research Laboratory
[2]University Hospital of Setif, Department of Pediatrics

Received Aug. 12, 2021; Accepted for publication Aug. 19, 2021; Published online Sept. 1, 2021
https://doi.org/10.17161/kjm.vol1415774

We read with great attention the recent case report published in the Kansas Journal of Medicine about the peculiar association of morphea, celiac disease, dermatitis herpetiformis, and dermatomyositis in a male adult.[1] We would like to highlight the genetic link between morphea and autoimmune disorders like celiac disease, along with the potent role of human leukocyte antigen (HLA) genes that may lay behind. In fact, numerous case reports in the literature depict similar lesions of morphea, notably in celiac patients with diabetes[2,3] and those individuals share a common pool of HLA alleles.[4]

Several studies investigating autoimmune diseases associated with morphea have identified an increased risk probably linked to a genetic (i.e., HLA) susceptibility.[5,6]

Genetically, several HLA alleles are associated with morphea and also strongly related to celiac disease and dermatomyositis,[7] as well as to other autoimmunes conditions like rheumatoid arthritis (HLA DRB1 *04)[8], multiple sclerosis (HLA DRB1*15 and HLA DQB1*06:02)[9], autoimmune thyroiditis (HLA-DR3)[10,11], and type 1 diabetes (HLA-DR3-DQ2 and HLA-DR4-DQ8).[12]

The near-future seems promising for a real "genetic card" (e.g., through HLA typing) offered to each patient with autoimmune disorders, and the early detection of all genetic, HLA-related risk is a strong perspective of personalized medicine for early diagnosis and individualized long-term management.

ACKNOWLEDGEMENTS

The authors are supported by the Directorate General for Scientific Research and Technological Development (DGRSDT), MESRS, Algeria. The sponsor had no involvement in the collection, analysis, and interpretation of data nor in the writing of the manuscript.

REFERENCES

1 Jibbe A, Neill BC, Tolkachjov SN. Concurrent dermatomyositis, celiac disease, and dermatitis herpetiformis in a patient with a history of morphea. Kans J Med 2021; 14:203-205. PMID: 34367491.
2 Firoz EF, Kamino H, Lehman TJA, Orlow SJ. Morphea, diabetes mellitus type I, and celiac disease: Case report and review of the literature. Pediatr Dermatol 2010; 27(1):48-52. PMID: 20199410.
3 Loo WJ, Farrell AM, Holt PJA. The coexistence of lichen sclerosus and morphea in the same lesion in a child with insulin dependent diabetes and celiac disease. Eur J Pediatr Dermatol 2000; 10(4):201-204.
4 Deja G, Sikora D, Pyziak-Skupien A, Klenczar K, Deja R, Jarosz-Chobot P. The usefulness of genotyping of celiac disease-specific HLA among children with type 1 diabetes in various clinical situations. J Diabetes Res 2020; 2020:7869350. PMID: 32149153.
5 Simmonds MJ, Gough SCL. Unravelling the genetic complexity of autoimmune thyroid disease: HLA, CTLA-4 and beyond. Clin Exp Immunol 2004; 136(1):1-10. PMID: 15030506.
6 Hemminki K, Li X, Sundquist J, Sundquist K. Familial associations of rheumatoid arthritis with autoimmune diseases and related conditions. Arthritis Rheum 2009; 60(3):661-668. PMID: 19248111.
7 Rebollo-Domínguez N, Vega-Memije M-E, Villaseñor-Ovies P, García-Lechuga M, Granados J, Rangel-Gamboa L. Major histocompatibility complex class II (HLA-DR) is associated with morphea and systemic sclerosis patients. Blood Genom 2018; 2(3):165-170.
8 Wysocki T, Olesińska M, Paradowska-Gorycka A. Current understanding of an emerging role of HLA-DRB1 gene in rheumatoid arthritis-from research to clinical practice. Cells 2020; 9(5):1127. PMID: 32370106.
9 De Silvestri A, Capittini C, Mallucci G, et al. The involvement of HLA class II alleles in multiple sclerosis: A systematic review with meta-analysis. Dis Markers 2019; 2019:1409069. PMID: 31781296.
10 Lee HJ, Li CW, Hammerstad SS, Stefan M, Tomer Y. Immunogenetics of autoimmune thyroid diseases: A comprehensive review. J Autoimmun 2015; 64:82-90. PMID: 26235382.
11 Cortés JMR, Zerón HM. Genetics of thyroid disorders. Folia Med (Plovdiv) 2019; 61(2):172-179. PMID: 31301652.
12 Pociot F, Lernmark Å. Genetic risk factors for type 1 diabetes. Lancet 2016; 387(10035):2331-2339. PMID: 27302272.

KANSAS JOURNAL of MEDICINE

Author Response: Morphea, Gluten, and Autoimmunity: HLA Behind the Scenes?

Mitchell S. Davis, M.D.[1], Brett C. Neill, M.D.[2], Atieh Jibbe, M.D.[3], Stanislav N. Tolkachjov, M.D.[2]
[1]HCA Las Palmas Del Sol, El Paso, TX
[2]Epiphany Dermatology, Dallas, TX
[3]University of Kansas Medical Center, Kansas City, KS
Department of Internal Medicine, Division of Dermatology

Received Aug. 18, 2021; Accepted for publication Aug. 19, 2021; Published online Sept. 1, 2021
https://doi.org/10.17161/kjm.vol1415821

We appreciated Boutrid and Rahmoune for their remarks regarding our report in the letter to the editor.[1] The authors first reference several case reports describing morphea-like lesions in patients with celiac disease and diabetes. Next, they highlighted the genetic links between several autoimmune diseases (AD): morphea, celiac disease, diabetes, rheumatoid arthritis, multiple sclerosis, and autoimmune thyroiditis. Coexistence of multiple AD commonly is seen, and the combination of at least three ADs is called multiple autoimmune syndrome.[2] This is analogous to multiple endocrinopathies seen in autoimmune polyendocrinopathy syndrome, also called polyglandular autoimmune syndromes, that have identified genetic mutations.[3] These clusters of disorders and named syndromes help to correlate disorders together, and if recognized, may lead to additional testing for early diagnosis and treatment.

We agreed with the authors that the association of various HLA genes with AD bolsters our understanding of the nature of the autoimmune conditions and has implications for improved medical care in the future. Several studies have identified specific HLA gene variants associated with an increased risk of the particular disorders mentioned in our paper. For example, HLA DQB1*02 is associated with celiac disease, dermatitis herpetiformis, and dermatomyositis.[4-8] Additionally, HLA DRB1*04 is associated with celiac disease, dermatitis herpetiformis, dermatomyositis, and morphea.[4,9]

The authors discussed a potential situation in the future where each patient with an AD could receive HLA testing. The utility of such a practice is evident. The recognition of relative risk for associated AD based on the genetic profile would facilitate earlier diagnoses of concurrent diseases and subsequently improved disease management. We commend Boutrid and Rahmoune for their commentary on our article which contributes knowledge and insight on this subject. We recommend further studies to investigate the genetic associations between autoimmune diseases. As we discussed in our paper, the investigation of clusters of autoimmune conditions (possibly with the help of HLA typing) may lead to new associations and the discovery of therapeutic targets.

REFERENCES

1 Jibbe A, Neill BC, Tolkachjov SN. Concurrent dermatomyositis, celiac disease, and dermatitis herpetiformis in a patient with a history of morphea. Kans J Med 2021; 14:203-205. PMID: 34367491.
2 Cojocaru M, Cojocaru IM, Silosi I. Multiple autoimmune syndrome. Maedica 2010; 5(2):132-134. PMID: 21977137.
3 Sperling MA, Angelousi A, Yau M. Autoimmune Polyglandular Syndromes. [Updated 2021 Apr 10]. In: Feingold KR, Anawalt B, Boyce A, et al. [Eds.] Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000-. https://www.ncbi.nlm.nih.gov/books/NBK279152/. Accessed August 17, 2021.
4 Gao X, Han L, Yuan L, et al. HLA class II alleles may influence susceptibility to adult dermatomyositis and polymyositis in a Han Chinese population. BMC Dermatol 2014; 14:9. PMID: 24894810.
5 Sankari H, Hietikko M, Kurppa K, et al. Intestinal TG3- and TG2-specific plasma cell responses in dermatitis herpetiformis patients undergoing a gluten challenge. Nutrients 2020; 12(2):467.
6 Hall MA, Lanchbury JS, Bolsover WJ, Welsh KI, Ciclitira PJ. HLA association with dermatitis herpetiformis is accounted for by a cis or trans-associated DQ heterodimer. Gut 1991; 32(5):487-490. PMID: 1674926.
7 Bonciani D, Verdelli A, Bonciolini V, et al. Dermatitis herpetiformis: From the genetics to the development of skin lesions. Clin Dev Immunol 2012; 2012:239691. PMID: 22778763.
8 Spurkland A, Ingvarsson G, Falk ES, Knutsen I, Sollid LM, Thorsby E. Dermatitis herpetiformis and celiac disease are both primarily associated with the HLA-DQ (alpha 1*0501, beta 1*02) or the HLA-DQ (alpha 1*03, beta 1*0302) heterodimers. Tissue Antigens 1997; 49(1):29-34. PMID: 9027962.
9 Jacobe H, Ahn C, Arnett F, Reveille JD. Major histocompatibility complex class I and II alleles which confer susceptibility or protection against morphea: Findings from the Morphea in Adults and Children cohort. Arthritis Rheumatol 2014; 66(11):3170-3177. PMID: 25223600.

KANSAS JOURNAL of MEDICINE

KANSAS JOURNAL OF MEDICINE

VOLUME 14 • 2021

journals.ku.edu/kjm

Have a manuscript ready to publish?
Visit our website for instructions on submitting a manuscript.

Frontiers: University of Kansas Clinical and Translational Science Institute is a collaborating partner of the Kansas Journal of Medicine

Office of Research
1010 N. Kansas, Wichita, KS 67214
316-293-2617 • Email: kjm@kumc.edu

VOLUME 14 • 2021

WHAT'S INSIDE: ORIGINAL RESEARCH • CASE REPORT

KANSAS JOURNAL of MEDICINE

TABLE OF CONTENTS

KANSAS JOURNAL of MEDICINE

Creating and Implementing a Protocol for the Management of Patients in Skeletal Traction: A Quality Improvement Project

Justin A. Cline, M.D.[1,2], Jack A. Nolte, B.S.[1], Gregory M. Mendez, M.D.[1,2], Jordan T. Willis, M.D.[1,2], Andrew J. Bachinskas, M.D.[1,2], Clint L. Benge, M.D.[1,2], Bradley R. Dart, M.D.[1,2]

[1]University of Kansas School of Medicine-Wichita, Wichita, KS

[2]Department of Orthopaedics

Received Feb. 11, 2021; Accepted for publication May 28, 2021; Published online Oct. 14, 2021
https://doi.org/10.17161/kjm.vol14.15179

ABSTRACT

Introduction. Skeletal traction use generally has decreased over generations and is used most often for temporary fracture stabilization. Proper nursing management of patients in skeletal traction is crucial. A hospital protocol was created and implemented to educate and direct registered nurses (RNs) in the care of patients requiring skeletal traction.

Methods. A skeletal traction management protocol was drafted and implemented as hospital policy. Twenty-nine RNs from an orthopaedic unit at a level 1 trauma center attended a financially compensated, 45-minute, in-person, off-shift educational session. An anonymous pre-test utilizing a 5-point Likert scale was completed to assess RN knowledge and comfort regarding the following topics of traction care: pin care, manual traction, frame assembly, weight application and removal, skin evaluation, neurovascular checks, and reporting issues. The RNs were provided with a copy of the new hospital policy and key points were highlighted and demonstrated. After the demonstration, the RNs were given a post-test to assess their perceived knowledge and comfort with traction care.

Results. Statistically significant improvements in RN knowledge and comfort were seen in six of the seven evaluated topics. The greatest increase was seen in the manual traction topic. No significant change regarding neurovascular checks was observed with this topic having the highest pre-test scores.

Conclusions. A hospital protocol was created successfully and implemented that significantly improved the level of RN knowledge and comfort with the management of patients requiring skeletal traction. Future studies should assess the effectiveness of annual education regarding the traction policy. ***Kans J Med 2021;14:240-242***

INTRODUCTION

The use of skeletal traction devices to treat musculoskeletal injuries and deformities dates to the time of Hippocrates with the use of wooden rods, levers, and ropes to aid in the reduction of fractures.[1] Skeletal traction systems became more sophisticated over generations with important figures like Russell, Steinmann, and Kirschner credited for advancing skeletal traction systems in the early 1900s.[2] The standard medical treatment of femur fractures at that time was a combination of closed reduction, continuous traction, and splinting. Patients would spend weeks in the hospital requiring continuous labor-intensive care, often being left with poor outcomes and long-term complications.[3] Nursing knowledge and management of skeletal traction systems was crucial to achieve proper function and prevent complications.

With the advent of anesthesia, antisepsis, and skeletal imaging in the late 19th century, more fractures began to be treated with some form of internal fixation. Consequently, skeletal traction became more of a temporary measure used prior to definitive surgical fixation.[3-5] Although this led to a decrease in the amount of time patients spent in continuous traction, the care of a patient in traction remained a key skill set for nursing staff. The importance of these nursing skills was highlighted in 1974, when "The Do's and Don'ts of Traction Care" was published, illustrating the important concepts with which nurses managing traction systems must be familiar.[6]

The nursing management of patients in skeletal traction is a demanding task and it remains a crucial skill set for nurses caring for orthopaedic trauma patients.[7] In their practice of skeletal traction care, nurses continuously monitor the traction system to ensure proper use without harm to the patient. They perform traction pin site care to prevent infections and their diligent efforts to monitor neurovascular status and mobilize the patient are invaluable in preventing complications.[8]

Skeletal traction devices are utilized most often as a means of temporary stabilization until definitive surgical fixation can take place. As continuous skeletal traction use has declined in the modern orthopaedic era, nursing education regarding specific traction systems and the care of a patient in traction also has decreased.[7,9] At our level 1 trauma center, a gap was noticed in the education and training of nurses in this area. Our orthopaedic floor nurses and aides were uncomfortable managing temporary traction systems due to a lack of education regarding the systems. The purpose of this quality improvement project was to educate our nursing staff on the set-up and maintenance of commonly used traction systems and to create a well-defined protocol outlining the care responsibilities regarding patients in skeletal traction.

METHODS

An orthopaedic skeletal traction policy was drafted (see Appendix at website: journals.ku.edu/kjm) and approved by the associated hospital system. Registered nurses (RNs) from the orthopaedic unit at the level 1 trauma hospital were enrolled in a required 45-minute in-person educational session regarding the new policy. They were assigned to one of three sessions based on scheduling availability and they were compensated for their time. Assessment of the policy implementation and associated educational session was performed with a pre-test and post-test design to quantify improvements in comfort and knowledge.

Sessions were initiated with anonymous completion of the "Skeletal Traction Pre-Test" (see Appendix at website: journals.ku.edu/kjm) by all present nursing staff. After collection of the pre-tests, a 30-minute presentation using Microsoft® PowerPoint® and visual demonstrations regarding the newly implemented skeletal traction policy was given by two orthopaedic residents. A copy of the policy and a simplified checklist (see Appendix at website: journals.ku.edu/kjm) were distributed to all the participants prior to the presentation and all pertinent points were highlighted. A vacant hospital bed with appropriate components of a skeletal traction system allowed for the demonstration of proper assembly and manipulation of the system. Tips, tricks,

and pitfalls of all topics were included in the presentation. All questions from the RNs during and after the presentation were answered. A nursing supervisor was present during the session to facilitate and answer any questions within the scope of nursing. After the demonstration, each individual anonymously completed the "Skeletal Traction Post-Test" (see Appendix at website: journals.ku.edu/kjm). The content of the pre-test and post-test were identical and used as a learning assessment tool to allow for quantification and statistical analysis.

After the three sessions had been completed, matched pre-test and post-test data were compiled into Microsoft® Excel®. All questions from the survey, except for two, were in the form of a 5-point Likert scale. These Likert scale items investigated nurse "knowledge" and "comfort" regarding specific aspects of skeletal traction systems and the care of patients in skeletal traction. Nurse knowledge was self-reported with "1" representing "no knowledge" and "5" indicating "expert knowledge". Similarly, nurse comfort was self-reported with "1" representing feeling "distressed by the task" and "5" representing feeling "at ease or comfortable with the task". The topics included pin care, manual traction, frame assembly, weight hanging and removal, evaluation of the skin, neurovascular checks, and an established protocol for reporting issues. All knowledge item responses were totaled, as were all comfort items, and differences between pre- and post-test were calculated. Of the remaining questions, one asked for the year the RN started working for the hospital system, and the other was a "yes or no" response to assess perception of any existing orthopaedic traction policy. The year the nurse started working on this unit was used as a surrogate for years of orthopaedic nursing experience by subtracting their response from the year of this survey.

After consultation with a biostatistician, pre-test and post-test Likert data were compared using a two-tailed Wilcoxon signed-ranks test. A p value of 0.05 was accepted as a statistically significant result. The continuous variable, years of nursing experience, was assessed for normality using the Kolmogorov-Smirnov Test. Results showed normality could not be assumed. Therefore, bivariate associations between Likert scale items, knowledge difference and comfort difference, and years of experience were evaluated with Spearman's Rho. All statistical tests were conducted with Social Science Statistics, an online statistics calculator found at https://www.socscistatistics.com/tests/. At the recommendation of the consulting biostatistician, the revised Standards for Quality Improvement Reporting Excellence (SQUIRE 2.0) were used as a framework during the preparation of this manuscript.[10]

RESULTS

Participants in the educational sessions included 29 RNs. Nursing experience on this unit ranged from new-hire nurses to veteran nurses with 27 years of experience. The median nursing tenure was 3.0 years (0.5, 6.0). Pre-test results demonstrated that 11 of the 29 nurses (38%) were under the impression that there was a prior skeletal traction policy in place, when in fact there was not.

Table 1 summarizes survey responses, reported as medians and interquartile ranges. With the exceptions of neurovascular check for both knowledge and comfort, results for all pre- and post-test item differences were significant with p values being 0.004 or less. The lowest pre-test item observed was for frame assembly comfort for which the median response was 2.0 (2.0, 4.0). This response increased to 4.0 (4.0, 4.0) for the post-test, which was the largest score improvement among all items tested. Conversely, neurovascular check knowledge and comfort questions demonstrated the highest pre-test scores and the least improvement in post-test scores.

Table 1. Comparison of pre- and post-test responses by subject area.

Subject area	Pre-test[1]	Post-test[1]	p[2]
Knowledge			
Pin care	3.0 (3.0, 4.0)	4.0 (4.0, 5.0)	< 0.001
Manual traction	3.0 (2.0, 3.0)	4.0 (4.0, 5.0)	< 0.001
Frame assembly	3.0 (2.0, 4.0)	4.0 (4.0, 4.5)	< 0.001
Weight removal/application	3.0 (2.0, 4.0)	4.0 (4.0, 5.0)	< 0.001
Skin evaluation	4.0 (3.0, 4.5)	4.0 (4.0, 5.0)	0.004
Neurovascular check	4.0 (4.0, 5.0)	5.0 (4.0, 5.0)	0.754
Reporting issues	4.0 (3.0, 4.0)	5.0 (4.0, 5.0)	0.001
Total knowledge	25.0 (20.0, 26.0)	29.0 (27.5, 29.0)	< 0.001
Comfort			
Pin care	3.0 (2.5, 4.0)	4.0 (4.0, 5.0)	< 0.001
Manual traction	3.0 (2.0, 3.0)	4.0 (3.0, 4.5)	< 0.001
Frame assembly	2.0 (2.0, 4.0)	4.0 (4.0, 4.0)	< 0.001
Weight removal/application	3.0 (2.0, 4.0)	4.0 (4.0, 5.0)	< 0.001
Skin evaluation	4.0 (3.0, 4.0)	4.0 (4.0, 5.0)	0.001
Neurovascular check	4.0 (4.0, 5.0)	5.0 (4.0, 5.0)	0.508
Reporting issues	4.0 (3.0, 4.0)	5.0 (4.0, 5.0)	0.001
Total comfort	24.0 (19.5, 26.0)	28.0 (27.5, 33.0)	< 0.001

[1]Median (interquartile range)
[2]Results are from Wilcoxon signed-rank test

Correlation between years of experience and pre-test total scores showed a low-to-moderate linear association: rho = 0.451, p = 0.014 for knowledge pre-test total, and rho = 0.463, p = 0.011, for comfort pre-test total. However, this association appeared to decline somewhat for post-test responses: rho = 0.402, p = 0.031 for knowledge total, with rho = 0.335, p = 0.076, for comfort total. When comparing years of experience to change in total scores, no significant linear associations were observed: rho = 0.060, p = 0.756 for knowledge difference, with rho = 0.063, p = 0.747 for comfort difference.

DISCUSSION

As surgical techniques have improved, skeletal traction in orthopaedic traumatology has transitioned from a definitive treatment modality to a temporary stabilization method. Proper nursing care of patients in traction is labor-intensive and is vital in preventing complications that can arise from bed confinement and traction pin sites.[11] For this quality improvement project, the aim was to fill an important educational gap that was reported by the nursing staff, as well as to produce a well-defined protocol that could be implemented on a local and system-wide scale.

We successfully created and implemented a hospital protocol for orthopaedic trauma patients in skeletal traction devices. We also provided a nursing education session and checklist to aid in their labor-intensive care of these patients. All nurses who participated in our

program showed a significant increase in their knowledge of and comfort with traction systems and in the care for these patients.

This study was conducted over a limited time period in a frequently changing sample of orthopaedic floor nurses. The subjects completed the pre-exam, experienced the educational course, and subsequently completed the post-exam questionnaire in the same setting. As the orthopedic floor nursing staff was ever growing and changing, it would be reasonable to repeat this session annually or semi-annually in an attempt to improve nursing knowledge and comfort with skeletal traction and verify the results of this study.

From a systems perspective, this skeletal traction management protocol may be a good educational tool for all orthopaedic nurses within the health care system. Further improvement may be possible by administering this educational course to the nursing staff on an annual basis. Future directions to study the efficacy of this nursing education program may include the longitudinal assessment of patients being treated with skeletal traction to determine if there are improved clinical outcomes and fewer adverse effects of treatment.

REFERENCES

[1] Flynn S. History of traction. Int J Orthop Trauma Nurs 2018; 28:4-7. PMID: 29033230.
[2] Peltier LF. A brief history of traction. J Bone Joint Sug Am 1968; 50(8):1603-1617. PMID: 4881165.
[3] Hernigou P. History of external fixation for treatment of fractures. Int Orthop 2017; 41(4):845-853. PMID: 27853817.
[4] Winant EM. The use of skeletal traction in the treatment of fractures of the femur. J Bone Joint Surg Am 1949; 31A(1):87-93. PMID:18122878.
[5] Kennedy RH. Treatment of fractures of the shaft of the femur: An analysis of one hundred twenty cases. Ann Surg 1938; 107(3):419-437. PMID: 17857146.
[6] Synnestvedt N. The dos and don'ts of traction care. Nursing 1974; 4(11):35-41. PMID: 4139675.
[7] Santy-Tomlinson J. Traction survival skills. Int J Orthop Trauma Nurs 2017; 24:1-2. PMID: 27561248.
[8] Mellett S. Care of the orthopaedic patient with traction. Nurs Times 1998; 94(22):52-54. PMID: 9687734.
[9] Matullo KS, Gangavalli A, Nwachuku C. Review of lower extremity traction in current orthopaedic trauma. J Am Acad Orthop Surg 2016; 24(9):600-606. PMID: 27454023.
[10] Ogrinc G, Davies L, Goodman D, Batalden P, Davidoff F, Stevens D. SQUIRE 2.0 (Standards for QUality Improvement Reporting Excellence): revised publication guidelines from a detailed consensus process. BMJ Qual Saf 2016; 25(12):986-992. PMID: 26369893.
[11] Althausen PL, Hak DJ. Lower extremity traction pins: Indications, technique, and complications. Am J Orthop (Belle Mead NJ) 2002; 31(1):43-47. PMID: 11827229.

Keywords: traction, orthopedics, quality improvement, trauma center, policy

KANSAS JOURNAL of MEDICINE

Variability in Rehabilitation Protocols after Superior Labrum Anterior Posterior Surgical Repair

Christina A. Hermanns[1], Reed G. Coda[1], Sana Cheema[1], Matthew L. Vopat, M.D.[2], Armin Tarakemeh[3], Kyle Veazey, D.P.T.[4], John P. Schroeppel, M.D.[3], Scott Mullen, M.D.[3], Bryan G. Vopat, M.D.[3]

[1]University of Kansas School of Medicine, Kansas City, KS

[2]University of Kansas School of Medicine-Wichita, Wichita, KS, Department of Orthopaedics

[3]University of Kansas Medical Center, Kansas City, KS, Department of Orthopedic Surgery

[4]University of Kansas Medical Center, Kansas City, KS, Department of Physical Therapy

Received March 22, 2021; Accepted for publication June 4, 2021; Published online Oct. 14, 2021
https://doi.org/10.17161/kjm.vol14.15286

ABSTRACT

Introduction. Rehabilitation after a superior labral anterior posterior (SLAP) repair is an important aspect of patient outcomes; however, no standardized rehabilitation protocol has been defined. The purpose of this paper is to assess the variability of rehabilitation after a SLAP repair to understand the need for standardization to improve patient outcomes.

Methods. Protocols for SLAP repairs were collected through a search for Academic Orthopedic Programs and a general Google search using the terms "[Program Name (if applicable)] SLAP Repair Rehab Protocol". Protocols were compared by sling, range of motion (ROM), physical therapy, return to sport (RTS), return to throwing, and biceps engagement and tenodesis recommendations. Protocols for non-operative or generalized shoulders were excluded.

Results. Sixty protocols were included. A total of 61.7% (37/60) recommended a sling for four to six weeks and 90% (54/60) included a full ROM recommendation, but time was variable. There were different exercises recommended, but pendulum swings were recommended by 53% (32/60), submaximal isometrics by 55% (33/60), and scapular strengthening by 65% (39/60). Of the sixty protocols, 33% (20/60) recommended return to sports in 24 weeks and 38.3% (23/60) recommended allowing throwing in 16 weeks.

Conclusions. There was variability in protocols for SLAP repair, especially time until full ROM, RTS, and biceps strengthening. Time in sling and scapular strengthening were the least variable. A lack of specificity within protocols in what return to throwing meant for functional ability made it difficult to compare protocols. Considering the large number of orthopedic programs, a relatively small number had published protocols. Further studies are needed to evaluate a standardized post-operative rehabilitation for SLAP repairs to improve outcomes.
Kans J Med 2021;14:243-248

INTRODUCTION

Superior labral anterior to posterior (SLAP) tears are a major cause of shoulder dysfunction, often found in overhead and throwing athletes.[1] They occur due to tensile overload when eccentric bicep contractions lift the bicep tendon off of the glenoid insertion which leads to labral injuries.[2] Traditionally, the management of SLAP lesions begins with non-operative treatment for three to six months, which can include supervised rehabilitation, nonsteroidal anti-inflammatory drugs, and intra-articular corticosteroid injections to improve the function and pain in the joint.[3] If conservative management fails to regain the patient's full range of motion (ROM) or return to the desired level of activity, surgical intervention may be considered.

Surgical treatment varies depending on the type of SLAP tear and the repair can be done through a variety of techniques. SLAP repairs have shown variable rates of success, ranging from some studies citing good to excellent outcomes, while others report less favorable results.[4-10] A systematic review by Gorantla et al.[11] found good to excellent results ranged from 40 to 94% of patients in studies, return to previous activity level ranged from 20 to 94%, and return of overhead athletes to previous level ranged from 22 to 64%. If significant biceps tendon pathology is also present, biceps tenodesis also may be performed at the same time as the SLAP repair.[3] The presence of concomitant surgery such as this would be expected to lead to changes in rehabilitation.

Suggestions for rehabilitation after surgical repair of a SLAP lesion have been outlined in the literature, but has never been reviewed in protocols used in practice. Manske et al.[12] described the rehabilitation in five phases based on a literature review: protective phase from week zero to six, moderate protection phase from week 7 to 12, minimum protection phase from week 13 to 20, advanced strengthening phase from week 21 to 26, and return to activity from months six to nine. However, as stated previously, these are just suggestions and a study has yet to find a standardized agreement for post-operative rehabilitation of SLAP repairs.

The glenohumeral joint is one of the most mobile in the body; its stability comes from interactions between the joint, muscles, tendons, capsule, osseous configuration, and the glenoid labrum.[12] Therefore, successful outcomes depend directly on a balance between mobilizing the shoulder while strengthening the rotator cuff and scapulothoracic musculature. Thus, after a SLAP repair, the post-operative rehabilitation of the surrounding musculature is essential to the recovery of the functional joint. However, in a systematic review to analyze the current treatment practices for SLAP lesions, Kibler et al.[1] found that there was a severe lack in published guidelines on rehabilitation recommendations. Therefore, the purpose of this study is to analyze the variability of all published rehabilitation protocols for post-operative care after a SLAP repair. If SLAP repair protocols can be gathered and analyzed, then general conclusions and trends of SLAP rehabilitation can be summarized and areas lacking consensus can be identified.

METHODS

A list of all orthopedic academic residency programs was obtained using the Fellowship and Residency Electronic Interactive Database Access (FREIDA) program search tool through the American Medical Association. These programs framed the Google search for "[Program Name] SLAP repair rehab protocol" to find all published protocols from academic orthopedic programs within the U.S. Any private practice protocols found during this search also were collected. An additional general search for "SLAP repair rehab protocol" was conducted to

search for any additional protocols. Due to this being a review of currently published post-operative protocols, an Institutional Review Board (IRB) approval was not needed.

Non-operative care, generalized shoulder rehabilitation, and non-English protocols were excluded. Records that were excluded due to being too general meant that the protocol covered broad rehabilitation for most procedures done to the shoulder (e.g., rotator cuff repair, Bankart repair, and total shoulder arthroplasty). A flow chart of this process is shown in Figure 1.

Each protocol was compared for variability in the inclusion, exclusion, and timing of sling immobilization, ROM guidelines, physical therapy exercises, return to throwing, return to sport (RTS), biceps strengthening, and if the protocol included additional guidelines for the presence of concomitant biceps tenodesis. For specific physical therapy exercises, only exercises that were present in more than 10% of protocols were included in the results of this paper.

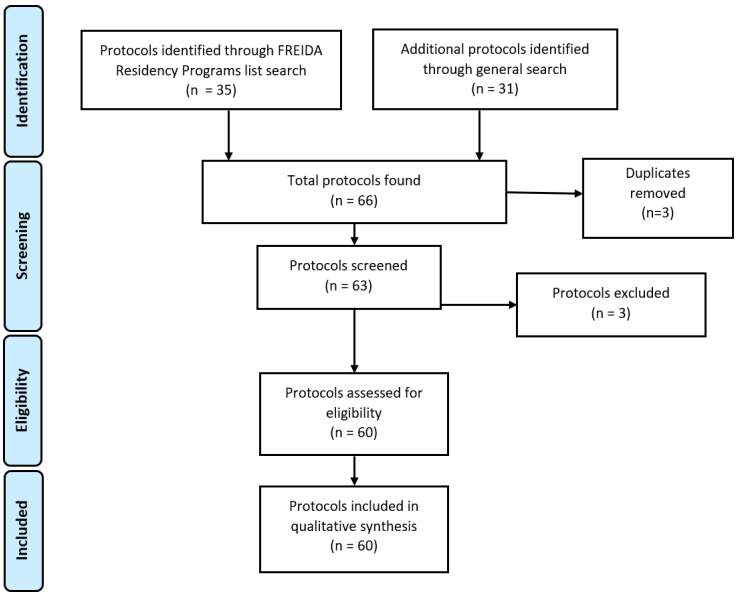


Figure 1. Flow diagram of methods of data collection used in this study.

RESULTS

A total of 60 protocols was included in this study. There were 27 U.S. academic residency programs that published SLAP rehabilitation protocols (14.7% of the 183 academic programs). Two academic programs had different published protocols from different physicians within their system; both were included in this study, making the total academic protocols used 29. There were 31 private practice protocols found and included in the study. A list of protocols included can be found in the Appendix.

Immobilization. A total of 97% (58/60) of protocols mentioned wearing a sling post-operatively (Figure 2). The majority of protocols (61.7%; 37/60) recommended that patients wear the sling until the four to six week timeframe, while 15% (9/60) recommended wearing the sling for two to four weeks, 13% (8/60) recommended for six or more weeks, and 6% (4/60) per surgeon's approval. However, 3% (2/60) did not specify the use of a sling post-operatively.

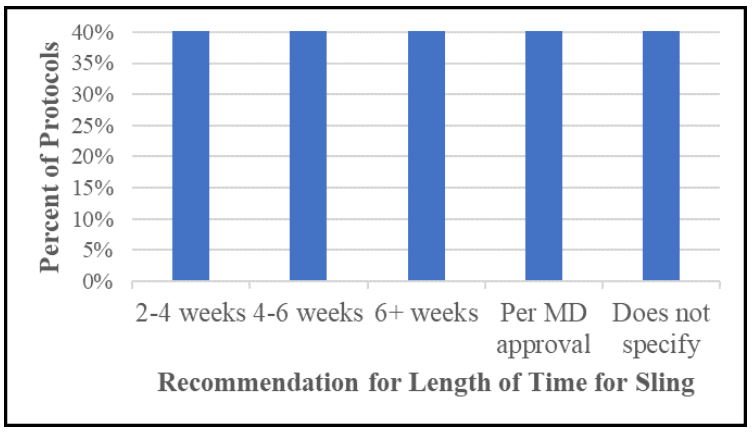


Figure 2. The length of time a protocol recommended wearing a sling and the number of protocols that recommended that timeframe.

Range of Motion (ROM). A total of 83% (50/60) of the protocols specified ROM recommendations starting at day or week zero, meaning immediately post-operatively (Figure 3). Sixty percent (36/60) of the protocols allowed passive ROM (PROM) immediately after surgery, while 8.3% (5/60) recommended no ROM, and 15% (9/60) allowed active assisted ROM (AAROM) of the shoulder. However, 16.7% (10/60) of the protocols did not specify post-operative ROM. Most patients were immobilized in a sling while instructed to do certain motion exercises such as pendulums, elbow, and wrist exercises which were counted as allowing passive or AAROM.

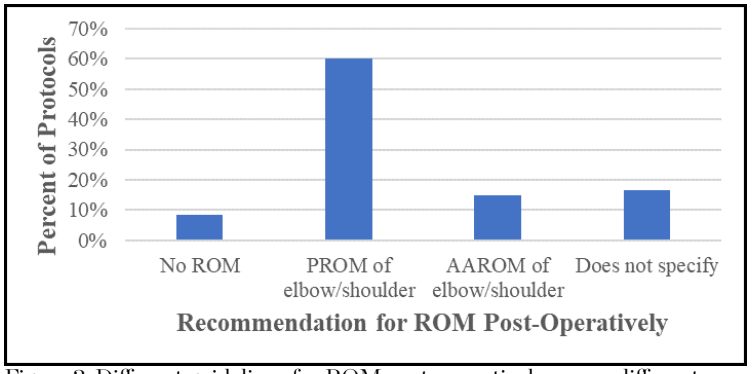


Figure 3. Different guidelines for ROM post-operatively across different protocols. (PROM: passive range of motion; AAROM: active assisted range of motion)

A total of 88.3% of protocols (53/60) included a guideline for full ROM at a certain week (Figure 4). One percent of protocols (1/60) left full ROM up to physician clearance, and 10% (6/60) did not specify full ROM. Of the protocols that specified a goal for full ROM, 18.3% (11/60) aimed for before eight weeks, 20% (12/60) for eight to ten weeks, 18.3% (11/60) for 10 to 12 weeks, 23% (14/60) for 12 to 14 weeks, 3% (2/60) for 14 to 16 weeks, and 5% (3/60) for 16+ weeks.

Exercises. A total of 65% (39/60) of protocols recommended scapular strengthening movements. Fifty-five percent (33/60) of protocols recommended using submaximal isometric exercises to strengthen the upper extremity. Fifty-three percent (32/60) of protocols recommended using pendulum swings, most of which recommended these begin relatively soon after surgery. All exercises that were mentioned in more than 10% of protocols can be seen in Figures 5 and 6.

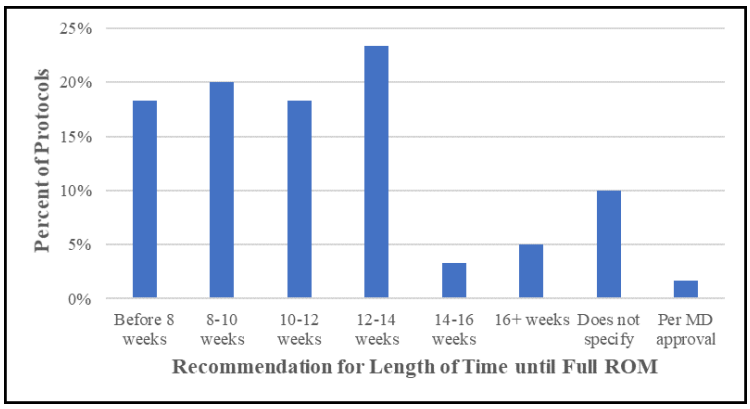


Figure 4. Time when full ROM of the shoulder is allowed and the percentage of protocols that recommended allowing full ROM at that time.

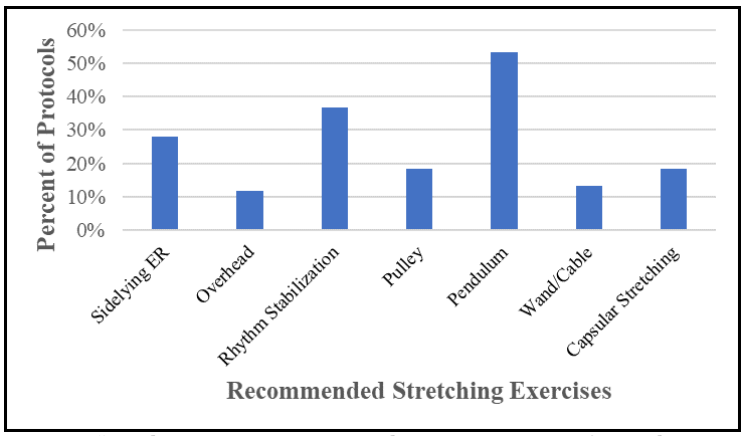


Figure 5. Stretching exercise recommendations to improve ROM and percentage of protocols that recommended that exercise. Only exercises that were present in more than 10% of protocols were included in this graph.

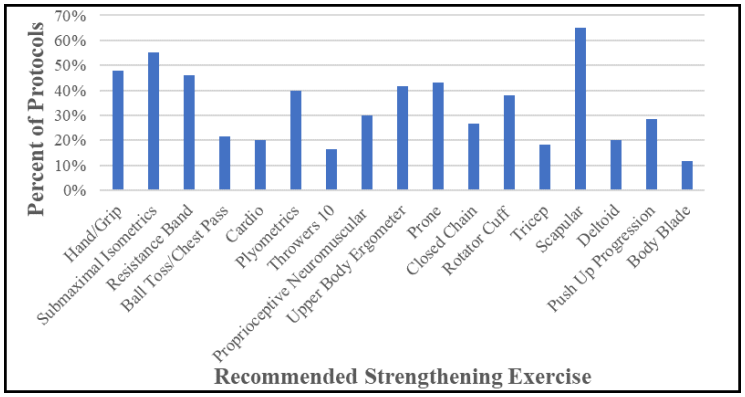


Figure 6. Specific physical therapy strengthening exercises and the percentage of protocols that included them. Only exercises that were present in more than 10% of protocols were included in this graph.

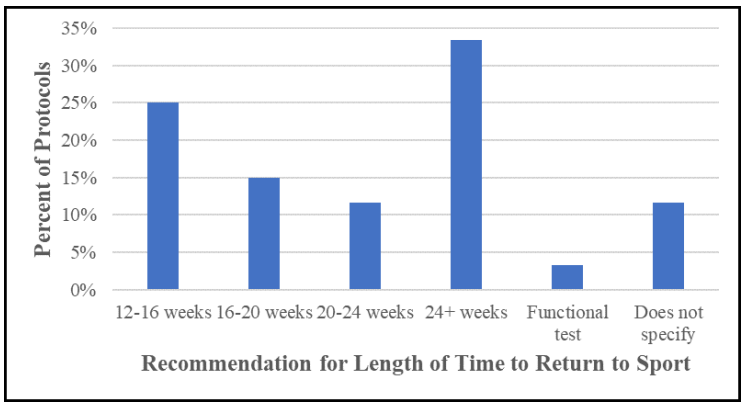


Figure 7. Percentage of protocols that included time of RTS post-operatively.

Return to Sport (RTS) and Throwing. A total of 88.3% (53/60) of protocols included RTS (Figure 7). The largest group of protocols, at 33% (20/60), recommended RTS at 24+ weeks, while 25% (15/60) recommended 12 to 16 weeks, 15% (9/60) recommended 16 to 20 weeks, and 11.6% (7/60) recommended 20 to 24 weeks. Only 3% (2/60) required functional testing, and 11.6% (7/60) did not specify time until RTS.

Of the 60 protocols, 68.3% (41/60) included return to throwing (Figure 8). Thirty-eight percent (23/60) of protocols allowed some sort of throwing motion to begin around 16 to 20 weeks. Ten percent (6/60) allowed return to throwing at 12 to 16 weeks, 10% (6/60) at 20 to 24 weeks, 8% (5/60) at 24+ weeks, 1.6% (1/60) per MD approval, and 31.6% (19/60) did not specify.

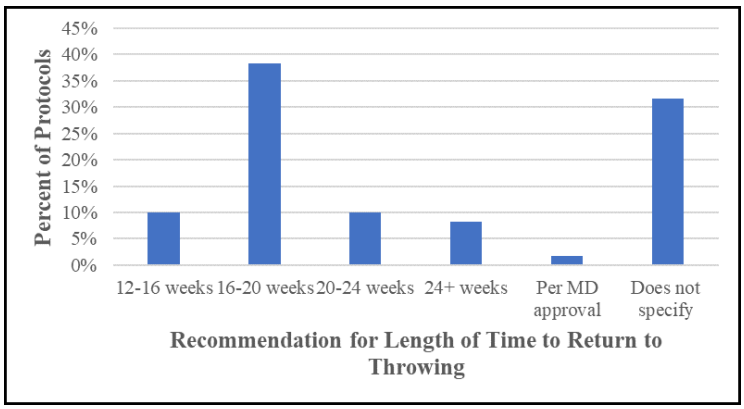


Figure 8. Percentage of protocols that included the initiation of throwing motions at different timeframes post-operatively.

Biceps Engagement and Tenodesis. A total of 36.7% (22/60) of the protocols specified a guideline for restraining biceps engagement until a certain time point after surgery to protect the healing process (Figure 9). Of those, 1.6% (1/60) allowed biceps engagement before six weeks, 18.3% (11/60) at six to eight weeks, 5% (3/60) at eight to ten weeks, and 11.6% (7/60) at 10 to 12 weeks. Sixty-three percent (38/60) of protocols did not specify a biceps engagement or strengthening timeframe.

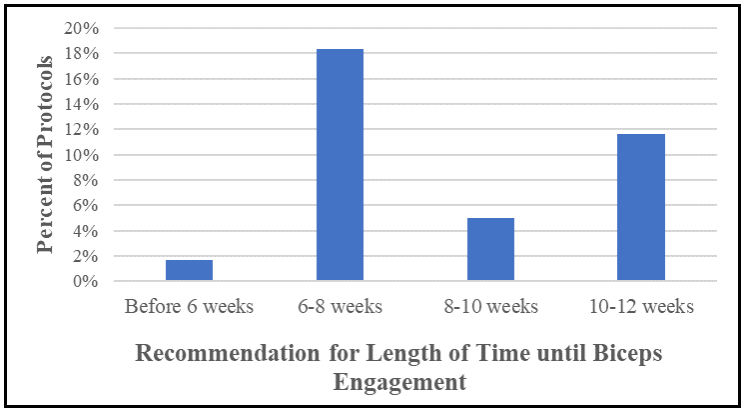


Figure 9. Percentage of protocols that recommend allowing bicep engagement at different time points post-operatively.

Only 6% (4/60) of protocols specified the presence of or differences in rehabilitation due to the addition of concomitant biceps tenodesis with a SLAP repair. Two of the four protocols did not change rehabilitation with the addition of biceps tenodesis. The other two added on the following precautions if biceps tenodesis also was performed: no resisted elbow flexion for six weeks or eight weeks depending on protocol, no resisted shoulder flexion for eight weeks, no lifting anything over one or two pounds for eight weeks, and avoiding 90/90 stretching with previous instability for six weeks.

DISCUSSION

This study illustrated a high variability across SLAP repair post-operative protocols, especially in terms of time to full ROM, rehabilitation exercises, RTS, and biceps engagement. There was also a lack of published protocols from most U.S. academic orthopedic programs, although a sizable number of protocols were found to be analyzed. There were some general trends in protocols, including most (77%, 46/60) protocols recommending four weeks of immobilization.

Most protocols (61.6%, 37/60) recommended wearing a sling for four to six weeks, but allowed some ROM after surgery. All protocols in which ROM was specified recommended immediate motion after surgery, although the recommendation on passive versus active assisted ROM was variable. In terms of time to full ROM, the variability in rehabilitation protocols matched up with a lack of guidelines in the literature.[1] Eighty percent (48/60) of protocols recommended a goal of full ROM by 12 weeks or sooner. The longest recommended timeframe for full ROM was 12 to 14 weeks with only 23.3% (14/60) of protocols. Based on the data in this study, if a patient had not achieved full ROM by around 12 weeks, they would be lagging based on protocol standards. However, Michener et al.[3] suggested that ROM should recover fully after a SLAP repair, but because the course of a patient's increasing motion ability throughout post-operative treatment has not been measured, the time to full ROM recommendations could not be determined. This may help explain the variability in time to full ROM seen across protocols.

The general guideline published by Michener et al.[3] outlines returning to an interval throwing program at approximately four months (16 weeks) post-operatively, and RTS at around six months (24 weeks) after surgery. These guidelines were created from a literature search of current research on how to optimally manage SLAP tears. The longest recommended RTS timeframe found in protocols was 24 weeks (33.3%, 20/60) and return to a throwing program was 16 to 20 weeks (38.3%, 23/60). This was consistent with the literature, but neither group of protocols that recommended these timeframes represented a majority of all protocols (33% and 38.3%, respectively). The variability in RTS may be due to the vague nature of what RTS meant in terms of activity and movement, as well as individualized rehabilitation programs and differences between patients. Thus, it may be more accurate to specify which sport they return to, such as contact (e.g., football and rugby) versus non-contact sports (e.g., tennis and golf), and their level of participation in that sport (e.g., professional or recreational). However, it would be beneficial to know a general timeline of how long it should take a patient to progress to a level of function that they will be ready to RTS so that a practitioner can have an idea of whether a patient is improving as expected. More studies are needed to evaluate what the exact RTS recommendation should be for each sport. Return to throwing may be similar as some protocols mentioned return to throwing as the beginning of a progression to previous throwing levels instead of an actual return to full throwing. In this study, the results regarding use of functional testing to clear an athlete for sports were limited in protocols. This was consistent with the lacking and limited evidence of upper extremity functional testing, especially in injured populations, in the current litereature.[13]

There is a need for an increased number of published protocols to standardize timelines with literature evidence as well as to detail specific guidelines to ensure that patients recover optimally from a SLAP repair, regardless of where their procedure was performed. Authors of this study acknowledge that SLAP injuries themselves include an array of injuries and each patient's expectations also may vary. Thus, this study illustrated that there is a need for additional studies to clinically look at standardized post-operative protocols for specific patients, sports, and severity of injury.

LIMITATIONS

This study was limited by the number of published protocols found and the lack of online publications of rehabilitation protocols by many institutions. Regarding categories such as exercise recommendations and ROM, there was a large variety of included recommendations and formatting of rehabilitation protocols, which made it difficult to consolidate all protocols. Many protocols were also vague in specifics of what motion they meant by recommending certain movements and exercises.

CONCLUSIONS

There was variability in protocols for SLAP repair, especially time until full ROM, RTS, and biceps strengthening. Time in sling and scapular strengthening were the least variable. A lack of specificity within protocols in what return to throwing meant for functional ability made it difficult to compare protocols. Considering the large number of orthopedic programs, a relatively small number had published protocols. Further studies are needed to evaluate a standardized post-operative rehabilitation for SLAP repairs to improve outcomes.

REFERENCES

[1] Kibler WB, Sciascia A. Current practice for the surgical treatment of SLAP lesions: A systematic review. Arthroscopy 2016; 32(4):669-683. PMID: 26553961.
[2] Beyzadeoglu T, Circi E. Superior labrum anterior posterior lesions and associated injuries: Return to play in elite athletes. Orthop J Sports Med 2015; 3(4):2325967115577359. PMID: 26665050;
[3] Michener LA, Abrams JS, Bliven KCH, et al. National Athletic Trainers' Association Position Statement: Evaluation, management, and outcomes of and return-to-play criteria for overhead athletes with superior labral anterior-posterior injuries. J Athl Train 2018; 53(3):209-229. PMID: 29624450.
[4] Steinhaus ME, Makhni EC, Lieber AC, et al. Variable reporting of functional outcomes and return to play in superior labrum anterior and posterior tear. J Shoulder Elbow Surg 2016; 25(11):1896-1905. PMID: 27497788.

[5] Denard PJ, Ladermann A, Burkhart SS. Long-term outcome after arthroscopic repair of type II SLAP lesions: Results according to age and workers' compensation status. Arthroscopy 2012; 28(4):451-457. PMID: 22264832.
[6] Schroder CP, Skare O, Gjengedal E, Uppheim G, Reikeras O, Brox JI. Long-term results after SLAP repair: A 5-year follow-up study of 107 patients with comparison of patients aged over and under 40 years. Arthroscopy 2012; 28(11):1601-1607. PMID: 22608888.
[7] Brockmeier SF, Voos JE, Williams RJ 3rd, Altchek DW, Cordasco FA, Allen AA. Outcomes after arthroscopic repair of type-II SLAP lesions. J Bone Joint Surg Am 2009; 91(7):1595-1603. PMID: 19571081.
[8] Cohen DB, Coleman S, Drakos MC, et al. Outcomes of isolated type II SLAP lesions treated with arthroscopic fixation using a bioabsorbable tack. Arthroscopy 2006; 22(2):136-142. PMID: 16458798.
[9] Douglas L, Whitaker J, Nyland J, et al. Return to play and performance perceptions of baseball players after isolated SLAP tear repair. Orthop J Sports Med 2019; 7(3):2325967119829486. PMID: 30873424.
[10] Gilliam BD, Douglas L, Fleisig GS, et al. Return to play and outcomes in baseball players after superior labral anterior-posterior repairs. Am J Sports Med 2018; 46(1):109-115. PMID: 28942657.
[11] Gorantla K, Gill C, Wright RW. The outcome of type II SLAP repair: A systematic review. Arthroscopy 2010; 26(4):537-545. PMID: 20362836.
[12] Manske R, Prohaska D. Superior labrum anterior to posterior (SLAP) rehabilitation in the overhead athlete. Phys Ther Sport 2010; 11(4):110-121. PMID: 21055704.
[13] Tarara DT, Fogaca LK, Taylor JB, Hegedus EJ. Clinician-friendly physical performance tests in athletes part 3: A systematic review of measurement properties and correlations to injury for tests in the upper extremity. Br J Sports Med 2016; 50(9):545-551. PMID: 26701926.

Keywords: shoulder injuries, orthopedic rehabilitation surgery, SLAP tears, range of motion, return to sport

APPENDIX

List of Protocols

Type of Institution	Protocols Obtained From:
U.S. Academic Orthopedic Program (n = 29)	Baylor School of Medicine Brigham and Women's Hospital Brown (University Orthopaedics) Case Medical Center University of Cincinnati Medical Center University of Colorado Columbia University University of Delaware Loma Linda Massachusetts General Hospital Orthopaedics RUSH - Midwest Orthopaedics Naval Medical Center NYU - Dr. Laith Jazrawi NYU - Dr. Eric Strauss Ohio State University Wexner Medical Center Saint Louis University St. Mary Hospital and Medical Center UCLA University of Florida UNM School of Medicine Keck School of Medicine of USC UT Health University of Wisconsin Sports Medicine Vanderbilt Sports Medicine Vanderbilt Sports Medicine Knee and Shoulder Center VCU Sports Medicine Clinic University of Virginia Health System University of Washington Medical Center William Beaumont Army Medical Center
Private Practice (n = 31)	Beaumont Hospital Summit Sports Medicine Boston Sports Medicine & Research Institute Center Sports Medicine and Orthopedics Central Texas Sports Medicine and Orthopedics Chicago Orthopaedics and Sports Medicine Elite Sports Medicine - Connecticut Children's Dr. Brian Cole Dr. Brian Waterman Crystal Clinic Orthopedic Center (partnership with Summa Health System) Dr. Geoffrey Abrams Dr. Richard F. Howard Dr. Steven Levin Ellis and Badenhausen Orthopaedics Gundersen Health System Highland Clinic Orthopaedics and Sports Medicine OrthoIndy - Bone, Joint, Spine, Muscle Jackson Orthopedic Specialists Trinity Clinic Orthopedic and Sports Medicine Keller Orthopedics Miami Institute for Joint Reconstruction Mountain Orthopaedics Raleigh Orthopaedic Clinic Ortho Illinois Ortho Carolina Ortho Virginia South Shore Hospital Southeast Georgia Health System St. Elizabeth Medical Center Tallgrass Orthopedic and Sports Medicine Western Orthopaedics

KANSAS JOURNAL of MEDICINE

Glycemic Control and Awareness of Insulin Therapy

Yegor Pashchenko, MS-4[1], Daniel H. Clausing, MS-4[1], Elizabeth Ablah, Ph.D., MPH[1,2], Hayrettin Okut, Ph.D.[1,2,3], Georges C. Elhomsy, M.D., FACP, FACE[1,4,5]
[1]University of Kansas School of Medicine-Wichita, Wichita, KS
[2]Department of Population Health
[3]Office of Research
[4]Department of Internal Medicine
[5]Wichita Diabetes and Endocrinology, Wichita, KS

Received March 24, 2021; Accepted for publication June 7, 2021; Published online Oct. 14, 2021
https://doi.org/10.17161/kjm.vol14.15298

ABSTRACT

Introduction. Glycemic control is associated with better health outcomes among patients with diabetes. No previous research has examined the relationship between knowledge of one's insulin dose and glycemic control. This study sought to determine if patients who accurately recalled their insulin dose achieved better glycemic control than patients who could not remember their dose.

Methods. Interviews were conducted with 106 patients. Data were collected during patients' appointments at two endocrinology clinics in Wichita, Kansas from May 29, 2018 to February 15, 2019. Adequate glycemic control was defined as an HbA1c of less than 7.5%. A multiple logistic regression model was developed to identify factors associated with glycemic control.

Results. Of the 109 patients asked to participate, 105 agreed to participate in the study. About half (45%, n = 48) were male. Patients' mean age was 50 years (SD = 17). Seventy-seven percent (n = 81) were overweight (body mass index (BMI) of 25 to 29.9) or obese (BMI >30). Patients who correctly stated their insulin dose had a mean Hemoglobin A1c (HbA1c) of 6.9% (SD = 0.98), whereas those who incorrectly stated their dose had a mean HbA1c of 9.5% (SD = 1.9; p <0.0001).

Conclusions. There was a significant relationship between knowledge of one's insulin dose and adequate glycemic control.

Kans J Med 2021;14:249-252

INTRODUCTION

Poor glycemic control is the leading cause of hospital admissions among patients with diabetes in the United States.[1] Adequate outpatient management could decrease the morbidity of the disease substantially. Previous work by Rohlfing et al.[2] established glycated hemoglobin (HbA1c) as an ideal marker of glycemic control among patients with diabetes. HbA1c became the gold-standard for glycemic monitoring because it has been correlated with adverse outcomes, especially microvascular complications.[3] Although the relationship between adverse health complications and elevated HbA1c is well-documented, and treatment protocols to maintain a normal blood glucose level are similarly well known, patients struggle to maintain adequate glycemic control.[4]

Although adequate glycemic control is elusive for many patients, improved glycemic control can occur when patients with diabetes receive information on the benefits of exercise, glucose monitoring, and a proper diet.[5] Greater patient knowledge about diabetes management can lead to better health outcomes.[6] Yet, no studies to date have documented whether knowledge of one's insulin dose was associated with one's glycemic control. The objective of this study was to determine if patients with insulin-dependent diabetes who could recall their insulin dose accurately achieve better glycemic control than patients who could not recall their dose.

METHODS

This study was approved by the University of Kansas Medical Center's Institutional Review Board.

Participants. Adults (18 years or older) with diagnosed insulin-dependent diabetes who agreed to participate in the study were interviewed at one of two endocrinology clinics in Wichita, Kansas. All participants were taking basal-bolus insulin for glucose control. The medical team consisted of one endocrinologist and two physician assistants. Patients were interviewed from May 29, 2018 through February 15, 2019. Patients who were non-verbal or missed their appointment were not eligible to participate in the study.

Instruments. A survey was administered via semi-structured, face-to-face interview. The 25-item interview tool included variables that can be associated with poor glycemic control, such as weekly time spent performing moderate physical activity,[7] body mass index (BMI),[8] depression diagnosis,[9] frequency of blood glucose checks,[10] and type of insurance.[11] Basic demographic information also was requested, including age, sex, race, ethnicity, and educational status. In addition to the interview, patient health information was abstracted from medical records. Abstracted data included number of missed clinic appointments in the last 12 months, number of other medications currently prescribed,[12] duration of insulin treatment, and their most recent HbA1c value.

Procedures. At the beginning of each appointment, eligible patients were asked if they were interested in participating. After obtaining consent, one researcher administered the interview. Each patient was interviewed in a private exam room. During the interview, the patient's responses were entered into a database. After the interview, the chart data were abstracted. The patient's prescribed insulin dose was abstracted from the chart and compared to the dose reported by the patient. If the self-reported and medical chart doses were the same, the patient was identified as having reported the insulin dose accurately.

Data Analysis. A sample size of 100 patients with diabetes (50 in each knowledge group) was determined to detect a difference of 40% between groups. Data were analyzed with SAS version 9.4 (2018, SAS Int. Inc., Cary, NC). Frequencies, proportions, means, and standard deviation were calculated. Likelihood ratio chi-square and Fisher's exact tests were used to test the significance of the association between two nominal or categorical variables. Prior to the main analyses, the Shapiro-Wilk test was conducted to test for normal distribution of outcomes. Hence, the rank transform approach to nonparametric methods was used as combination of PROC RANK and PROC GLM in SAS. Several longstanding nonparametric tests including Kruskal-Wallis are either exactly equivalent to rank transform tests or are nearly

equivalent to them. 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. Mann-Whitney U test and t-test methods were used to test the differences between means of two independent groups. Univariate linear regression models were used to test the association among HbA1c, number of minutes of moderate exercise each week and BMI. All statistical tests at $p \leq 0.05$ were considered significant.

RESULTS

Of the 109 patients who met inclusion criteria, 105 patients agreed to participate in the study (96%). The mean patient age was 50 years (SD = 17; Table 1). Most of the sample (80%, n = 84) reported they were Caucasian, and 53% percent of patients (n = 56) were female. Sixty-two percent of patients (n = 65) reported having completed high school or some college. Fifty-seven percent (n = 60) of patients reported being employed. Approximately three-quarters of patients (78%, n = 82) were overweight (BMI 25 - 29.9) or obese (BMI >30). Forty-five percent of patients (n = 48) had inadequate glycemic control (≥ 7.5%), with a mean HbA1c of 9.5% (SD = 1.9). More than half of patients (55%, n = 58) had adequate glycemic control, with a mean HbA1c of 6.6% (SD = 0.98).

Bivariate analysis suggested that patients who correctly stated their insulin dose had a mean HbA1c of 6.9% (SD = 0.98), whereas those who incorrectly stated their insulin dose had a mean HbA1c of 9.5% (SD = 1.9, $p < 0.0001$). A regression analysis was conducted to determine the association between the insulin dose error (the number of insulin units greater than or less than reported by the patient) and their resultant HbA1c. For every 29.5 units of insulin less than the patient's prescribed dose, the resultant HbA1c increased by one point. There also was a positive correlation between minutes of moderate physical activity per week and HbA1c ($p = 0.02$).

Although a greater insulin dose error and more minutes of exercise were the only variables associated with elevated HbA1c in bivariate analyses, a multivariate model suggested that other factors also contribute to an elevated HbA1c. Specifically, major depressive disorder ($p = 0.03$), elevated BMI ($p = 0.04$), type of insurance ($p < 0.0001$), increased duration of insulin use ($p = 0.01$), a greater number of missed clinic appointments ($p < 0.0001$), fewer glucose checks ($p = 0.026$), and a greater number of prescribed medications ($p = 0.02$) also were associated significantly with elevated HbA1c ($F(19,72) = 7.57$, $p < 0.0001$, $R2 = 0.666$). Patients who correctly stated their insulin dose, on average, had a 2.6% lower HbA1c value than patients who incorrectly stated their insulin dose, when accounting for these other variables in the model. Additionally, for every 100 minutes of moderate physical activity, patients were likely to have a 0.2% increase in HbA1c ($p = 0.02$).

Table 1. Patient characteristics.

Patient characteristics*	n (%)
Age	
18 - 25	8 (8)
26 - 35	23 (22)
36 - 45	13 (12)
46 - 55	13 (12)
56 - 65	23 (22)
66 - 75	20 (19)
76 or older	6 (6)
Education level	
High school or less	33 (31)
Some college	32 (30)
College degree	29 (28)
Graduate degree	10 (9)
Race and ethnicity	
Caucasian	89 (84)
African American	9 (6)
Hispanic	4 (4)
Asian American	5 (4)
Other or more than one race/ethnicity	3 (3)
Employment status	
Employed	53 (50)
Retired	28 (27)
Disabled	11 (10)
Unemployed	13 (12)
Student	4 (4)
Body Mass Index	
Normal weight	23 (17)
Overweight	27 (23)
Obese	55 (60)
Glycemic control	
Adequate glycemic control (HbA1c less than 7.5%)	59 (55)
Inadequate glycemic control (HbA1c greater than or equal to 7.5%)	47 (45)

*Some categories do not add up to the total number of participants because some patients left a survey question blank or selected multiple options (e.g., they were retired and disabled or Hispanic and African American).

DISCUSSION

The purpose of this study was to determine if there was an association between knowledge of one's insulin dose and glycemic control. The current study suggested that patients who accurately reported their insulin dose had a lower mean HbA1c than those who inaccurately reported their insulin dose. These findings are consistent with other studies that have examined the association between glycemic control and diabetes knowledge, such as proper diet,[5] diabetes medication awareness,[6] and symptom recognition of hypoglycemia.[13] This might suggest that increasing patient involvement in diabetes management can lead to better glycemic control. It was also possible that this association is a biproduct of healthier patients being more involved in their healthcare.

In the current study, patients who inaccurately reported their insulin dose were more likely to have a higher HbA1c. For every 30 units that patients under-reported their insulin dose, their HbA1c increased by one percentage point. This suggested that the magnitude of a patient's insulin dose error correlated to the amount that their HbA1c was elevated.

In addition to insulin dose error, the current study also suggested that other factors are associated with poor glycemic control: longer duration of insulin use, fewer daily blood glucose checks,[14] certain comorbid medical factors, and social factors. Another factor that varies between individuals with diabetes is the number of times they check their blood sugar every day. This study suggested that patients who check their glucose more often had lower HbA1c values. This was consistent with previous literature.[14]

In addition to diabetes management factors, other medical comorbidities, such as depression and high BMI, also were associated with increased HbA1c values. A study by Lustman et al.[15] suggested that untreated depression was associated with poor diabetes medication adherence. The current study suggested there was not an association between poor glycemic control and having a diagnosis of depression. One potential reason for this discrepancy was that all participants in the current study who reported a diagnosis of depression were being treated for their depression; however due to the limited scope of the survey, the extent, severity, and medication responsiveness of their depression was not taken into account during data analysis. Moreover, Brieler et al.[16] suggested that the use of antidepressants can improve glycemic control among depressed patients with diabetes. This might suggest that recognizing, diagnosing, and treating depression can lead to better glycemic control. Another interpretation might be that patients with good glycemic control are less likely to feel depressed.

The current study suggested that BMI was associated with glycemic control. This was inconsistent with a study by Koga et al.[17] that suggested no correlation with BMI. A 2001 study by Boulé et al.[8] suggested that greater physical activity lead to lower HbA1c levels, whereas the current study suggested an association between more time spent exercising and worse HbA1c values, which was also inconsistent with the findings of Boulé et al.[8] It is unclear why more exercise would be associated with poorer glycemic control. One explanation is that some of the participants in the present study were farmers or other outside laborers who had high levels of physical activity, but who also experienced barriers to accessing their insulin during the workday. Another explanation was that an unmeasured factor was associated with both increased activity and poorer glycemic control (e.g., type of exercise), and this factor was not assessed by the survey. Regardless of the reason for this odd relationship, medical comorbidities like depression status and BMI are important factors to explore in predicting glycemic control.

In addition to considering the role of medical comorbidities when determining the factors that affect glycemic control, the role of concomitant social factors also was important. One such social factor in the current study was missed clinic appointments. The study suggested that patients who miss six or more clinic appointments had higher HbA1c values than patients who missed one or fewer clinic appointments. This supported previous research by Karter et al.,[18] indicating that patients who missed more than 30% of their appointments had higher HbA1c values, with a mean HbA1c of 8.6%. Another social factor explored in the current study was the association between being a patient on Medicaid and glycemic control. The current study suggested no association, which was inconsistent with a study by Healy et al.[11] where being a Medicaid patient was associated with poor diabetes medication adherence. The lack of association between Medicaid status and poor glycemic control in the current study could be attributed to the small sample size and lack of variability in participants' insurance type.

Limitations. The current study had several potential limitations. As a cross-sectional study, a causal relationship between glycemic control and other factors could not be established. Due to time constraints, only five to ten minutes were dedicated to interviewing each patient; this limited the number of potential factors that could be surveyed regarding glycemic control. For example, it could have been useful to include data about patients' attitudes toward healthcare, literacy,[19] medical knowledge,[20] living situation,[21] relationship status, number of children, diet characteristics,[9] completing a depression screening, and access to transportation.[22] Additionally, the interview only included patients during an eight-month period; this may have resulted in a less representative sample due to seasonal variation. The studies smaller sample size created some oddities in generating a model. For example, individual categories within variables, such as five missed clinic appointments vs. four, were not necessarily correlated with different HbA1c values, but they were considered significant and included in the model if there were at least two distinct groups (e.g., six missed clinic appointments were associated with higher HbA1c than zero missed clinic appointments). Finally, the interview questions could be subject to recall bias and self-reporting bias which should be considered when interpreting the results of this study.

CONCLUSIONS

This study suggested that patients who have adequate knowledge of insulin dose have better glycemic control, when controlling for insulin dose, minutes of exercise, depression status, BMI, and type of insurance. Additionally, patients who reported higher levels of moderate physical activity had higher HbA1c values.

REFERENCES

[1] Centers for Disease Control and Prevention. National Diabetes Statistics Report, 2017. Atlanta, GA: Centers for Disease Control and Prevention, U.S. Dept of Health and Human Services; 2017.
[2] Rohlfing CL, Wiedmeyer HM, Little RR, England JD, Tennill A, Goldstein DE. Defining the relationship between plasma glucose and HbA1c: Analysis of glucose profiles and HbA1c in the Diabetes Control and Complications Trial. Diabetes Care 2002; 25(2):275-278. PMID: 11815495.
[3] Ohkubo Y, Kishikawa H, Araki E, et al. Intensive insulin therapy prevents the progression of diabetic microvascular complications in Japanese patients with non-insulin-dependent diabetes mellitus: A randomized prospective 6-year study. Diabetes Res Clin Pract 1995; 28(2):103-117. PMID: 7587918.
[4] Akbar DH, Al-Gamdi AA. Common causes of admission in diabetics. Saudi Med J 2000; 21(6):539-542. PMID: 11500701.
[5] Duncan I, Ahmed T, Li Q, et al. Assessing the value of the diabetes educator. Diabetes Educ 2011; 37(5):638-657. PMID: 21878591.
[6] Al-Qazaz HK, Sulaiman SA, Hassali MA, et al. Diabetes knowledge, medication adherence and glycemic control among patients with type 2 diabetes. Int J Clin Pharm 2011; 33(6):1028-1035. PMID: 22083724.

[7] Umpierre D, Ribeiro PA, Kramer CK, et al. Physical activity advice only or structured exercise training and association with HbA1c levels in type 2 diabetes: A systematic review and meta-analysis. JAMA 2011; 305(17):1790-1799. PMID: 21540423.
[8] Boulé NG, Haddad E, Kenny GP, Wells GA, Sigal RJ. Effects of exercise on glycemic control and body mass in type 2 diabetes mellitus: A meta-analysis of controlled clinical trials. JAMA 2001; 286(10):1218-1227. PMID: 11559268.
[9] Katon W, Russo J, Lin EH, et al. Diabetes and poor disease control: Is comorbid depression associated with poor medication adherence or lack of treatment intensification? Psychosom Med 2009; 71(9):965-972. PMID: 19834047.
[10] Buckingham B, Caswell K, Wilson DM. Real-time continuous glucose monitoring. Curr Opin Endocrinol Diabetes Obes 2007; 14(4):288-295. PMID: 17940454.
[11] Healy SJ, Black D, Harris C, Lorenz A, Dungan KM. Inpatient diabetes education is associated with less frequent hospital readmission among patients with poor glycemic control. Diabetes Care 2013; 36(10):2960-2967. PMID: 23835695.
[12] Balkrishnan, R. Predictors of medication adherence in the elderly. Clin Ther 1998; 20(4):764-771. PMID: 9737835.
[13] Angamo MT, Melese BH, Ayen WY. Determinants of glycemic control among insulin treated diabetic patients in Southwest Ethiopia: Hospital based cross sectional study. PLoS One 2013; 8(4):e61759. PMID: 23620789.
[14] Miller KM, Beck RW, Bergenstal RM, et al. Evidence of a strong association between frequency of self-monitoring of blood glucose and hemoglobin A1c levels in T1D exchange clinic registry participants. Diabetes Care 2013; 36(7):2009-2014. PMID: 23378621.
[15] Lustman PJ, Clouse RE. Depression in diabetic patients: The relationship between mood and glycemic control. J Diabetes Complications 2005; 19(2):113-122. PMID: 15745842.
[16] Brieler JA, Lustman PJ, Scherrer JF, Salas J, Schneider FD. Antidepressant medication use and glycaemic control in co-morbid type 2 diabetes and depression. Fam Pract 2016; 33(1):30-36. PMID: 26743722.
[17] Koga M, Matsumoto S, Saito H, Kasayama S. Body mass index negatively influences glycated albumin, but not glycated hemoglobin, in diabetic patients. Endocr J 2006; 53(3):387-391. PMID: 16717395.
[18] Karter AJ, Parker MM, Moffet HH, et al. Missed appointments and poor glycemic control: An opportunity to identify high-risk diabetic patients. Med Care 2004; 42(2):110-115. PMID: 14734947.
[19] Rothman R, Malone R, Bryant B, Horlen C, DeWalt D, Pignone M. The relationship between literacy and glycemic control in a diabetes disease-management program. Diabetes Educ 2004; 30(2):263-273. PMID: 15095516.
[20] Bains SS, Egede LE. Associations between health literacy, diabetes knowledge, self-care behaviors, and glycemic control in a low income population with type 2 diabetes. Diabetes Technol Ther 2011; 13(3):335-341. PMID: 21299402.
[21] Forsander GA, Sundelin J, Persson B. Influence of the initial management regimen and family social situation on glycemic control and medical care in children with type I diabetes mellitus. Acta Paediatr 2000; 89(12):1462-1468. PMID: 11195237.
[22] Syed ST, Gerber BS, Sharp LK. Traveling towards disease: Transportation barriers to health care access. J Community Health 2013; 38(5):976-993. PMID: 23543372.

Keywords: glycemic control, medication adherence, hemoglobin A1c, patient education, health knowledge

KANSAS JOURNAL of MEDICINE

Can You Repeat What You Just Said? A Case of Unusual Hearing Loss

John Netherton, D.O.[1,2], Rachna Kalia, M.D.[1,2], Kennedy Kirkpatrick, MBA, MS-3[1]
[1]University of Kansas School of Medicine-Wichita, Wichita, KS
[2]Department of Psychiatry and Behavioral Sciences

Received April 2, 2021; Accepted for publication May 19, 2021; Published online Oct. 14, 2021
https://doi.org/10.17161/kjm.vol14.15331

INTRODUCTION

Synthetic opioids are a class of psychoactive drugs that are designed to relieve pain. Synthetic opioids are constructed so that they have a base structure that is akin to naturally derived opiates and have similar effects.[1] These include drugs such as fentanyl, methadone, and tramadol among others. Synthetic opioids have significant advantages over naturally derived opiates including decreased cost, higher potency, and faster production speed, however they are not without drawbacks.

As of 2017, an estimated two out of three opioid-involved overdose deaths involved synthetic opioids.[2] While overdose deaths already were increasing in the months preceding the 2019 novel coronavirus disease (COVID-19) pandemic, the latest numbers suggested an acceleration of synthetic opioid overdose deaths during the pandemic.[3] The classic signs of opioid intoxication include altered mental status, decreased respiratory rate, decreased tidal volume, decreased bowel sounds, and miosis.

This report presents a rare case of a young patient who developed toxic leukoencephalopathy and transient hearing loss after a presumed synthetic opioid overdose. The purpose of this case report was to draw attention to these less common complications and provide a review of the literature.

CASE REPORT

A 19-year-old male with history of depression, substance use disorder, and a previous suicide attempt presented to the burn care unit by emergency medical services after being found at home with severely altered mentation, a scald wound on the chest, and possible aspiration pneumonia following ingestion of an unknown substance. On arrival, he was unresponsive and would not follow commands. He had crackles in the bases of the left lung with oxygen saturation at 74%, he was covered in urine and feces, and had an estimated total body surface area burn of 6% to the chest with blistering. Due to significant distress, the decision was made to intubate. Urine drug screen on admission was positive for cannabis, but negative for any other illicit substances. Other labs, including complete blood count, comprehensive metabolic panel, and urinalysis, were unremarkable except slightly elevated liver function tests and lactic acid. Initial computed tomography (CT) of the chest showed a focal consolidation in the left lower lobe consistent with aspiration pneumonia and initial head CT without contrast was negative for acute processes. An electrocardiogram showed sinus tachycardia. He remained intubated for the next 24 hours while his burns and aspiration pneumonia were addressed by surgical and pulmonary teams.

The patient's mother was contacted for past medical history and potential substances ingested. She was unaware of the patient's recent whereabouts or what he may have ingested prior to current admission. His mother reported an overdose four months prior on benzodiazepines, cocaine, marijuana, and a synthetic blend of fentanyl and oxycodone/acetaminophen. She stated that the patient was involved in "research chemicals" that he ordered over the internet. The patient's psychiatric history included one inpatient hospitalization for suicidal ideation as an adolescent, two previous suicide attempts, prior incarceration for battery of an officer, and a history of depression. At presentation, he was not being treated for his depression and had no outpatient psychiatrist.

Following extubation on the second day of admission, his mental status remained severely altered. He would open his eyes in response to sternal rub, but would not follow commands and remained nonverbal. He continued to be incontinent of urine and feces. On day three, the patient started communicating verbally; however, speech was nonsensical, and he appeared to be responding to internal stimuli. He was not oriented to time, place, or situation.

With lack of improvement of his mentation by day six, the psychiatry service was consulted. Their working diagnosis was unspecified schizophrenia spectrum and other specified disorder, synthetic opioid withdrawal psychosis, or anoxic brain injury due to toxic ingestion. Magnetic resonance imaging (MRI) of the brain was ordered to rule out underlying causes. In addition, risperidone 1 mg twice daily was started for agitation and aggression toward staff.

The MRI of the brain showed symmetric bilateral diffusion restriction with fluid-attenuated inversion recovery (FLAIR) abnormality in the centrum semiovale, occipital lobes, and splenium of corpus callosum consistent with anoxic brain injury. A lumbar puncture was negative. A diagnosis of toxic leukoencephalopathy likely caused by an overdose on a synthetic opioid such as fentanyl was established.

The patient's mentation improved over the following days. He was oriented to self and was able to feed himself for the first time. Physical therapy evaluation noted significant motor impairments with persistent posterior lean on standing, inability to take more than two steps with the help of a walker, and severe balance impairment with a left lower extremity limp.

On day 13, the patient was evaluated again by the psychiatry team. He was oriented to time, location, and person for the first time. He was able to maintain a full conversation and admitted to overdosing on a "pressed pill" at a friend's house before waking up in the hospital. He stated that these pills were manufactured in Mexico and often contain synthetic opioids. He reported that this was the first time when he could remember anything prior to his overdose. He was unaware how long he had been in the hospital.

Further evaluation revealed overall improvement in his cognition. However, the patient was noted to have significant hearing impairment, as evidenced by asking the care team to repeat multiple questions at a significantly louder volume. He was able to hear low pitch volumes better than higher pitch. This was noted to be a new deficit that he did not have prior to current hospitalization. The initial differential for his sudden bilateral hearing loss included encephalitis, tumor, noise-induced loss, autoimmune disorder, and/or ototoxic medications;

however, all were eventually ruled out. Extensive workup for encephalitis was unremarkable and a brain MRI did not show evidence of a tumor or autoimmune disease such as multiple sclerosis. There was no collateral information indicating he was exposed to a loud/long lasting noise and was not prescribed any medications that are typically ototoxic.

Two weeks following admission, risperidone was stopped. He no longer had visual or auditory hallucinations, was alert and oriented, and reported to be at his cognitive baseline. The remainder of patient's hospital course was complicated by fevers with left forearm cellulitis and thrombophlebitis which prolonged his hospital stay. The patient's hearing slowly improved. After stabilization and resolution of his infection, he was discharged home 24 days after admission.

DISCUSSION

Ototoxicity and toxic leukoencephalopathy are known, albeit rare, distinct complications of synthetic opiate overdose.[4-13] To our knowledge, this is the first reported case in which these complications have co-occurred.

Despite the prevalence of opioid abuse, a relatively small number of cases of leukoencephalopathy as the result of inhalation, intravenous injection, or ingestion of opioids have been reported.[4] The most studied cause of toxic leukoencephalopathy has been the inhalation of heroin, colloquially known as "chasing the dragon", and has been recognized since the 1980s. About 160 cases have been documented as of 2018. Cases also have been reported as a result of abusing other opioids such as methadone, oxycodone, and fentanyl, though these occurrences appear to be rarer.

Clinical features of toxic leukoencephalopathy secondary to opioid overdose may include the following: cerebellar dysfunction, confusion, motor restlessness, mutism, and/or incontinence, though no particular symptom is considered pathognomonic.[5-7] The pathogenesis of neurologic injury related to opioid overdose is unknown. One theory suggested mitochondrial dysfunction may play a role, as mitochondrial changes have been seen histologically on brain biopsy specimens.[5] The diagnosis should be suspected in patients with a history of substance abuse, especially a history of opioid abuse. A urine drug screen can be helpful, but synthetic opioids often do not show up on a standard screen; therefore, history that can be confirmed by reliable collateral sources can provide diagnostic value. Brain MRI commonly shows diffuse, symmetrical hyperintensities on T2 and FLAIR sequences, affecting primarily white matter, and the frontal lobes are relatively spared.[7] There was some evidence that giving antioxidants (e.g., CoQ, vitamin C, vitamin E) may result in varying levels of improvement, however, data are limited and had mixed results.[8-11]

Sensorineural hearing loss is another unusual complication of an opioid overdose.[12] Symptoms can be as mild as transient tinnitus and can be as severe as permanent deafness. It has been associated with several mu receptor agonists including heroin, oxycodone, methadone, and tramadol, among others. The exact mechanism of opioid induced hearing loss is unknown, but theories included ischemic cochlear injury secondary to artery vasospasm, abnormalities in transporting proteins and receptors, and/or direct effect of opioids on opioid receptors.[13]

The cochlea is a highly metabolic structure and distinctly susceptible to ischemia. Opioids stimulate production of endothelin-1, an endogenous vasoconstrictor, theoretically leading to vasospasm and cochlear ischemia.[13] The blood-labyrinth barrier maintains homeostasis of inner ear fluid. Variation in the permeability of this barrier between opioid users, according to differences in the molecular weight of opioid drugs, may contribute to opioid induced hearing loss. Finally, opioid receptors (mu, kappa, and delta) are present in the inner ear, although their physiologic role here is not determined. Endogenous opioid peptides likely play a role in auditory neuromodulation and it is possible that activation of these receptors by an exogenous opioid may impair this process and lead to hearing loss.

The clear majority of opioid associated hearing loss cases are bilateral.[12] In a retrospective review of 41 cases reporting hearing loss after opioid overdose in New Jersey Poison Center records over the last two decades, 12 reported complete deafness, 15 reported hypoacusis, 10 reported tinnitus, and 4 cases reported mixed auditory dysfunction. Of these cases, 7 reported complete resolution, 8 reported partial resolution, 4 reported no resolution, with the remainder not including resolution data. Another theoretical cause of hearing loss after opioid overdose was hypoxia related to respiratory suppression, however, 61% of the 41 cases reported no presence of a hypoxic event after their overdose, making this etiology less likely, or perhaps a secondary contributor to hearing loss.

This case revealed two rare complications of synthetic opioid overdose that should be kept on the differential diagnosis for patients who present with altered mental status, especially younger patients with history of substance abuse. This case was relevant given the increasing rate of synthetic opioid overdose in the United States and increasing need for awareness of potential overdose sequelae.[14] We propose that both toxic leukoencephalopathy and hearing loss likely were underreported phenomena associated with synthetic opioid overdose and suggest additional case reports and epidemiological studies be done to elicit their rate of incidence further.

REFERENCES

[1] [No authors] LiverTox: Clinical and Research Information on Drug-Induced Liver Injury [Internet]. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases, 2012. Opioids, November 24, 2020. PMID: 31643200.

[2] Wilson N, Kariisa M, Seth P, Smith H, Davis NL. Drug and opioid-involved overdose deaths - United States, 2017-2018. MMWR Morb Mortal Wkly Rep 2020; 69(11):290-297. PMID: 32191688.

[3] U.S. Centers for Disease and Control and Prevention. Overdose deaths accelerating during COVID-19. December 17, 2021. https://www.cdc.gov/media/releases/2020/p1218-overdose-deaths-covid-19.html. Accessed April 6, 2021.

[4] Alambyan V, Pace J, Miller B, et al. The emerging role of inhaled heroin in the opioid epidemic: A review. JAMA Neurol 2018; 75(11):1423-1434. PMID: 29987325.

[5] Wolters EC, van Wijngaarden GK, Stam FC, et al. Leucoencephalopathy after inhaling "heroin" pyrolysate. Lancet 1982; 2(8310):1233-1237. PMID: 6128545.

[6] Kriegstein AR, Shungu DC, Millar WS, et al. Leukoencephalopathy and raised brain lactate from heroin vapor inhalation ("chasing the dragon"). Neurology 1999; 53(8):1765-1773. PMID: 10563626.

[7] Long H, Deore K, Hoffman RS, Nelson LS. A fatal case of spongiform leukoencephalopathy linked to "chasing the dragon". J Toxicol Clin Toxicol 2003; 41(6):887-891. PMID: 14677803.
[8] Gacouin A, Lavoue S, Signouret T, et al. Reversible spongiform leucoencephalopathy after inhalation of heated heroin. Intensive Care Med 2003; 29(6):1012-1015. PMID: 12637976.
[9] Jee RC, Tsao WL, Shyu WC, et al. Heroin vapor inhalation-induced spongiform leukoencephalopathy. J Formos Med Assoc 2009; 108(6):518-522. PMID: 19515634.
[10] Cordova JP, Balan S, Romero J, et al. 'Chasing the dragon': New knowledge for an old practice. Am J Ther 2014; 21(1):52-55. PMID: 21519216.
[11] Bartlett E, Mikulis DJ. Chasing "chasing the dragon" with MRI: Leukoencephalopathy in drug abuse. Br J Radiol 2005; 78(935):997-1004. PMID: 16249600.
[12] Mozeika AM, Ruck BE, Nelson LS, Calello DP. Opioid-associated hearing loss: A 20-year review from the new jersey poison center. J Med Toxicol 2020; 16(4):416-422. PMID: 32468345.
[13] Oroei M, Peyvandi, AA, Mokhtarinejad F. Opioid drugs and sensorineural hearing loss. Addict Health 2018; 10(1):64-66. PMID: 30627386.
[14] Vivolo-Kanter AM, Seth P, Gladden M, et al. Vital signs: Trends in emergency department visits for suspected opioid overdoses – United States, July 2016-September 2017. MMWR Morb Mortal Wkly Rep 2018; 67(9):279-285. PMID: 29518069.

Keywords: opioids, synthetic drugs, hearing loss, leukoencephalopathy, drug overdose

KANSAS JOURNAL of MEDICINE

Incidental Detection of Massive Left Ventricular Calcification by Myocardial Perfusion Imaging: A Case of Imaging Illustrations

Robert T. Tung, M.D.[1], Johannes Heyns, M.D.[2]
Department of Veterans Affairs, Eastern Kansas HealthCare System, Topeka, KS
[1]Cardiology Section
[2]Radiology Department

Received April 10, 2021; Accepted for publication May 25, 2021; Published online Oct. 14, 2021
https://doi.org/10.17161/kjm.vol14.15359

INTRODUCTION

Cardiac calcification is not uncommon, but massive left ventricular (LV) myocardial calcification is rare and can be an uncommon cause of congestive heart failure.[1,2] Myocardial calcification can be associated with metastatic deposition, infarction, or other endocrine disorders.[3] It represents abnormal accumulation of calcium salts in the myocardium and includes two basic forms: dystrophic and metastatic.[4] Dystrophic calcification is more prevalent than metastatic calcification. It represents deposition of calcium salts in previously damaged tissue with normal calcium metabolism and is seen commonly in patients with myocardial infarction or primary myocardial disease.[5]

Metastatic calcification is caused by deposition of calcium salts in previously normal tissue due to disturbance in calcium or phosphorus metabolism seen in disorders like hyperparathyroidism, chronic renal disease, widespread bone destruction from metastases, or myeloma.[3] Depending on the degree of calcification, it can be detected by chest x-ray, echocardiography, or computed tomography (CT) of the chest. Chest CT is the optimal modality for identifying and characterizing myocardial calcifications as illustrated in this case. Myocardial calcification is an important marker of underlying pathology and knowledge of its potential etiology are important to provide accurate differential diagnosis.

We report a case with illustrated images of massive LV calcification detected incidentally during regadenoson single photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI) and confirmed by chest computed tomography.

CASE REPORT

This case was a 70-year-old patient who had a history of atrial fibrillation (AF), symptomatic of dyspnea and congestive heart failure. At that time, his AF was converted by electrical cardioversion with resolution of his symptoms. A year later, he presented with several months' history of progressive and marked dyspnea with minimal exertion. He underwent regadenoson MPI for cardiac evaluation. His electrocardiogram (ECG) showed a normal sinus rhythm, first degree atrioventricular (AV) block, and T wave inversion in the inferolateral leads suggestive of myocardial ischemia (Figure 1). His MPI demonstrated mildly decreased LV ejection fraction of 49% without evidence of myocardial ischemia or infarction; however, significant LV

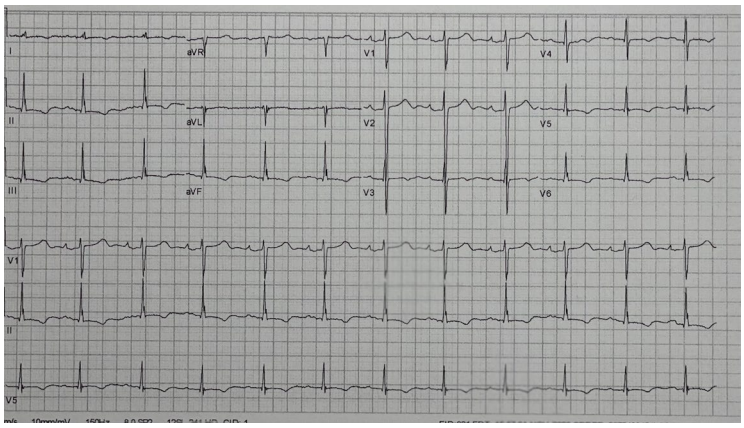


Figure 1. The electrocardiogram showed normal sinus rhythm, first-degree AV block, and T-wave inversion in the inferolateral leads.

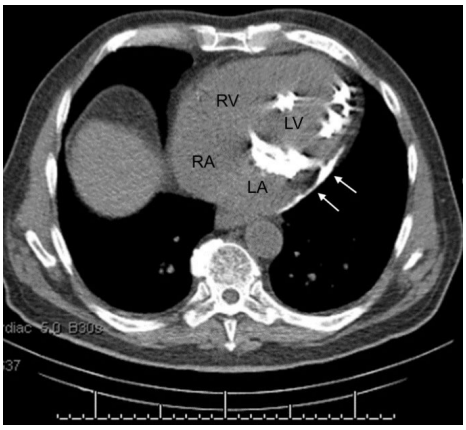


Figure 2. The axial image of low-dose CT during MPI demonstrated a significant amount of calcification at mitral valvular annulus, LV myocardium at septum, and free wall as well as pericardium (white arrows). [LA = left atrium; LV = left ventricle; RA = right atrium; LV = left ventricle.]

calcification (Figure 2) was observed on the low-dose CT used for attenuation correction during MPI.

Subsequently, other imaging studies, including chest x-ray, echocardiography, and chest CT, were obtained for further evaluation. The chest x-ray (Figure 3) showed extensive cardiac calcification, and the echocardiogram (Figure 4) revealed significant calcification of mitral valve annulus, LV septum, and mid free wall. However, his chest CT (Figure 5) revealed massive myocardial calcification involving only LV and its overlaying pericardium.

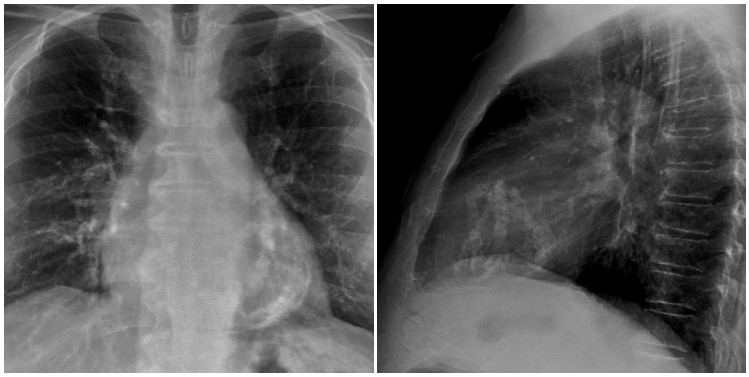


Figure 3. The posteroanterior (left) and lateral (right) views of patient's chest x-ray.

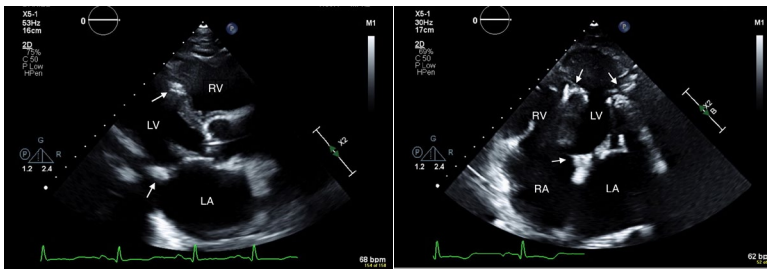


Figure 4. The parasternal view (left) and 4-chamber view of echocardiogram (right) showed calcification of mitral annulus, LV septum, and free wall (indicated by white arrows). [LA = left atrium; LV = left ventricle; RA = right atrium; LV = left ventricle.]

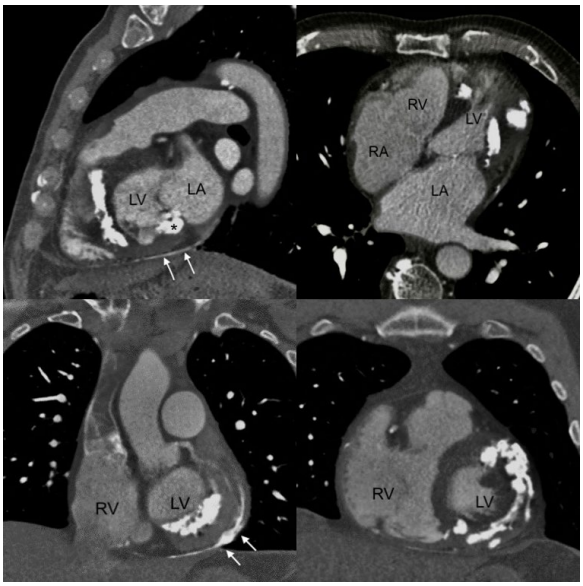


Figure 5. The sagittal (upper left), axial (upper right), and coronal images (lower left and right) of the chest CT demonstrated calcification of LV myocardium, mitral valve annulus (* in upper left image), and pericardium (white arrows in upper and lower left images) over the LV. [LA = left atrium; LV = left ventricle; RA = right atrium; LV = left ventricle.]

The patient had no past history of malignancy, endocrine disorder, tuberculosis, or recent traveling to other countries. Extensive laboratory evaluation revealed elevated NT-proB-type Natriuertic Peptide (1113.5 pg/ml; normal < 100 pg/ml) and C-reactive protein (1.21 mg/dL, normal < 0.5 mg/dL), but normal findings of complete blood count, basic chemistry profile, troponin-I, sedimentation rate, antinuclear antibody, antimitochondrial antibody, serum calcium/phosphate level, vitamin D level, and thyroid and parathyroid hormone levels. His echocardiography showed: (1) normal LV systolic function with calcification in the LV septum, mid free wall and mitral valve annulus (Figure 4) and normal right ventricular (RV) size and systolic function; (2) moderate bi-atrial enlargement with mild mitral regurgitation, moderate tricuspid regurgitation; and (3) severe pulmonary hypertension and LV diastolic dysfunction. Cardiac catheterization demonstrated: (1) no angiographic evidence of coronary artery disease; (2) moderately severe pulmonary hypertension with pulmonary artery systolic pressure of 67 mmHg; (3) elevated pulmonary capillary wedge pressure, measured at 28 mmHg; (4) elevated LV end-diastolic pressure, measured 29 mmHg; and (5) no evidence of ventricular interdependence on simultaneous LV/RV pressure measurement.

The final diagnosis was congestive diastolic heart failure due to massive LV myocardial calcification of unknown etiology. He was treated with aggressive diuresis and other guideline-driven medical therapy successfully with marked improvement of his dyspnea on exertion during follow-up.

DISCUSSION

The SPECT MPI is a well-established, commonly used diagnostic test for evaluation of coronary artery disease (CAD).[6] To improve quality of the study, low-resolution CT is used commonly for artifact attenuation and anatomical correction during SPECT MPI.[7] The low-resolution, unenhanced CT portion of the MPI is considered low-quality, therefore, labelled by manufacturers as "non-diagnostic". In many centers, it is used only for image fusion and attenuation correction, and these images are not reviewed routinely or reported by cardiologists. Incidental findings on low-resolution CT during cardiac MPI are frequent, but clinically significant ones are relatively infrequent[8]; however, some might be of important clinical significance.[8-11]

There is no uniform or consensus recommendations of reporting incidental findings during cardiac CT imaging. They ranged from no recommendations,[12,13] to optional,[14] to recommended or mandatory reporting.[15,16] This report described, for the first time, the incidental detection of a massive LV myocardial calcification by low-resolution CT during cardiac MPI in a patient presented as congestive heart failure. Therefore, it was appropriate and necessary to review low-resolution CT images during cardiac MPI to detect incidental but clinically significant findings.

CONCLUSIONS

Massive LV myocardial calcification is rare and can be an uncommon cause of congestive heart failure. To ensure high-quality patient care, low-resolution CT used for attenuation correction during cardiac MPI should be reviewed routinely and interpreted to identify incidental but clinically significant findings as demonstrated by this case.

REFERENCES

1 Torfs M, Salgado R, Van Herck P, Corthouts B, Robert D, Parizel PM. A curious case of acute myocardial calcifications. Circulation 2016; 133(10):e426-427. PMID:26951826.

2 El-Bialy A, Shenoda M, Saleh J, Tilkian A. Myocardial calcification as a rare cause of congestive heart failure: A case report. J Cardiovasc Pharmacol Ther 2005; 10(2):137-143. PMID: 15965565.

3 Nance JW, Crane GM, Halushka MK, Fishman EK, Zimmerman SL. Myocardial calcifications: Pathophysiology, etiologies, differential diagnoses, and imaging findings. J Cardiovasc Comput Tomogr 2015; 9(1);58-67. PMID: 25456525.

4 Perkins JA. Tissue renewal, regeneration, and repair. In: V Kumar, AK Abbas, N Fausto, JC Aster (Eds.). Robbins and Cotran Pathologic Basis of Disease. Eighth Edition. Philadelphia: WEB Saunders, 2010, pp 79-110. ISBN: 9781455753406.

5 Shackley BS, Nguyen TP, Shivkumar K, Finn PJ, Fishbein MC. Idiopathic massive myocardial calcification: A case report and review of the literature. Cardiovasc Pathol 2011; 20(2):e79-83. PMID:20598909.

6 Hendel RC, Berman DS, Di Carli MF, et al. ACCF/ASNC/ACR/AHA/ASE/SCCT/SCMR/ SNM 2009 appropriate use criteria for cardiac radionuclide imaging: A report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, the American Society of Nuclear Cardiology, the American College of Radiology, the American Heart Association, the American Society of Echocardiography, the Society of Cardiovascular Computed Tomography, the Society for Cardiovascular Magnetic Resonance, and the Society of Nuclear Medicine. Circulation 2009; 119(22):e561-587. PMID: 19451357.

[7] Hendel RC, Corbett JR, Cullom J, DePuey EG, Garcia EV, Bateman TM. The value and practice of attenuation correction for myocardial perfusion SPECT Imaging: A joint position statement from the American Society of Nuclear Cardiology and the Society of Nuclear Medicine. J Nucl Cardiol 2002; 9(1):135-143. PMID: 11845140.
[8] Coward J, Nightingale J, Hogg P. The clinical dilemma of incidental findings on the low-resolution CT images from SPECT/CT MPI studies. J Nucl Med Technol 2016; 44(3):167-172. PMID: 27102662.
[9] Osman MM, Cohade C, Fishman E, Wahl RL. Clinically significant incidental findings on the unenhanced CT portion of PET/CT studies: Frequency in 250 patients. J Nucl Med 2005; 46(8):1352-1355. PMID: 16085594.
[10] Goetze S, Pannu HK, Wahl RL. Clinically significant abnormal findings on the "non-diagnostic" CT portion of low-amperage-CT attenuation-corrected myocardial perfusion SPECT/CT studies. J Nucl Med 2006; 47(8):1312-1318. PMID: 16883011.
[11] Tung RT, Heyns J, Dryer L. Incidental findings of pulmonary and hilar malignancy by low-resolution computed tomography used in myocardial perfusion imaging. Fed Pract 2020; 37(Suppl 2):S27-21. PMID: 32952384.
[12] Holly TA, Abbott BG, Al-Mallah M, et al. Single photon-emission computed tomography. J Nucl Cardiol 2010; 17(5):941-973. PMID: 20552312.
[13] Dorbala S, Ananthasubramaniam K, Armstrong IS, et al. Single photon emission computed tomography (SPECT) myocardial perfusion imaging guidelines: Instrumentation, acquisition, processing, and interpretation. J Nucl Cardiol 2018; 25(5):1784-1846. PMID: 29802599.
[14] Tilkermeier P, Bourque J, Doukky R, Sanghani R, Weinberg R. ASNC imaging guidelines for nuclear cardiology procedures: Standardized reporting of nuclear cardiology procedures. J Nucl Cardiol 2017; 24(6):2064-2128. PMID: 28916938.
[15] Dorbala S, DiCarli MF, Delbeke D, et al. SNMMI/ASNC/SCCT guideline for cardiac SPECT/CT and PET/CT 1.0. J Nucl Med 2013; 54(8):1485-1507. PMID: 23781013.
[16] Dilsizian V, Bacharach SL, Beanlands RS, et al. ASNC imaging guidelines/SNMMI procedure standard for positron emission tomography (PET) nuclear cardiology procedures. J Nucl Cardiol 2016; 23(5):1187-1226. PMID: 27392702.

Keywords: vascular calcification, myocardial perfusion imaging, SPECT CT, incidental findings

KANSAS JOURNAL of MEDICINE

Hepatic Epithelioid Hemangioendothelioma Discovered Incidentally on Computerized Tomography

Luke Johnson, M.D.[1], Ryan Ford, M.D.[1], Paul A. Johnson, M.D.[2]
[1]University of Kansas School of Medicine-Wichita, Wichita, KS
Department of Internal Medicine
[2]University of Kansas School of Medicine-Salina, Salina, KS

Received March 30, 2021; Accepted for publication May 25, 2021; Published online Oct. 14, 2021
https://doi.org/10.17161/kjm.vol14.15326

INTRODUCTION

Hepatic epithelioid hemangioendothelioma (HEHE) is an exceedingly rare vascular tumor first described by Weiss and Enzinger in 1982.[1] It is a neoplasm that can arise in many different parts of the body, but most frequently involves the liver, lung, and bone.[2] It disproportionately affects females with a ratio of 3:2 and 50% of cases are discovered incidentally. HEHE is misidentified in up to 80% of cases. It can be mistaken for angiosarcoma, metastatic carcinoma, hepatocellular carcinoma (HCC), or cholangiocarcinoma. While 25 - 40% of patients are asymptomatic, common presenting symptoms include right upper-quadrant pain, fatigue, nausea, vomiting, weakness, ascites, anorexia, and weight loss.[2-4] Up to 37% of patients have distant metastases at the time of diagnosis and rapid progression is seen in up to 75% of cases where there are multifocal lesions.[2,4] This report presents a unique case of HEHE found incidentally on computerized tomography (CT).

CASE REPORT

A 40-year-old female with no known past medical history presented to the emergency department (ED) with fatigue and shortness of air. The shortness of air gradually worsened over a period of weeks until she presented to the ED. Her vitals were stable and she did not require supplemental oxygen. Chest x-ray was unremarkable for any acute cardiopulmonary process. CT angiography of the chest was negative for pulmonary embolism, but demonstrated a heterogenous liver with discrete hypoattenuating areas concerning for metastatic lesions.

Laboratory evaluation was unremarkable aside from a slight leukocytosis. Magnetic resonance imaging (MRI) of the abdomen days later demonstrated multiple peripheral, contrast enhancing 3-centimeter nodules throughout the liver (Figure 1). Subsequent needle biopsy showed scattered nodular fibrotic lesions, a small number of slightly atypical cells within the fibrotic tissue, and focal hepatic necrosis with scarring. Immunohistochemistry (IHC) stains were positive for CD34 and CAMTA-1. All of these findings were consistent with the diagnosis of hepatic epithelioid hemangioendothelioma. The patient was not a candidate for resection or ablation due to the amount and distribution of her lesions. She was referred for evaluation for liver transplantation and subsequently underwent orthotopic liver transplantation less than one year after diagnosis (Figure 2).

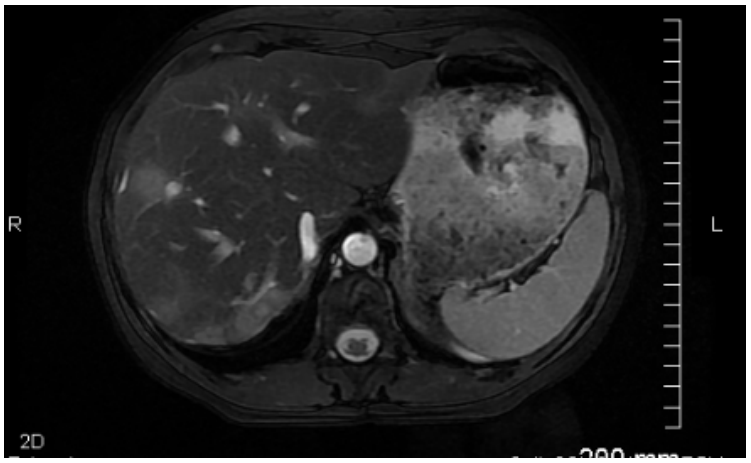


Figure 1. T2 sagittal view of MRI abdomen shows multiple, predominantly peripheral, contrast enhancing nodules in the liver.

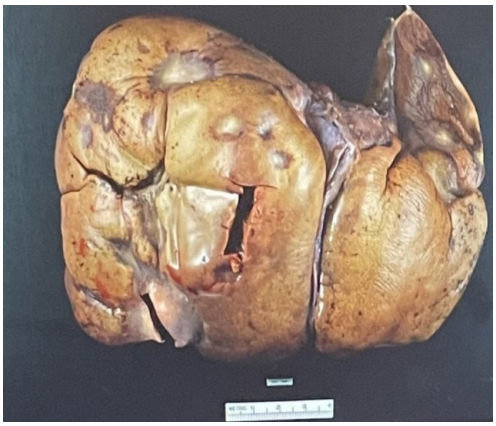


Figure 2. Gross pathology of this patient's liver status-post liver transplantation. [Courtesy of: Mayo Clinic Liver Transplant Program]

DISCUSSION

HEHE can be differentiated from common mimickers by a combination of histology, IHC, and molecular characteristics. Initial diagnostic workup includes CT, MRI, or ultrasound. Lesions appear hypoechoic on ultrasound.[3] Non-contrast CT shows nodules with a hypodense appearance, while CT with contrast shows small lesions (< 2 cm) with homogenous enhancement and large lesions with peripheral or heterogenous enhancement.[2] Lesions appear hypointense on T1 weighted MRI and hyperintense on T2 weighted MRI.

HEHE lesions vary in size from less than one centimeter to more than ten centimeters in diameter and over 75% of cases have lesions in both liver lobes.[5] When presenting as multifocal, there is a peripheral or subcapsular growth pattern. Lesions also can differ based on disease progression with late disease showing a pattern of coalescence.[2]

Histologically, HEHE manifests as nests and cords of spindle to epithelioid cells with mild to moderate atypia, abundant pale to eosinophilic cytoplasm, indistinct cell boundaries, and intracytoplasmic vacuolations in a fibromyxoid stroma.[4] Older lesions appear sclerotic, calcified, or necrosed.[2]

IHC stained HEHE cell tissues typically are positive for CD34 (94% of cases), CD31 (86% of cases), and Factor VIIIa (99% of cases).[2]

Other positive staining factors include vimentin, type IV collagen, and D2-40 which helps to differentiate from other angiomatous lesions. IHC staining of common mimickers is as follows: (1) metastatic carcinoma does not stain positive for any of the above markers; (2) cholangiocarcinoma does not stain positive for any of the above markers; (3) HCC is negative for the above factors except for CD34 following sinusoidal capillarization; and (4) angiosarcoma stains positive for CD34, CD31, and Factor VIIIa while losing expression of these markers upon undergoing dedifferentiation. In 86% of cases, molecular translocation results in *WWTR1-CAMTA1* fusion.[2] Fine needle aspiration and small biopsy is an effective method for diagnosis; however, it holds a 10% false negative rate.[5]

There is no consensus for a gold standard of treatment, however, there is agreement that treatment should consider the involvement of both liver lobes, lesion size/number, and disease progression.[4] Treatment includes radiation, chemotherapy, liver resection, and liver transplant. While agents targeting anti-angiogenesis have had the most success in clinical trials, common chemotherapeutics include doxorubicin, vincristine, interferon-alpha, 5-fluorouracil, thalidomide, and monoclonal antibodies against vascular endothelial growth factor. Characteristics most favorable to liver resection included: less than 10 lesions, tumor diameter of less than 10 cm, less than four extrahepatic lesions, and single lobe involvement. Liver transplant is the treatment of choice for diffuse, multifocal lesions, and rapidly progressive disease.[4,6]

Patients with radiologically stable disease should undergo an initial three-month surveillance period with subsequent treatment for tumors rapidly enlarging at a rate of more than three centimeters in three months.[6] Survival rates are liver transplant (54.5%), liver resection (75%), chemotherapy/radiation (30%), and surveillance without follow-up intervention (4.5%).[2]

A poor prognosis is associated with a tumor size of more than 10 cm in diameter in patients who received liver resection versus liver transplant.[6] Increased uptake by 18F-fluorodeoxyglucose PET/CT imaging following anti-angiogenic chemotherapy signifies a worse clinical outcome. Risk factors for recurrence are macrovascular infiltration, time to liver transplant of at least 120 days, and hilar lymph node infiltration.[5] A scoring system assessing the risk of HEHE recurrence following liver transplant stated that the five-year disease-free survival rate was significantly higher in patients with a lower score of 2 or less (93.9%) versus a higher score of 6 or more (38.5%).[5]

HEHE is a rare malignancy that often presents with nonspecific clinical symptoms, nonspecific labs, and imaging that easily misdirects. It carries a high misdiagnosis rate and an even worse clinical outcome when treated improperly. It has potential to progress rapidly and there was no consensus for treatment. It is difficult to overstate the need for a multifaceted diagnostic approach that considers imaging, histology, immunohistochemistry, and molecular markers.

REFERENCES

[1] Weiss SW, Enzinger FM. Epithelioid hemangioendothelioma: A vascular tumor often mistaken for a carcinoma. Cancer 1982; 50(5):970-981. PMID: 7093931.
[2] Studer LL, Selby DM. Hepatic epithelioid hemangioendothelioma. Arch Pathol Lab Med 2018; 142(2):263-267. PMID: 29372848.
[3] Llueca A, Piquer D, Maazouzi Y, et al. Hepatic epithelioid hemangioendothelioma: A great mimicker. Int J Surg Case Rep 2018; 53:25-28. PMID: 30366173.
[4] Din N, Rahim S, Asghari T, Abdul-Ghafar J, Ahmad Z. Hepatic epithelioid hemangioendothelioma: Case series of a rare vascular tumor mimicking metastases. Diagn Pathol 2020; 15(1):120. PMID: 32977811.
[5] Kou K, Chen Y, Zhou J, Sun X, Sun D, Li S, Lv G. Hepatic epithelioid hemangioendothelioma: Update on diagnosis and therapy. World J Clin Cases 2020; 8(18):3978-3987. PMID: 33024754.
[6] Cao L, Hong J, Zhou L, Ye Y, Liu Y, Yu J, Zheng S. Selection of treatment for hepatic epithelioid hemangioendothelioma: A single-center experience. World J Surg Oncol 2019; 17(1):183. PMID: 31699108.

Keywords: epithelioid hemangioendothelioma, liver neoplasms, local neoplasm recurrence, treatment, diagnosis

KANSAS JOURNAL of MEDICINE

A Case of Pediatric Catatonia

Susan Ciccolari Micaldi, M.D., M.A., Christopher W. Dao, D.O., Dannette N. Napier, D.O., Joycy Samson, M.D.
University of Kansas School of Medicine-Wichita, Wichita, KS
Department of Psychiatry and Behavioral Sciences

Received Dec. 9, 2020; Accepted for publication July 6, 2021; Published online Oct. 14, 2021
https://doi.org/10.17161/kjm.vol14.14985

INTRODUCTION

Karl Ludwig Kahlbaum was the first to describe catatonia in 1868.[1] Although it has been described as an adult condition, Kahlbaum observed that the majority of the adults had their first symptoms of catatonia in childhood, and described catatonia as a syndrome of abnormal motor function.[2] Catatonic symptoms can be divided into motor (e.g., posturing, catalepsy, waxy flexibility), behavioral (e.g., negativism, mutism), affective (e.g., uncontrollable emotional reactions, withdrawal), and regressive (e.g., enuresis).

Pediatric catatonia usually presents acutely, but its onset can be insidious.[2] Duration can be brief or chronic for weeks or months. Though schizophrenia was believed, for a long time, to be the major cause of catatonia, the syndrome is now known to occur in a wide range of psychiatric and medical conditions.[3] Catatonia in children and adolescents occur most commonly in the context of the schizophrenia spectrum followed by affective disorders. Trauma also plays an important role in the onset of catatonic presentations in youths.[2]

In addition to psychiatric diagnoses, in more than 20% of cases of pediatric catatonia, an underlying medical condition could be identified.[2] Systemic autoimmune disorders, such as systemic lupus erythematosus and autoimmune encephalitis, are the two common classes of autoimmune disorders associated with catatonia.

The most common autoimmune encephalitis underlying catatonia are anti-NMDA-receptor (anti-NMDAR) encephalitis and pediatric autoimmune neuropsychiatric disorders associated with streptococcal infection (PANDAS).[2] Various drugs or toxic compounds can cause catatonia in youths, including steroids, lithium, phencyclidine, and cannabis abuse. Furthermore, catatonia can be associated with metabolic and genetic conditions such as Wilson's disease and porphyria.

Regarding treatment, benzodiazepines and, in particular, lorazepam, are the first line treatment for pediatric catatonia.[2] At times, dosing in the range of 15 mg daily is necessary for resolution of symptoms. Lorazepam treatment needs to be maintained until the underlying cause of catatonia is found and appropriately treated.

Antipsychotic medications, specifically first-generation, worsen catatonia especially in the acute phase.[2] However, neuroleptics can be used with caution to treat the underlying psychiatric disorders when catatonia symptoms are stabilized. Electroconvulsive therapy should be considered when catatonia does not respond to benzodiazepine treatment.[2]

CASE REPORT

This case concerned a young patient who, while admitted to our psychiatric adolescent unit, developed symptoms of catatonia in the context of a difficult-to-reach diagnosis due to the patient's lack of verbal communication and detailed prior history. The patient was a 16-year-old African American female in state custody with a complicated and somewhat uncertain psychiatric, psychosocial, medical, and family history. She was transferred from a neighboring hospital's pediatric intensive care unit (PICU) to the adolescent inpatient psychiatric unit, after medical stabilization, following a witnessed intentional overdose at her foster mother's home on 82 tablets of her prescribed clonidine 0.1 mg.

The note from the emergency department reported the patient as having a history of schizophrenia and bipolar disorder with multiple past inpatient psychiatric hospitalizations. The patient's home medications were clonidine 0.1 mg three times a day (TID) and risperidone 2 mg two times a day (BID). During her three-day PICU course, she was reported to be uncooperative, primarily nonverbal, with psychomotor retardation, and with an episode of enuresis on the hospital floor. Once deemed medically stable, she was transferred to the psychiatric unit on day four of her medical admission.

According to the case manager, the patient's history was not clear. Her mother had died of cancer six years prior, while she was living with her. The patient also had reported that when she was seven years old and in out-of-state foster care, she was abused physically and sexually by the foster family and would attempt suicide if she were to return to that home. After her mother's untimely death, the patient went to live with her father and two half-sisters, one of which reportedly suffered from schizophrenia. School records indicated that she was a straight-A student until halfway through ninth grade, when she was first psychiatrically hospitalized.

Six months before coming to our unit, the patient's father sent her to live with his friends since she required a high level of care. While staying at the friends' house, she had an episode of acute agitation and assaulted responding law enforcement officers. She was re-hospitalized and taken into state custody.

According to the patient's foster mother, she had lived with her on two occasions. The first time she resided with the foster mother for a few weeks right after entering the foster system (about six months prior to admission to our unit). The medications she was prescribed at that time were unknown. According to the foster mother, during the patient's first stay with her, she was talkative, and she would laugh and joke with the foster mother and other girls in the home. However, the mother had installed nanny cameras throughout the house, and the patient was observed debating with her father over the phone when alone. The patient was removed from the home after assaulting another female foster child residing with the same foster mother.

The second time the patient resided with the foster mother was after discharge from a later psychiatric hospitalization, just five days prior to her admission to our hospital. In contrast to her previous stay, upon return to the foster mother's place, the patient was primarily nonverbal, but was taking care of basic needs. However, this situation dramatically worsened after she resumed contact with her father. Afterwards, she began refusing her medications (risperidone 2 mg BID and clonidine 0.1 mg TID).

The week prior to admission to our unit, the patient was described by the foster mother as isolated, pacing, anxious, depressed, and was seen talking to herself. On the day of admission to the PICU, she grabbed the bottle of clonidine from the foster mother's hands and quickly ingested all the pills in the bottle (82 tablets).

Past Psychiatric History. Based on the case manager's report and review of documents from prior hospitalizations, about two years before the patient was admitted to our unit, she began demonstrating aggressive behavior at home at the same time her half-sister with schizophrenia moved in with the family. Six months before her first psychiatric hospitalization (18 months before she was admitted to our unit), her primary care provider (PCP) found a moderate degree of depression and anxiety on Patient Health Questionnaire-9 and General Anxiety Disorder-7 evaluations (sleep and psychomotor symptoms were the most severe). She was diagnosed with Adjustment Disorder with mixed anxiety and depression.

One week prior to her first hospitalization, she reported to her PCP severe anxiety and depression with additional symptoms of fatigue and social withdrawal. She also related that dizziness had begun eight months prior, and that bilateral lower extremities joint pain and numbness had begun three months prior. She also requested contraception and was given a medroxyprogesterone acetate injection. She had no history of psychotic symptoms up to this point.

One week later, following a physical altercation with her father, the patient was admitted for her first psychiatric hospitalization with suicidal/homicidal ideation and psychosis, including auditory and visual hallucinations. Police reports indicated that the patient accused her father of sexually molesting her. She was acting "strange and nonsensical", and was agitated, self-harming, and assaultive with police. The patient made and retracted allegations of sexual assault by her father multiple times throughout that stay. A urine drug screen was positive for methamphetamine.

Throughout that admission, the patient was assaultive towards staff, sexually inappropriate, had enuresis on the floor and chairs, and required intra-muscular benzodiazepines and antipsychotics as needed for agitation and medication refusal. Multiple medication changes were made, and she was cross titrated from chlorpromazine 50 mg four times a day (QID) to discharge medication of olanzapine 15 mg at bedtime (qHS) and benztropine 1 mg daily (QD) with a discharge diagnosis of schizophrenia.

After spending one month in the hospital, the patient was admitted again, shortly after discharge, for another three-week psychiatric hospitalization due to depressive symptoms, including anhedonia, sleep disturbances, low mood, constant suicidal ideation, and critical and demeaning auditory hallucinations. According to those hospital records, her father described her as having symptoms consistent with a "catatonic state" and blamed the medications. The patient again made repeated allegations, with subsequent retractions, that her father had sexually abused her. She was diagnosed with complex post-traumatic stress disorder (PTSD) and was discharged home to her father on fluoxetine 10 mg QD.

Six months after her initial hospitalization, the patient's younger sister reported to the PCP that she had to assist her with showering and dressing. This was one year before this team saw her. The patient had two more inpatient psychiatric hospitalizations in the following few months with records documenting that she demonstrated varying degrees of avolition, psychomotor retardation, self-care failure, mutism, unresponsiveness, depression, and suicidality.

About one year before being admitted to our hospital, at the funeral of a family member, the patient reportedly exhibited psychotic symptoms, involving a demonic persecutory delusion along with dysregulated behavior, which required inpatient psychiatric admission. Her case manager was unable to obtain those records. Aside from her second hospitalization, when she was prescribed only fluoxetine, the antipsychotic medications ordered at discharge consistently were stopped by her father, with complaints that his daughter was in a "zombified state" and not able to talk.

Records documented additional hospitalizations with suicide attempts via hanging once, intentional overdose twice, as well as self-harm via cutting. Also, a report was documented wherein the patient was found by the police task force to be involved in sex trafficking in exchange for methamphetamine.

Family Medical History. The patient's family medical history included that her father had been diagnosed with depression and rheumatoid arthritis, her half-sister with depression, her other half-sister with schizophrenia, and her maternal uncle with completed suicide. Her mother died of cancer of unknown type.

Treatment Course. Assessment of the patient was hindered by her inability to engage in a diagnostic interview (she remained primarily mute except for occasional one-word replies or rare short sentences) and to provide information about the onset, characterization, and progression of her psychiatric symptoms. On observation, she demonstrated notable latency, psychomotor retardation, significant social withdrawal, blank staring, and flat affect. Given the patient's history of trauma at an early age (e.g., witness to custodial mother dying of cancer when she was seven years old, possible physical and sexual abuse, including sex trafficking), her history of methamphetamine use (with extent unknown), her family medical history, and incomplete past hospitalizations and PCP records, all in the context of her initial clinical presentation, this team formulated the following list of initial diagnoses:

- Unspecified Schizophrenia Spectrum Disorder and Other Psychotic Disorder
- Complex PTSD
- Rule out Major Depressive Disorder, recurrent episode severe, with psychotic features
- Rule out Catatonia associated with another mental disorder
- Rule out Adjustment Disorder with mixed disturbance of emotions and conduct
- Rule out Substance/Medication-Induced Psychotic Disorder (including cognitive and behavioral changes due to past methamphetamine use)

Given the patient's lack of meaningful participation in any interview, it was difficult to discern whether she was exhibiting symptoms of a

Schizophrenia Spectrum Disorder or psychotic symptoms in the context of a severe episode of Major Depressive Disorder. When she first came to the unit, she was eating and, throughout the day, ambulating to and from the day room, though primarily isolating to her room. On her fourth day on our service, a weekend call team felt strongly that she was experiencing psychotic symptoms and responding to internal stimuli. Specifically, she was darting her eyes around as if trying to locate the voices talking to her or the people out to get her. On the same weekend, she required intramuscular haloperidol for an episode of acute agitation. The weekend team restarted the patient's home risperidone, but at the much lower dose of 0.5 mg BID instead of 2 mg BID she was prescribed prior to admission to our unit.

In the couple of days that followed, the patient was started on sertraline 25 mg to address her apparent depressive symptoms, anxiety, and PTSD. During that time, she became very intrusive, resisting staff's attempts to redirect her physically when invading peers' rooms, entering closely into staff and peers' personal space, and staring at them intensely. Staff reported her as "fixated" on certain staff members, following them around and becoming frightening to certain staff and peers. During that time, she also started displaying stereotypies, as she began frequently and gently poking peers, staff, and objects in slow motion and without apparent purpose. She began blocking unit entrances, required "constant redirection", and was placed on one-on-one sitter precaution.

Over the next week, her risperidone was titrated up to 1 mg in the morning (qAM) and 0.5 mg qHS to target psychotic symptoms. On day 10, she began lying on the floor and resisting encouragement to move to her bed. Over the following five days, she progressed to lying on the floor facing her bed, refusing to look or respond to staff, and became completely mute (negativism). Additional behaviors indicative of catatonia developed, including limited oral intake, mannerisms, (e.g., sticking sanitary pads to walls and chewing on them, while refusing to use feminine hygiene products properly during menstruation), and an episode of posturing. Also, on examination, she demonstrated some waxy flexibility.

The neurology service was consulted, but the patient refused multiple attempts by staff to obtain a brain Magnetic Resonance Imaging (MRI) and an electroencephalogram (EEG). The pediatrics service was consulted to monitor the patient's general medical status, including nutrition and hydration, eating nonfood items (Pica), and potential development of decubitus ulcers, and rhabdomyolysis.

Once catatonia became apparent, our team discontinued risperidone and initiated treatment of catatonia, while continuing sertraline 25 mg qAM. Lorazepam was started at 1 mg BID with target doses up to 8 - 12 mg total daily dose, if needed. Challenges were encountered with the treatment of the patient's catatonia. Firstly, our hospital did not have a PICU and the nearby hospital with a PICU did not have an inpatient psychiatry unit or service, outside of consult liaison. Because the patient would not allow for intravenous (IV) administration and due to the potential risk for respiratory depression, lorazepam had to be titrated slowly and administered orally, with intramuscular dosing as needed for refusal. Secondly, the patient experienced symptoms consistent with orthostatic hypotension, though without falls, but refused to allow our team to obtain vital signs. Consequently, intake and output were tracked, and individual psychotherapy was attempted.

The patient's symptoms improved mildly within a day of lorazepam initiation. She tearfully verbalized having nightmares and flashbacks to the nursing team (but otherwise remained primarily mute). She demonstrated some gradual improvement in oral intake, getting off the floor, and ambulating for brief periods of time throughout the day as lorazepam was titrated up to 3 mg PO TID over the next five days.

Dosing was changed to smaller QID doses to avoid sedation and, over the five following days, lorazepam was titrated to 2.5 mg PO QID. The patient showed improvement in eating, moving around, and participating in interviews though primarily with nodding and shaking of her head. Since the nursing staff reported the patient appearing off balance, overly sedated, and refusing vitals, dosing was decreased to 2 mg QID for safety. The dose was increased again to 2.5 mg PO QID five days later, with some additional mild improvement in symptoms, including the patient speaking in sentences at times, improvement in self-care/hygiene, increased ambulation, improvement in cooperation with taking medications, and allowing a brain MRI, but with symptoms fluctuating in severity. The patient continued to require a high level of care with much encouragement to get off the floor and complete activities of daily living.

On day 13, the patient attempted suicide by drowning via sticking her head in the toilet. Meanwhile, the result of the brain MRI without contrast was within normal limits. Laboratory tests were ordered by our team to rule out autoimmune encephalitis as a possible underlying etiology of the patient's catatonic symptoms and sent to the Mayo Clinic laboratory.

Later, lorazepam was titrated up to 11 mg total daily to address the patient's catatonia. During this time, she continued to make suicide attempts, swallowing labels and plastics, while hiding plastic condiment containers in her blankets. When she began showing improvement in her catatonic symptoms, lorazepam was decreased gradually to 2 mg QID over the course of one week. During that time, the patient's laboratory results returned positive for anti-GAD65, N and P/Q type paraneoplastic antibodies, and levels of anti-streptolysin O were elevated. Therefore, the patient was transferred to a pediatric hospital in a neighboring major city to receive workup for autoimmune encephalitis and multidisciplinary care.

While at the pediatric hospital, the patient continued to attempt to swallow plastic items. During that hospitalization, she underwent a battery of tests, including EEG, which showed mild diffuse cerebral dysfunction and encephalopathy. Two attempts were made to complete a lumbar puncture, but failed due to inability to retrieve any cerebrospinal fluid.

Based on the workup completed, the negative MRI result, and a multidisciplinary discussion including the psychiatry, neurology, and oncology services, the patient's symptomatology was deemed not to be due to an autoimmune or oncological etiology, but rather a psychiatric one. Hence, after about one week, she was transferred back to our inpatient psychiatric unit.

On arrival, the patient's mutism seemed improved. The treatment team attempted to decrease lorazepam to 6 mg daily in divided doses (QID). However, she gradually became mute again. At this time, lorazepam was titrated back up to 8 mg total daily and a second opinion was obtained with another child psychiatrist to clarify the patient's psychiatric diagnoses. She was diagnosed with Schizoaffective Disorder with Catatonia as the primary diagnosis, but Major Depressive Disorder, recurrent episode severe with psychotic features, remained in the differential diagnosis. Given the patient's multiple trials of previous antipsychotic medications, she was started on clozapine and titrated up to 100 mg PO BID.

A psychologist also was consulted to start the patient on a behavioral plan with a reward system whenever she tended to her activities of daily living and left her room to participate in milieu therapy.

Over the next month, the patient showed gradual improvement in her symptoms and was transferred to a psychiatric residential treatment facility (PRTF) for further stabilization. While at the facility, clozapine was titrated to 150 mg PO BID with good response. Lorazepam was tapered slowly to 0.5 mg PO TID without recurrence of catatonic symptoms. Sertraline 25 mg daily was continued.

The patient's case manager reported that the patient was conversing much better with others. The case manager also related that the patient indicated that her thoughts were clearer, and she wanted to continue taking her medications. She remained at the PRTF while plans were being made for her next living situation.

DISCUSSION

Pediatric catatonia is a rare occurrence with high risk for morbidity and mortality.[3] It can occur in children and adolescents in the context of psychiatric and medical conditions.

Our case of pediatric catatonia was in the context of a psychotic disorder whose assessment was complicated by the inability of the patient to participate in a meaningful diagnostic interview (she was mostly nonverbal) and by the lack of collateral information from guardians (the patient entered the foster system a few months prior to admission to our hospital).

The case confirmed the need for psychiatrists to first rule out medical causes of pediatric catatonia, then address catatonic symptoms with, at times, high doses of benzodiazepines carefully titrated and divided throughout the day to reduce side effects.[2] The need for physicians to be patient regarding emergence of positive response to benzodiazepine treatment and to taper the regimen slowly, once catatonic symptoms have stabilized, was underscored.

Even if the literature indicates that antipsychotics worsen catatonia symptoms,[2] this case seemed to confirm that neuroleptics have a place in the treatment of catatonia: when the patient's catatonic symptoms appeared to have stabilized and a psychotic disorder became the clear underlying etiology, an antipsychotic (clozapine, which has low binding affinity for the dopamine D2 receptor like quetiapine) was added to the treatment regimen with positive results.

Finally, the difficulty of this case needs to be framed in the context of the current state of inpatient hospital care where brief hospitalizations are the mainstay and longer ones are discouraged. The aforementioned case fueled plenty of disagreements and conflicts among the many agencies involved in her care.

REFERENCES

[1] Barnes MP, Saunders M, Walls TJ, Saunders I, Kirk CA. The syndrome of Karl Ludwig Kahlbaum. J Neurol Neurosurg Psychiatry 1986; 49(9):991-996. PMID: 3760905.

[2] Benarous X, Raffin M, Ferrafiat V, Consoli A, Cohen D. Catatonia in children and adolescents: New perspectives. Schizophr Res 2018; 200:56-67. PMID: 28754582.

[3] Hauptman AJ, Benjamin S. The differential diagnosis and treatment of catatonia in children and adolescents. Harv Rev Psychiatry 2016; 24(6):379-395. PMID: 27824634.

Keywords: catatonia, pediatrics, child psychiatry

KANSAS JOURNAL of MEDICINE

KANSAS JOURNAL OF MEDICINE

VOLUME 14 • 2021

journals.ku.edu/kjm

Have a manuscript ready to publish?
Visit our website for instructions on submitting a manuscript.

Frontiers: University of Kansas Clinical and Translational Science Institute is a collaborating partner of the Kansas Journal of Medicine

Office of Research
1010 N. Kansas, Wichita, KS 67214
316-293-2617 • Email: kjm@kumc.edu

VOLUME 14 • 2021

WHAT'S INSIDE: ORIGINAL RESEARCH • CASE REPORT

KANSAS JOURNAL of MEDICINE

TABLE OF CONTENTS

KANSAS JOURNAL of MEDICINE

Is a Video Worth a Thousand Words? Educating Preclinical Medical Students on Sterile Scrubbing, Gowning, and Gloving Virtually and In-Person

Ashlie A. Elver, B.S.[1], Maxwell C. Braasch, MPH[1], Stefano Byer, B.S.[1], Lisa Gilmer, M.D.[1,2], Kevin J. Sykes, Ph.D., MPH[1,3], Chad Tuchek, M.D.[1,4], Peter DiPasco, M.D., FACS, FSSO[1,5]

[1]University of Kansas School of Medicine, Kansas City, KS

[2]Department of Pediatrics

[3]Department of Otolaryngology - Head and Neck Surgery

[4]Department of Neurosurgery

[5]Department of Surgery

Received May 31, 2021; Accepted for publication July 6, 2021; Published online Nov. 5, 2021
https://doi.org/10.17161/kjm.vol14.15545

ABSTRACT

Introduction. Programs that offer early exposure to surgery for medical students foster interest in and positive perceptions of surgery. The COVID-19 pandemic led to suspension of these activities at our institution, the University of Kansas School of Medicine. In response to the lack of virtual alternatives, a pilot virtual surgery enrichment program was implemented for first-year students in place of in-person surgical exposure. The aim of this study was to compare the efficacy of in-person and virtual-based surgical education programs to expose preclinical medical students about the surgical realm of medicine.

Methods. First-year medical students participated in either a virtual (Group A) or in-person (Group B) week-long surgical enrichment program. Group assignments were dictated by COVID restrictions on each of our three medical school campuses: Salina, Wichita, and Kansas City. Pre- and post-surveys with a 14-question multiple-choice assessment of surgical knowledge were distributed to participants. Paired Wilcoxon Signed Rank tests and Mann-Whitney-U tests were used for statistical analysis.

Results. There were 14 participants in Group A and 7 participants in Group B. Both groups improved significantly from pre- to post-assessment score. (Group A, $p = 0.01$; Group B, $p = 0.04$). There was no difference between groups in the magnitude of score improvement from pre- to post-assessment ($p = 0.59$).

Conclusions. This pilot program demonstrated that virtual platforms can be a method to provide meaningful clinical experiences in surgery to preclinical medical students restricted from clinical activities. Further development of mentorship in virtual surgical programs and assessment of subjective experience is needed. ***Kans J Med 2021;14:265-268***

INTRODUCTION

The first two years of medical school, termed "preclinical years", are traditionally didactic based. Many schools offer structured programs for students to participate in clinical areas of interest early in their training to facilitate career exploration. In surgery, early exposure to positive experiences and mentorship are important influences on the decision to pursue surgery as a career.[1,2] Also, early clinical participation in surgery improves surgical knowledge and performance in the operating room (OR) during surgery clerkships.[3]

Unfortunately, the coronavirus pandemic led to suspension of clinical activities for students who were deemed non-essential personnel.[4] While clinical activities are core to third and fourth-year medical students completing clinical clerkships, they are lower educational priority for first and second-year students during the didactic portion of their training. However, structured programs facilitating early exposure to surgery have become a part of the standard model of a well-rounded medical education.[5] To address this gap in preclinical education, a virtual surgical enrichment program (VSEP) was created.

Virtual platforms seemed a far-fetched method to deliver quality surgical education, but have demonstrated successful performance measures in new virtual surgical clerkships, and even generated interest to pursue surgical careers.[6] The opportunities for preclinical students to participate in surgery remain limited. It is nonetheless critical to provide students with these opportunities. Virtual pilot programs for surgical education, such as the one described in this paper, must be developed and expanded to restore pre-existing standards in medical education.

METHODS

Scholarship, Enrichment, and Remediation (SER) week is a required shadowing program in the pre-existing curriculum of first and second-year students at our institution and occurs at the end of each systems-based academic block (seven total).[7] Students spend the week immersed in clinical areas of interest with faculty and residents in the specialty of their choosing. One group of first-year medical students (MS-1s) who choose surgical specialties for their SER week in December 2020 were invited to participate in this study. No predetermined study enrollment goal was set. With the unpredictable changes in clinical activities available to students during the COVID pandemic, the priority was capturing as many students at one point in time instead of enrolling students over multiple months to reach a specific study size, as the former could add unintended confounding bias to our results. A VSEP alternative was created for MS-1s who were restricted from in-person clinical activities. This was designated Group A. Students who participated in-person, as a result of differences in COVID protocols across our three campuses, were designated Group B. This cohort was thought to represent the usual standard of SER week and served as the control for the purposes of this study.

Design of Virtual Platform. The VSEP was designed with three major components. First, Group A students were asked to watch an educational video with technical skills about sterile scrubbing, gowning, and gloving. Second, students joined surgical teams each day for virtual rounds. Third, an intra-operative video stream was assembled for students to observe surgeries in real time with a mechanism to ask questions.

The primary objective of this study was assessment of surgical knowledge after participation in virtual or in-person surgical SER week. Students in Group A primarily gained this knowledge from the educational video on sterile scrubbing, gowning, and gloving. This video was created in collaboration with institutional experts in surgery and medical education, and operating room (OR) staff educators. The video was distributed electronically to preclinical students via a sharable link to the unlisted video on YouTube™ (https://youtu.be/xy2EwPjgJEA).

Only students in Group A had access to this digital content. Students in Group B acquired surgical knowledge from in-person OR experiences with faculty, residents, and staff on their respective surgical specialties.

Pre- and Post-Survey. A pre- and post-survey was distributed before and after surgical SER week in December 2020. Both surveys included an identical 14-question multiple choice assessment of surgical knowledge that was created by the authors in collaboration with institutional experts. Each multiple choice item was associated with an image demonstrating proper or improper sterile technique. Additional data collected in the surveys were age, gender, previous OR experience and education, and interest in surgical careers before and after SER week. Informed consent for this study was obtained when the pre-survey was distributed to participants. Participants were informed of the study purpose, main outcomes, anticipated benefits, and lack of risks of participation.

The primary outcome of this study was assessment of surgical knowledge, as measured by the 14-question multiple choice assessment in the pre- and post-survey. The secondary outcome was interest level in surgery, as measured in the pre- and post-survey.

Statistical Analysis. Chi-square and two-tailed t-test were performed to analyze categorical and continuous variables, respectively. Paired Wilcoxon Signed Rank Test was used to determine improvement of assessment score from pre- to post-survey in each group. The Mann-Whitney U Test was used to compare pre- and post-assessment scores across groups, and assess differences in magnitude of change in pre- and post-scores between groups. A p value of < 0.05 was determined to be statistically significant. The data were analyzed using IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp, Armonk, New York). Approval to conduct this study was obtained from our institutional review board and declared exempt from human subject review.

RESULTS

There were 65 MS-1s who participated in surgical SER week in December 2020. There were 14 respondents (28%) of the 50 students who participated in the pilot VSEP, this was designated Group A. There were 7 respondents (46.7%) of the 15 students who participated in-person, this was designated Group B. The overall response rate was 21/65 (32.3%).

Respondent characteristics are displayed in Table 1. There were no significant differences in demographics or previous OR experiences. Exposure to prior OR education was not different between groups, including attendance at surgical skills workshops ($p = 0.16$) or specific training in sterile scrubbing, gowning, and gloving ($p = 0.47$). Interest to pursue surgical careers was not statistically significant between groups before ($p = 0.40$) or after ($p = 0.19$) participation in SER week.

Score improvement from pre- to post-assessment of surgical knowledge is displayed in Table 2. The assessment scores of all study respondents improved significantly after participation in surgical SER week (95% CI: 11-29; $p = 0.001$). Additionally, assessment scores of respondents in Group A (95% CI: 7.1-29; $p = 0.01$) and Group B (95% CI: 20-39; $p = 0.04$) improved significantly from pre- to post-assessment.

Comparison of pre- and post-assessment of surgical knowledge between Group A and Group B is displayed in Table 3. There was no statistically significant difference in either the pre-assessment score between Group A and Group B ($p = 0.44$) or the post-assessment score between Group A and Group B ($p = 0.13$). There was no statistically significant difference in the magnitude of score improvement between groups ($p = 0.59$).

Table 1. Characteristics of 21 respondents in surgical SER week in December 2020.

	Group A n = 14	Group B n = 7	p value[a]
	n (%)		
Age (years)[b]	23 [23 - 24]	24 [23 - 28]	0.30
Female	8 (57)	4 (57)	1.00
Attended surgical education workshops	6 (43)	6 (86)	0.16
Number of previous OR experiences[b]	3 [0 - 6.25]	3 [0 - 8]	0.79
Previously scrubbed into a surgery	2 (14)	0	0.28
Previously educated on sterile scrubbing, gowning, and gloving			0.47
Yes	6 (43)	3 (43)	
No	3 (21)	3 (43)	
Unsure	5 (36)	1 (14)	
Interest in pursuing surgical careers at the beginning of this surgical experience			0.40
Very interested	8 (57)	6 (86)	
Somewhat interested	5 (36)	1 (14)	
Not interested	1 (7.1)	0	
Interest in pursuing a surgical career at the conclusion of this surgical experience			0.19
Very interested	9 (64)	7 (100)	
Somewhat interested	3 (21)	0	
Not interested	2 (14)	0	

Abbreviations: SER, Scholarship, Enrichment, and Remediation; OR, operating room.
[a]$p < 0.05$ statistically significant
[b]Median [interquartile range]

Table 2. Pre- and post-assessment scores in 14 virtual and 7 in-person SER week respondents in December 2020.

	Median pre-assessment score (%)	Median post-assessment score (%)	p value[a]	95% confidence interval
	Median [interquartile range]			
Both groups (n = 21)	50 [39 - 61]	71 [64 - 79]	0.001	11 - 29
Group A (n = 14)	50 [36 - 59]	68 [57 - 73]	0.01	7 - 29
Group B (n = 7)	57 [43 - 64]	71 [64 - 86]	0.04	20 - 39

Abbreviations: SER, Scholarship, Enrichment, and Remediation.
[a]$p < 0.05$ statistically significant

Table 3. Differences between pre- and post-assessment scores in virtual vs. in-person SER week respondents in December 2020.

	Group A (n = 14)	Group B (n = 7)	p value[a]
	Median [interquartile range]		
Median pre-assessment score (%)	50 [36 - 59]	57 [43 - 64]	0.44
Median post-assessment score (%)	68 [57 - 73]	71 [64 - 86]	0.13
Median difference between pre- and post-assessment scores (%)	+21 [5.4 - 29]	+29 [0 - 36]	0.59

Abbreviations: SER, Scholarship, Enrichment, and Remediation.
[a]$p < 0.05$ statistically significant

DISCUSSION

The virtual platform was effective in teaching surgical knowledge, similar to what was found in virtual surgery clerkships.[6] The interest in surgery did not change or differ between groups. Therefore, neither experience was superior to the other for the primary and secondary outcomes of this study. The lack of change in interest level was reported by other in-person surgical immersion programs from the literature.[8-10] One such reason may be the selection bias introduced by students choosing to participate likely are interested in surgery already. Interestingly, more students who were not interested in surgery participated virtually. This suggested that the easy accessibility and low-pressure nature of virtual platforms may attract wider audiences.

This study did not explore the subjective experience of the students or the perception of mentorship. Mentorship is a key aspect of early clinical experiences. Multiple strategies are available to enhance mentorship in the virtual setting, including allocating time for student and resident "hangouts" for questions and advice.[6] Incorporation of a mentorship focus in virtual-based surgical education should be a goal of these modalities and warrants further attention.

This study was limited by a small sample of 21 participants over a short, one-week surgical experience. However, varying local restrictions of the three campuses at the study institution created a pragmatic opportunity to compare a virtual pilot program to an in-person experience. Although it appeared that virtual-based surgical educational experiences may be reliable methods of education of select surgical competencies, further studies are needed to explore this trend with larger groups, and thus, higher statistical power.

This study was the first known to have assessed preclinical students' ability to learn basic surgical competencies through in-person or virtually based surgical education experiences using an objective measure of competency assessment. While not validated, the objective knowledge assessment in this study was constructed carefully with input from expert surgeons, surgical educators, and medical educators. This new measure was superior to gauging knowledge merely on participant self-reported confidence in their knowledge of this topic. Assessing procedural skills, such as sterile scrubbing, gowning, and gloving techniques, with an assessment based on images of individuals demonstrating proper or improper technique, was preferred over assessing a procedural skill with text alone. This added tremendous value to the visually based assessment tool used in this study. While it would have been beneficial to perform an in-person assessment of these procedural skills instead of a picture-based assessment, that was not possible due to pandemic related infection control measures, such as limited in-person exposures and social distancing in the clinical learning environment.

The generalizability of this study was limited by a small sample of 21 participants over a short period of time. However, the authors intended the study design to be completed with a single cohort of as many participants as possible. This was because of the evolving pandemic and changing student restrictions introduced bias into including future cohorts after December 2020. Despite this, the sample size of this study was sufficient to address the primary and secondary study aims adequately. The overall response rate was low and unequally distributed among groups. The fact that virtual learners were less likely to participate may allude to a lower motivation to acquire technical skills that lack immediate relevance. It was possible that in-person learners felt a stronger desire to be prepared for their performance in the OR. The addition of in-person skills assessment to virtual learning should be explored to improve motivation.

CONCLUSIONS

The use of readily available video-based technology can be applied through programs such as described in this paper to facilitate experiential participation of students in different areas of medicine. A virtual surgical education program to teach scrubbing, gowning, and gloving for students was as effective as an in-person educational program as measured by the study's knowledge assessment. This study demonstrated a virtual surgical education program can provide a quality educational experience for students without access to in-person programs due to resource limitations caused by financial constraints, limited local expertise, or a pandemic. In addition, these results showed that some clinical content can be taught effectively prior to an in-person educational session, thus allowing in-person education to build more on foundational concepts and focus on application in clinical settings.

REFERENCES

[1] Al-Heeti KN, Nassar AK, Decorby K, Winch J, Reid S. The effect of general surgery clerkship rotation on the attitude of medical students towards general surgery as a future career. J Surg Educ 2012; 69(4):544-549. PMID: 22677595.
[2] Marshall DC, Salciccioli JD, Walton SJ, Pitkin J, Shalhoub J, Malietzis G. Medical student experience in surgery influences their career choices: A systematic review of the literature. J Surg Educ 2015; 72(3):438-445. PMID: 25544332.
[3] Gawad N, Moussa F, Christakis GT, Rutka JT. Planting the 'SEAD': Early comprehensive exposure to surgery for medical students. J Surg Educ 2013; 70(4):487-494. PMID: 23725936.
[4] Moletta L, Pierobon ES, Capovilla G, et al. International guidelines and recommendations for surgery during Covid-19 pandemic: A systematic review. Int J Surg 2020; 79:180-188. PMID: 32454253.
[5] Dhillon J, Salimi A, ElHawary H. Impact of COVID-19 on Canadian medical education: Pre-clerkship and clerkship students affected differently. J Med Educ Curric Dev 2020; 7:2382120520965247. PMID: 33134548.
[6] Shin TH, Klingler M, Han A, et al. Efficacy of virtual case-based general surgery clerkship curriculum during COVID-19 distancing. Med Sci Educ 2020; 1-8. PMID: 33200037.
[7] Kallail KJ, Shaw P, Hughes T, Berardo B. Enriching medical student learning experiences. J Med Educ Curric Dev 2020; 7:2382120520902160. PMID: 32030355.

[8] Hicks KE, Doubova M, Winter RM, Seabrook C, Brandys T. Surgical Exploration and Discovery Program: Early exposure to surgical subspecialties and its influence on student perceptions of a surgical career. J Surg Educ 2019; 76(5):1248-1257. PMID: 30904391.
[9] Zuccato JA, Kulkarni AV. The impact of early medical school surgical exposure on interest in neurosurgery. Can J Neurol Sci 2016; 43(3):410-416. PMID: 26711669.
[10] Greene B, Head L, Gawad N, Hamstra SJ, McLean L. Surgical Exploration and Discovery Program: Inaugural involvement of otolaryngology - head and neck surgery. J Otolaryngol Head Neck Surg 2015; 44(1):3. PMID: 25649902.

Keywords: medical education, pilot projects, coronavirus, medical students, operating rooms

KANSAS JOURNAL of MEDICINE

Treatment of Cardiac Surgical Wounds with Silver Dressings

Ashlie A. Elver, B.S.[1], Katy Wirtz, RN, BSN[2], Jinxiang Hu, Ph.D.[1,3], Emmanuel Daon, M.D.[1,4]

[1]University of Kansas School of Medicine, Kansas City, KS
[2]University of Kansas Health System, Kansas City, KS
University of Kansas School of Medicine, Kansas City, KS
[3]Department of Biostatistics and Data Science
[4]Department of Cardiovascular and Thoracic Surgery

Received May 24, 2021; Accepted for publication July 8, 2021; Published online Nov. 5, 2021
https://doi.org/10.17161/kjm.vol14.15506

ABSTRACT

Introduction. Mediastinitis is a deadly surgical site infection (SSI) after cardiac surgery. Although rare, mortality is as high as 47%. Best practices for infection prevention to eliminate this deadly complication must be identified. Surgical dressings impregnated with silver have been shown to reduce SSIs in other surgical specialties. The aim of this study was to determine if the routine use of silver surgical dressings is beneficial to prevent mediastinitis after cardiac surgery.

Methods. A single-center retrospective study was performed on patients who underwent sternotomy from 2016 to 2018 at the University of Kansas Medical Center. Prior to June 2017, all cardiac surgical patients were treated with gauze surgical dressings and designated as Group A. The routine use of silver-impregnated surgical dressings was implemented in June 2017; patients after this change in practice were designated as Group B. Patient characteristics and rates of deep and superficial sternal wound infections (SWI) were compared.

Results. There were 464 patients in Group A and 505 in Group B. There were seven SWIs in Group A (7/464, 1.5%) and five in Group B (5/505, 1%; p = 0.57). Of these, there was one deep SWI per group (p = 0.61) and six superficial SWIs in Group A compared to four in Group B (p = 0.74). Severe COPD was higher in Group A (p = 0.04) and peak glucose was higher in Group B (p = 0.02).

Conclusions. The analysis conferred no benefit with silver-impregnated surgical dressings to prevent mediastinitis. Choice of gauze surgical dressings may be preferable to reduce cost.

Kans J Med 2021;14:269-272

INTRODUCTION

Surgical site infection (SSI) is a burdensome healthcare-associated infection (HAI) affecting nearly all surgical operations, with potentially devastating outcomes.[1] Specifically in cardiac surgery, patients are susceptible to superficial and deep sternal wound infections (SWI), noted by some to occur in 8.49% of sternotomies.[2] Deep sternal wound infection (DSWI), or mediastinitis, is the most serious SWI and has mortality rates reported as high as 47%.[3] Many efforts were made to optimize infection prevention strategies that became standard of care resulting in a 32% decrease in infection rates from 2008 to 2012.[4] Some of these strategies included skin and nares decontamination, antibiotic prophylaxis, strict perioperative glucose control, and surgical closure techniques (i.e., figure-of-eight, Robicsek).[5,6] Despite this, the incidence of DSWI remains unacceptably high at 0.5% to 6% and warrants further investigation.[7]

Contamination of the sternal wound by normal skin flora is an important route for infection in the postoperative period. Pathogens can gain access to deeper tissues when dehiscence is present due to the normal breathing mechanics at the destabilized wound.[8-12] Theoretically, reducing the bioburden around the incision in the postoperative period could interrupt this process and allow time for wound healing. Guidelines for infection prevention focus on the pre- and intra-operative periods, while less clear guidance is given in the postoperative period. In this situation, exogenous routes seeding deep tissue infections after leaving the operating room deserve further consideration.

One idea gaining popularity in postoperative wound care is the use of silver surgical dressings to harness the natural bactericidal and bacteriostatic properties of silver.[13] Silver has long been used successfully in device coating and chronic wound and burn care, and more recently has shown promising results to prevent SSI.[14-21] The mechanism of silver-impregnated surgical dressings presents an opportunity to decontaminate the incision while the sternum heals. Early reports were compelling, and one study noted zero cases of mediastinitis after replacing gauze with silver dressings. But the reproducibility of these findings was variable, and the pursuit of high-quality data slowed down.[22-25] However uncertain, the potential to save one patient from suffering this complication instituted a department wide change to use silver dressings in all cardiothoracic surgical patients.

Cost-conscious care is a principle of high-value healthcare. Benefit-cost analysis evaluates the benefits of interventions with their costs, such as postoperative silver dressings at this institution. The immediate cost of silver dressings is $26.82 for each sternal dressing. The potential benefits are mitigating future costs of mediastinitis and reduced morbidity and mortality for patients. The aim of this study was to evaluate this intervention and its ability to achieve the intended goal of reducing postoperative complications at this institution.

METHODS

This single-center study was approved by the institutional review board at the University of Kansas Medical Center. A retrospective cohort study was performed on adults 18-years-old and older who underwent sternotomy for cardiac surgery from June 2016 to June 2018. Patients with active infection at the time of operation and those undergoing open heart transplant were excluded due to higher susceptibility to infections. Left ventricular assist device placements were excluded because sternal incisions are not uniformly performed in these cases. Sternotomy incisions were treated with gauze dressings (GD) in all patients before June 2017; this was Group A and served as the control group. Sternotomy incisions after June 2017 were treated with silver-impregnated dressings (SD) after a department wide change in practice was implemented; this was Group B and served as the treatment group. All operations were performed by board-certified cardiothoracic surgeons and patients received the same perioperative infection prevention protocol aligned with institutional standards. GD used in Group A were replaced on postoperative day two and removed on postoperative day three or until wound was dry. CarraKlenz™ wound cleanser (Medline

Industries, Northfield Illinois) was used during dressing changes. Commercially available SD used in Group B were removed on postoperative day seven as recommended by the manufacturer (Argentum Medical, Geneva Illinois).

Sternal wound infections were diagnosed by surgeons according to the criteria from the U.S. Centers for Disease Control and Prevention.[26] Superficial sternal wound infection (SSWI) involved tissue above the fascial plane with at least one of the following: 1) purulent drainage; 2) organisms isolated from the wound; 3) tenderness, swelling, or heat present and wound opened by surgeon; or 4) diagnosis by surgeon. DSWI, or mediastinitis, involved tissue below the fascial plane (with or without infected retrosternal space) and met at least one of the following: 1) purulent drainage; 2) wound dehiscence or opened by surgeon with organisms identified in mediastinal tissue or fluid and fever (> 38°C) or tenderness present; or 3) evidence of infection on gross anatomical or histopathologic exam.

Data were collected using electronic medical record and the Society of Thoracic Surgeons database. Patient demographics including age, sex, body mass index (BMI), smoking history, and comorbidities were collected. Severe chronic obstructive pulmonary disease (COPD) was defined as FEV_1 < 50% of predicted value. Recorded operative details included cardiac bypass time, valve operation, blood products, peak lab values, ventilation time, and length of stay.

Data were analyzed using SAS statistical software version 9.4 (SAS Institute, Cary, NC). Continuous and normally distributed data were presented as mean with standard deviation and categorical data were presented as percentages. Fisher exact test was used for analysis of categorical data and student t-test was used for analysis of continuous variables.

RESULTS

There were 464 patients in Group A and 505 patients in Group B. There were significantly more patients with severe COPD in Group A (39/464, 8.4%) compared to Group B (26/505, 5.1%; p = 0.04). There were no statistical differences in other demographic variables including age (62.2 ± 13 years vs. 61.2 ± 13.3 years in Group B; p = 0.23), female sex (128/464, 27.6% vs. 160/505, 31.7% in Group B; p = 0.16), BMI (30 ± 5.6 kg/m^2 vs. 30 ± 6.3 kg/m^2 in Group B; p = 0.99), Hemoglobin A1C (6 ± 1.7 mg/dL vs. 6.1 ± 1.7 mg/dL in Group B; p = 0.41), current smokers (260/464, 56% vs. 291/505, 57.6% in Group B; p = 0.62), diabetes (177/464, 38.1% vs. 170/505 in Group B, 33.7%; p = 0.15), hypertension (386/464, 83.2% vs. 410/505, 81.2% in Group B; p = 0.42), dyslipidemia (361/464, 77.8% vs. 400/505, 78.2% in Group B; p = 0.59), dialysis (17/464, 3.7% vs. 13/505 2.6% in Group B, p = 0.33), emergent procedures (35/464, 7.5% vs. 44/505, 8.7% in Group B; p = 0.51), or valvular procedures (190/464, 41% vs. 193/505, 38.2% in Group B; p = 0.38).

Average intraoperative peak glucose levels were significantly higher in Group B (186.9 ± 62.1 mg/dL) compared to Group A (179.1 ± 41.3 mg/dL; p = 0.02). All other operative characteristics were not statistically different, including cardiac bypass time (106.5 minutes ± 46.6 vs. 109.1 minutes ± 53.2 in Group B; p = 0.41), peak creatinine (1.6 mg/dL ± 1.6 vs. 1.5 ± 1.5 mg/dL in Group B; p = 0.45), ventilation time (17.4 hours ± 46.9 vs. 20.6 ± 48.6 hours in Group B; p = 0.30), blood products (186/464, 40% vs. 189/505, 37.4% in Group B; p = 0.40), or length of stay (8.1 days ± 5.9 vs. 7.6 days ± 5.3 in Group B; p = 0.19).

Table 1. Comparison of baseline characteristics between patients who received gauze surgical dressings before June 2017, and patients who received silver-impregnated surgical dressings after June 2017.

	Gauze dressings Group A, N = 464	Silver dressings Group B, N = 505	p value[a]
Characteristics	**Mean (± Standard Deviation)**		
Age, years	62.2 (13)	61.2 (13.3)	0.23
BMI, kg/m^2	30 (5.6)	30 (6.3)	0.99
Hemoglobin A1C, mg/dL	6 (1.7)	6.1 (1.7)	0.41
Cardiac bypass time, min	106.5 (46.6)	109.1 (53.2)	0.41
Peak glucose, mg/dL	179.1 (41.3)	186.9 (62.1)	0.02[a]
Peak creatinine, mg/dL	1.6 (1.6)	1.5 (1.5)	0.45
Ventilation time, hour	17.4 (46.9)	20.6 (48.6)	0.30
Length of stay, days	8.1 (5.9)	7.6 (5.3)	0.19
	n (%)		
Sex, female	128 (27.6)	160 (31.7)	0.16
Current smoker	260 (56)	291 (57.6)	0.62
Severe COPD[b]	39 (8.4)	26 (5.1)	0.04[a]
Diabetes	177 (38.1)	170 (33.7)	0.15
Hypertension	386 (83.2)	410 (81.2)	0.42
Dyslipidemia	361 (77.8)	400 (78.2)	0.59
Dialysis	17 (3.7)	13 (2.6)	0.33
Emergent operation	35 (7.5)	44 (8.7)	0.51
Valve procedure	190 (41)	193 (38.2)	0.38
Blood products	186 (40)	189 (37.4)	0.40

[a]p < 0.05, statistically significant
[b]FEV_1 < 50% of predicted

SWI developed in seven patients in Group A (7/464, 1.5%) and in five patients in Group B (5/505, 1%; p = 0.57). Of these, six wounds in Group A and four wounds in Group B were classified as superficial (p = 0.74). One wound in both Group A and Group B was classified as deep (p = 0.61; Table 2).

Table 2. Incidence of sternal wound infections (SWI) in patients who received gauze surgical dressings before June 2017, and patients who received silver-impregnated surgical dressings after June 2017.

	Gauze dressings Group A, N = 464	Silver dressings Group B, N = 505	p value[a]
	n (%)		
Total SWI	7 (1.5)	5 (1)	0.57
Deep	1 (0.4)	1 (0.2)	0.61
Superficial	6 (1.3)	4 (0.8)	0.74

[a]p < 0.05, statistically significant

DISCUSSION

The interest in silver dressings in cardiac surgery began when Huckfeldt reported a reduction in SWIs with SD down to zero compared to traditional gauze in adult cardiac patients.[25] Adding to the interest, Totaro demonstrated the addition of SD in patients with mediastinitis refractory to wound vacuum-assisted closure caused wound cultures to turn negative.[27] This prompted further investigation. In 2016, a randomized control trial was conducted in pediatric patients undergoing sternotomy for cardiac surgery to compare silver and gauze dressings. No infections occurred in either group and the authors concluded silver and gauze were equally effective.[23] More recently, Raman also reported no difference between silver and gauze in a single center retrospective study of adult cardiac patients.[22] The findings reported in the literature were variable, making the clinical significance of SD unclear.

Our study did not indicate benefit with the use of SD to prevent mediastinitis or even superficial sternal infections. The incidence of infection in our study population was similar to what was reported in the literature, and like Raman,[22] we were not able to reproduce the promising results reported by Huckfeldt[25] in 2004. This may suggest institutional-specific bias present in Huckfeldt's study. However, without randomized controlled trials in the adult cardiac population, the benefit remains unclear.

Our study results could have been influenced by the differences between study groups noted at baseline. Patients with COPD are known to be at increased risk of developing SWI.[28,29] We had significantly more patients with severe COPD in Group A, which could have exacerbated the observed benefit in Group B. Strict glycemic control during the perioperative period is known to reduce the risk of developing SWI.[28-30] We noted a significantly higher peak glucose level in Group B compared to the control, which could have underestimated benefit of SD. However, the peak glucose level did not exceed the level associated with elevated risk (> 200 mg/dL).[31] Thus, we do not believe either of these differences would have changed the results in a meaningful way.

Our study was limited by its retrospective nature and lack of randomization. Over the duration of the study, it was possible that small changes in practice could have introduced confounders. The overall incidence of mediastinitis was low in both study groups making it difficult to draw conclusions in this retrospective study. This was a single-center study and results may not be generalizable, although incidence was like that of the general population.

CONCLUSIONS

A retrospective analysis assessed the use of silver-impregnated surgical dressings compared to gauze surgical dressing in hopes of preventing mediastinitis. The analysis showed no benefit with the use of silver-impregnated surgical dressings. Based on these results, treatment of the sternal incision with gauze may be preferred to reduce cost. Further investigation of optimal wound care during the postoperative period is needed in the effort to eliminate this costly and deadly complication.

REFERENCES

[1] U.S. Centers for Disease Control and Prevention. Acute care hospital surveillance for surgical site infections. http://www.cdc.gov/nhsn/acute-care-hospital/ssi/index.html. Accessed June 26, 2021.
[2] Edwards JR, Peterson KD, Mu Y, et al. National Healthcare Safety Network (NHSN) report: Data summary for 2006 through 2008, issued December 2009. Am J Infect Control 2009; 37(10):783-805. PMID: 20004811.
[3] El Oakley RM, Wright JE. Postoperative mediastinitis: Classification and management. Ann Thorac Surg 1996; 61(3):1030-1036. PMID: 8619682.
[4] U.S. Centers for Disease Control and Prevention. 2014 National and State Healthcare-Associated Infections Progress Report. 2016. https://www.cdc.gov/hai/progress-report/index.html. Accessed October 1, 2020.
[5] Lazar HL, Salm TV, Engelman R, Orgill D, Gordon S. Prevention and management of sternal wound infections. J Thorac Cardiovasc Surg 2016; 152(4):962-972. PMID: 27555340.
[6] Association for Professionals in Infection Control and Epidemiology. Guide for the Prevention of Mediastinitis Surgical Site Infections Following Cardiac Surgery. 2008. https://www.apic.org/eliminationguides. Accessed October 1, 2020.
[7] Hever P, Singh P, Eiben I, Eiben P, Nikkhah D. The management of deep sternal wound infection: Literature review and reconstructive algorithm. JPRAS Open 2021; 28:77-89. PMID: 33855148.
[8] Goh SSC. Post-sternotomy mediastinitis in the modern era. J Card Surg 2017; 32(9):556-566. PMID: 28833518.
[9] von Eckardstein AS, Lim CH, Dohmen PM, et al. A randomized trial of a skin sealant to reduce the risk of incision contamination in cardiac surgery. Ann Thorac Surg 2011; 92(2):632-637. PMID: 21704290.
[10] Mossad SB, Serkey JM, Longworth DL, Cosgrove DM 3rd, Gordon SM. Coagulase-negative staphylococcal sternal wound infections after open heart operations. Ann Thorac Surg 1997; 63(2):395-401. PMID: 9033307.
[11] Gårdlund B, Bitkover CY, Vaage J. Postoperative mediastinitis in cardiac surgery - microbiology and pathogenesis. Eur J Cardiothorac Surg 2002; 21(5):825-830. PMID: 12062270.
[12] Losanoff JE, Richman BW, Jones JW. Disruption and infection of median sternotomy: A comprehensive review. Eur J Cardiothorac Surg 2002; 21(5):831-839. PMID: 12062271.
[13] Kumar Pandian SR, Deepak V, Kalishwaralal K, Viswanathan P, Gurunathan S. Mechanism of bactericidal activity of silver nitrate – A concentration dependent bi-functional molecule. Braz J Microbiol 2010; 41(3):805-809. PMID: 24031558.
[14] Krieger BR, Davis DM, Sanchez JE, et al. The use of silver nylon in preventing surgical site infections following colon and rectal surgery. Dis Colon Rectum 2011; 54(8):1014-1019. PMID: 21730792.
[15] Epstein NE. Do silver-impregnated dressings limit infections after lumbar laminectomy with instrumented fusion? Surg Neurol 2007; 68(5):483-485. PMID: 17961738.
[16] Zegelman M, Guenther G, Waliszewski M, et al. Results from the International Silver Graft Registry for high-risk patients treated with a metallic-silver impregnated vascular graft. Vascular 2013; 21(3):137-147. PMID: 23508393.
[17] Ogbemudia AO, Bafor A, Edomwonyi E, Enemudo R. Prevalence of pin tract infection: The role of combined silver sulphadiazine and chlorhexidine dressing. Niger J Clin Pract 2010; 13(3):268-271. PMID: 20857782.
[18] Nherera L, Trueman P, Roberts C, Berg L. Silver delivery approaches in the management of partial thickness burns: A systematic review and indirect treatment comparison. Wound Repair Regen 2017; 25(4):707-721. PMID: 28742235.
[19] Moir J, Serra MP. The use of silver nitrate in wound management. Ann Ital Chir 2012; 83(1):45-48. PMID: 22352216.
[20] Storm-Versloot MN, Vos CG, Ubbink DT, Vermeulen H. Topical silver for preventing wound infection. Cochrane Database Syst Rev 2010; (3):CD006478. PMID: 20238345.
[21] Siah CJ, Yatim J. Efficacy of a total occlusive ionic silver-containing dressing combination in decreasing risk of surgical site infection: An RCT. J Wound Care 2011; 20(12):561-568. PMID: 22240882.
[22] Raman V, Thompson-Brazill KA, Kane K, et al. Silver-impregnated dressing does not decrease incidence of surgical site infection after adult cardiac surgery. Innovations (Phila) 2018; 13(4):296-299. PMID: 30124586.
[23] Staveski S, Abrajano C, Casazza M, et al. Silver-impregnated dressings for sternotomy incisions to prevent surgical site infections in children. Am J Crit Care 2016; 25(5):402-408. PMID: 27587419.
[24] Schwartz J, Goss S, Facchin F, et al. A prospective two-armed trial assessing the efficacy and performance of a silver dressing used postoperatively on high-risk, clean surgical wounds. Ostomy Wound Manage 2014; 60(4):30-40. PMID: 24706401.

[25] Huckfeldt R, Redmond C, Mikkelson D, Finley PJ, Lowe C, Robertson J. A clinical trial to investigate the effect of silver nylon dressings on mediastinitis rates in postoperative cardiac sternotomy incisions. Ostomy Wound Manage 2008; 54(10):36-41. PMID: 18927482.
[26] U.S. Centers for Disease Control and Prevention. The NHSN Surgical Site Infection Event (SSI). 2021. https://www.cdc.gov/nhsn/pdfs/pscmanual/9pscssicurrent.pdf. Accessed June 26, 2021.
[27] Totaro P, Rambaldini M. Efficacy of antimicrobial activity of slow release silver nanoparticles dressing in post-cardiac surgery mediastinitis. Interact Cardiovasc Thorac Surg 2009; 8(1):153-154. PMID: 18948308.
[28] Risnes I, Abdelnoor M, Almdahl SM, Svennevig JL. Mediastinitis after coronary artery bypass grafting risk factors and long-term survival. Ann Thorac Surg 2010; 89(5):1502-1509. PMID: 20417768.
[29] Phoon PHY, Hwang NC. Deep sternal wound infection: Diagnosis, treatment, and prevention. J Cardiothorac Vasc Anesth 2020; 34(6):1602-1613. PMID: 31623967.
[30] Furnary AP, Wu Y. Eliminating the diabetic disadvantage: The Portland Diabetic Project. Semin Thorac Cardiovasc Surg 2006; 18(4):302-308. PMID: 17395026.
[31] Trick WE, Scheckler WE, Tokars JI, et al. Modifiable risk factors associated with deep sternal site infection after coronary artery bypass grafting. J Thorac Cardiovasc Surg 2000; 119(1):108-114. PMID: 10612768.

Keywords: standard of care, mediastinitis, surgical wound infection, cardiac surgical procedures, postoperative period

KANSAS JOURNAL of MEDICINE

Trends in Internet Safety Education by Healthcare Providers

Gary King, M.D., Thuy Bui, MPH, Julian Dedeaux, Ph.D., Carolyn R. Ahlers-Schmidt, Ph.D., Kari Harris, M.D.
University of Kansas School of Medicine-Wichita, Wichita, KS
Department of Pediatrics

Received Oct. 29, 2020; Accepted for publication July 15, 2021; Published online Nov. 5, 2021
https://doi.org/10.17161/kjm.vol14.14805

ABSTRACT

Introduction. The purpose of this study was to explore healthcare provider training, comfort, and provision of internet safety counseling. Prior research has demonstrated increased parental concern regarding the pervasive access to the internet by children, including the potential impacts of risky internet behavior and adverse media exposure.

Methods. A self-reported survey was provided to a convenience sample of 31 healthcare providers during a mental health training seminar. Responses were analyzed using descriptive statistics.

Results. Internet safety counseling, especially regarding risky online behavior, was not a focal point of provider-patient interaction in the sample population. This finding was reinforced with more than half of the respondents indicating that they infrequently or never provide internet safety counseling (n = 17, 56%). While research has placed an emphasis on the importance of discussing the risks of exposure to violence, drugs, and sexually explicit media online, this study found that the topics most often discussed were setting time limits (77%), limiting access to media devices (67%), and supervising internet use (50%). This may be due in part to the fact that most respondents (n = 17, 57%) reported never receiving training on internet safety counseling.

Conclusions. Overall, significant deficits were identified in internet safety counseling training for professionals and provision of education for families. These finding were inconsistent with the American Academy of Pediatrics recommendations around media use counseling and a point of urgent concern given the increasing time spent on media devices, particularly during the COVID pandemic.

Kans J Med 2021;14:273-276

INTRODUCTION

Internet access is nearly ubiquitous to American youth with access becoming virtually unlimited through mobile devices. The COVID pandemic has encouraged social distancing, and as a result, children's access to the internet is becoming increasingly pervasive. As of 2015, 92% of adolescents go online daily.[1,2] Approximately 75% of adolescents own a smart phone with 25% reporting they are online "almost constantly". In addition, 76% of adolescents maintain at least one social media profile. This prevalence is not only relevant in adolescent youth. Nearly all homes with small children (98%) own a mobile device, an increase from 75% in 2013 and 52% in 2011.[3] Further, 50% of five-year-old children go online daily and nearly 75% of four-year-old children have their own mobile device.[4,5] Although data were lacking on media use during the COVID pandemic, these prior statistics supported the American Academy of Child and Adolescent Psychiatry's (AACAP) concern that quarantined youth have unprecedented access to potentially harmful media content and that risk needs to be mitigated.[6]

Parents were concerned about potential adverse impacts of the internet on their children, most notably the impact of exposure to violent and sexual content.[7] Parental concerns were placed appropriately given research has shown poor outcomes of child exposure to risky behaviors. Specifically, children who consume media rich in alcohol advertisements were more likely to initiate use.[8-10] The same influential effect has been shown for sexually explicit media, including pornography.[11,12] These risks can be applied to other online safety concerns such as cyberbullying and increased risk of suicidal ideation.[13] To mitigate these risks, trusted adults need to engage in conversation with youth emphasizing media safety.[14,15] Taken together, parental mediation of media use has been shown to decrease risky behaviors.[16,17] More than ever, parents should be intentional about helping youth develop positive media habits. This can be done by modeling healthy behaviors, setting limits, and co-viewing.[7]

In addition to parents, healthcare providers play an important role in delivering internet safety education to youth.[15,18,19] Parents trust healthcare providers to provide appropriate recommendations for the health and well-being of their children. The American Academy of Pediatrics (AAP) has released a policy statement, "Media Use in School-Aged Children and Adolescents", outlining best practices for parents and pediatric healthcare providers.[18] This statement included information on the AAP's Family Media Plan, which can be an asset to parents during quarantine as well as non-quarantine times. Healthcare providers have a unique opportunity to support parents in providing resources and anticipatory guidance on internet safety. Despite this policy statement, only one in five parents were aware of the AAP's recommendation, indicating a gap in communication between parents and pediatric healthcare providers. Although pediatricians have been tasked with educating parents on this topic, to what extent this happens remained unclear.

Three study objectives were investigated:

1. To explore the extent and type of counseling provided by healthcare providers on internet safety.
2. To explore the type and extent of training that healthcare providers have received on internet safety, their comfort level, and barriers to providing counseling.
3. To determine if internet safety counseling differs between provider demographic groups.

METHODS

Prior to engaging in the study, Institutional Review Board approval was obtained through University of Kansas School of Medicine-Wichita Human Subjects Committee. An anonymous, self-reported, 14-item survey was developed to capture information related to healthcare provider demographics, training, and experience with internet safety counseling. Prior to use, the survey was reviewed by an expert panel for readability.

Healthcare providers attending a local mental health training seminar in late 2018 were asked to participate in this study. Participation was voluntary, informed consent was obtained, and no incentives were

provided. Participants included community and academic physicians, resident physicians, and physician extenders (i.e., nurse practitioners, physician assistants) who provide primary care to children. Non-practicing healthcare providers and providers who do not serve children were excluded from the study.

Data were entered into the encrypted and HIPAA compliant REDCap® online data capture application. Descriptive statistics were calculated from the database.

RESULTS

Of 31 potential participants, a total of 30 (n = 30, 97%) completed the survey. Of the 30 respondents, most were pediatricians (n = 24, 80%), female (n = 21, 70%), and had been in practice for an average of 10.5 years (SD = 9.8; Table 1). The majority of providers characterized their practice as urban (n = 20, 67%), and cared for children in all age ranges (≥ 80%). The mean provider's age was 42.3 years (SD = 9.9). Most providers reported having children of their own, with only 17% (n = 5) reporting they had no children. No statistically significant correlations were found between provider demographics and provider delivery of internet safety counseling.

Most providers (n = 17; 57%) reported having never received training on internet safety counseling. Of those who had received training (n = 13; 43%), independent study and informal training were most common, followed by in-person lectures, and online courses (Table 2). Few reported the adequacy of their training as good and none as very good. Regardless of training, few respondents (n = 8; 27%) felt comfortable or very comfortable with their knowledge on internet safety. An equal amount (n = 8; 27%) of providers reported that they felt uncomfortable with their level of knowledge.

The majority (n = 17; 57%) of respondents reported providing internet safety counseling during well child and adolescent visits infrequently or never. When counseling was provided, only 3% (n = 1) waited to initiate counseling until the patients started high school. Topics discussed most often by providers included setting time limits (n = 23; 77%), limiting access to media devices (n = 20; 67%), and supervising internet use (n = 15; 50%; Figure 1). Topics involving avoidance of risky internet behavior were discussed routinely by 37% (n = 11) of respondents and risks of adverse internet exposure were discussed only by 27% (n = 8).

Ninety percent of respondents (n = 27) indicated time constraint as a barrier to providing internet safety counseling, followed by 47% (n = 14) having limited knowledge on the topic, 40% (n = 12) forgetting to provide counseling, and 30% (n = 9) having a lack of resources.

DISCUSSION

The results of this study demonstrated provider training, comfort, and delivery of internet safety counseling were less than optimal with over half of providers never or infrequently providing counseling. Only 20% of providers reported counseling most of the time. Parents have reported internet safety as a top concern, specifically regarding exposure to sexual and violent content, or risky internet behaviors.[3,7] While providers in this study reported discussing risky internet behaviors, the rates of these discussions were at lower frequency than other topics, such as setting time limits. This result illustrated a gap in care, as media topics that parents were most concerned about were being discussed infrequently by their child's healthcare provider.

Table 1. Descriptive demographics of sample population.

	M	SD
Age	42.3	9.9
Years in practice	10.5	9.8
	n	**%**
Gender		
Males	9	30
Females	21	70
Geographic region		
Rural (population < 50K)	9	30
Urban (population > 50K)	20	67
Missing	1	3
Specialty		
Pediatrics	24	80
Family Medicine	5	17
Other	1	3
Age groups seen		
Infants/young children (0 - 5 years)	26	87
School aged (6 - 11 years)	26	87
Adolescents (12 - 17 years)	23	77
Providers as parents		
Infants/young children (0 - 5 years)	9	30
School aged (6 - 11 years)	13	43
Adolescents (12 - 17 years)	12	40
Adult children (18 years)	8	27
None	5	17

The optimal time for introduction of internet safety to children is not known. Nevertheless, many key stakeholders, including parents, adolescents, teachers, and healthcare providers agreed that internet safety counseling should be started at a young age, between six to eight years.[20] However, given the increasing prevalence of very young children accessing the internet regularly,[3-5] it would be prudent for internet safety education to be introduced with the onset of internet use. This study found only 13% of providers initiated conversations about internet safety with the parents of very young children, and 33% start during elementary school.

The AAP has recognized that pediatricians have an important role in providing guidance to patients and families regarding internet safety in their policy statement "Media Use in School-Aged Children and Adolescents".[18] In this statement, the AAP emphasized the development and use of a personalized Family Media Use Plan that considers the child's age, health, temperament, developmental stage, and individual needs. The use of this tool has been encouraged during the COVID pandemic.[20] This study found that the primary barriers to providing internet safety counseling center around time constraints and lack of provider knowledge on the topic. Increasing awareness of the important role providers have in mitigating risks associated with unsafe internet

use may reduce these barriers. Providers should be offered resources and education on adverse media exposure, including ways to initiate discussions with families. Some authors suggested expanding the HEADS (Home; Education/Employment; Activities; Drugs/Depression/Diet; Sex/Suicide/Safety) psychosocial history-taking pneumonic as a useful tool to include elements of media use, thereby assisting providers to engage patients and families on discussions of internet safety.[21,22]

Table 2. Physician training and practice on internet safety counseling.

Training format	**n**	**%**
Independent study	9	30
Informal setting	6	20
In-person lecture	5	17
Online training	4	13
None	17	57
Adequacy of training		
Very good	0	0
Good	4	13
Adequate	7	23
Poor	2	7
Very poor	0	0
Did not receive training	13	43
Missing	4	13
Comfort with knowledge		
Very comfortable	2	7
Comfortable	6	20
Neutral	14	47
Uncomfortable	8	27
Very uncomfortable	0	0
Frequency of practice		
Always	0	0
Most of the time	6	20
Sometimes	7	23
Infrequently	13	43
Never	4	13
Age of initiation of internet safety counseling		
High school	1	3
Middle school	8	27
Elementary school	10	33
Pre-school	3	10
Infant/toddler	1	3
Do not provide internet safety counseling	6	20

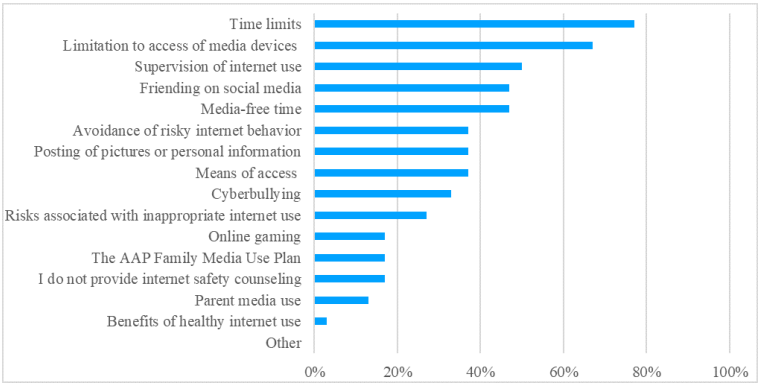


Figure 1. Provider report of topics routinely discussed.

The AAP's policy statement has provided much of the educational background needed for providers to offer internet safety counseling, although some providers would benefit from more structured education modalities.[18] In short, the AAP recommended that families include the following components in their Family Media Use Plan in addition to traditional media recommendations: 1) how media is accessed, 2) where it is accessed, 3) when it is accessed, 4) how long the child is spending on media, 5) who they are interacting with both on- and off-line, 6) what is appropriate to share online, 7) what the child is accessing, 8) risks and avoidance of inappropriate content, 9) consequences of accessing inappropriate content, 10) how to respond to online attacks, and 11) parental role modeling of healthy internet use.

Limitations. This study had several limitations. First, the small sample size may limit the generalizability of these results to the larger pediatric healthcare community, however, sampled providers came from various regions of the state representing diversity in healthcare practices. Second, the study survey did not delineate providers' levels of training (i.e., attending physician, resident physician, or physician extender) which may have affected training experience. In addition, age and level of training also may impact providers' personal level of comfort with the internet and technology in general which may in turn impact their comfort providing internet safety education to patients. Third, the survey was conducted during a voluntary mental health training event which may introduce a sample bias of respondents interested in mental health, including internet safety. Finally, the COVID pandemic emerged during compilation of this manuscript. Although data were collected prior to the pandemic, it was perhaps more valuable given the increased access youth have during this time and supported that internet safety counseling should be a priority. Despite these limitations, provider training, comfort, and delivery of internet safety counseling were insufficient to meet current recommendations.

Future Research. This study examined the trends in internet safety counseling by a small cohort of healthcare providers, practicing in the midwestern part of the United States. The results of the study found that provider training, comfort, and provision of internet safety counseling below optimum. To determine if these trends were reflective of the greater population of healthcare providers caring for children, future studies designed to target a larger, multi-regional study population may qualify the seriousness of this problem better. With a larger sample, future studies may consider exploring the influence of provider demographic characteristics on training and practice of internet safety counseling.

CONCLUSIONS

Healthcare providers have a unique opportunity to support parents and children in providing resources and anticipatory guidance on internet safety. Nonetheless, significant deficits were identified in provider training, comfort, and provision of internet safety counseling for families. Further studies need to be performed to evaluate the significance of these findings on a wider scale. Providers need to be cognizant of their role in mitigating risk associated with unsafe media exposure by offering internet safety counseling to patients and their families.

ACKNOWLEDGEMENTS

We would like to thank the University of Kansas School of Medicine-Wichita Department of Pediatrics and The REACH Institute for allowing us to survey the attendees of their mental health seminar. We also acknowledge Dr. Julian Dedeaux for his assistance in bringing this manuscript to completion.

REFERENCES

[1] Anderson M. Parents, teens and digital monitoring. January 7, 2016. http://www.pewInternet.org/2016/01/07/parents-teens-and-digital-monitoring. Accessed October 2, 2018.
[2] Lenhart A. Teens, social media, and technology overview. April 9, 2015. http://www.pewInternet.org/2015/04/09/teens-social-media-technology-2015. Accessed October 2, 2018.
[3] Common Sense. The Common Sense census: Media use by kids age zero to eight. 2017. https://www.commonsensemedia.org/sites/default/files/uploads/research/csm_zerotoeight_fullreport_release_2.pdf. Accessed October 2, 2018].
[4] Kabali HK, Irigoyen MM, Nunez-Davis R, et al. Exposure and use of mobile media devices by young children. Pediatrics 2015; 136(6):1044-1050. PMID: 26527548.
[5] Swindle TM, Ward WL, Whiteside-Mansell L, Bokony P, Pettit D. Technology use and interest among low-income parents of young children: Differences by age group and ethnicity. J Nutr Educ Behav 2014; 46(6):484-490. PMID: 25087748.
[6] American Academy of Child and Adolescent Psychiatry. Media habits during COVID-19: Children and teens on screens in quarantine. https://www.aacap.org/App_Themes/AACAP/Docs/resource_libraries/covid-19/Screen-Time-During-COVID.pdf. Accessed May 18, 2020.
[7] C.S. Mott Children's Hospital. Mott Poll Report. Bullying and internet safety are top health concerns for parents. August 21, 2017. http://mottpoll.org/reports-surveys/bullying-and-Internet-safety-are-top-health-concerns-parents. Accessed November 12, 2020.
[8] Litt DM, Stock ML. Adolescent alcohol related risk cognitions: The roles of social norms and social networking sites. Psychol Addict Behav 2011; 25(4):708-713. PMID: 21644803.
[9] Robinson TN, Chen HL, Killen JD. Television and music video exposure and risk of adolescent alcohol use. Pediatrics 1998; 102(5):E54. PMID: 9794984.
[10] Winpenny EM, Marteau TM, Nolte E. Exposure of children and adolescents to alcohol marketing on social media websites. Alcohol Alcohol 2014; 49(2):154-159. PMID: 24293506.
[11] Ashby SL, Arcari CM, Edmonson MB. Television viewing and risk of sexual initiation by young adolescents. Arch Pediatr Adolesc Med 2006; 160(4):375-380. PMID: 16585482.
[12] Bailin A, Milanaik R, Adesman A. Health implications of new age technologies for adolescents: A review of the research. Curr Opin Pediatr 2014; 26(5):605-619. PMID: 25160783.
[13] Litwiller BJ, Brausch AM. Cyber bullying and physical bullying in adolescent suicide: The role of violent behavior and substance use. J Youth Adolesc 2013; 42(5):675-684. PMID: 23381779.
[14] Coyne SM, Radesky J, Collier KM, et al. Parenting and digital media. Pediatrics 2014; 40(suppl 2):S112-S116. PMID: 29093044.
[15] Harris KR, Hopper MT. Preventing teen pregnancy at pre-adolescence. In: Akella D (Ed.). Socio-cultural influences on teenage pregnancy and contemporary prevention measures. Hershey, PA: IGI Global, 2019. pp. 166-188. ISBN: 1522561080.
[16] Collier KM, Coyne SM, Rasmussen EE, et al. Does parental mediation of media influence child outcomes? A meta-analysis on media time, aggression, substance use, and sexual behavior. Dev Psychol 2016; 52(5):798-812. PMID: 26914217.
[17] Starr CR, Ferguson GM. Sexy dolls, sexy grade-schoolers? Media and maternal influences on young girls' self-sexualization. Sex Roles 2016; 67(7-8):463-476.
[18] Council on Communications and Media. Media use in school-aged children and adolescents. Pediatrics 2016; 138(5):e20162592. PMID: 27940794.
[19] Moreno MA, Egan KG, Bare K, Young HN, Cox ED. Internet safety education for youth: Stakeholder perspectives. BMC Public Health 2013; 13:543. PMID: 23738647.
[20] American Academy of Pediatrics. Teens & COVID-19: Challenges and opportunities during the outbreak. June 5, 2020. https://www.healthychildren.org/English/health-issues/conditions/chest-lungs/Pages/Teens-and-COVID-19.aspx. Accessed November 12, 2020.
[21] Contemporary Pediatrics. HEEADSSS 3.0: The psychosocial interview for adolescents updated for a new century fueled by media. January 1. 2014. https://www.contemporarypediatrics.com/view/heeadsss-30-psychosocial-interview-adolescents-updated-new-century-fueled-media. Accessed November 12, 2020.
[22] Norris ML. HEADSS up: Adolescents and the internet. Pediatr Child Health 2007; 12(3):211-216. PMID: 19030361.

Keywords: internet, primary care, pediatrics, social media

KANSAS JOURNAL of MEDICINE

A Disclosure About Death Disclosure: Variability in Circulatory Death Determination

Christopher P. Robinson, D.O., M.S.[1], Suzanne L. Hunt, M.S.[2], Gary S. Gronseth, M.D.[3], Sara Hocker, M.D.[4], Eelco F.M. Wijdicks, M.D., Ph.D.,[4], Alejandro A. Rabinstein, M.D.[4], Sherri A. Braksick, M.D.[3,4]

[1]University of Florida, Gainesville, FL
Department of Neurology
University of Kansas Medical Center, Kansas City, KS
[2]Department of Biostatistics and Data Science
[3]Department of Neurology
[4]Mayo Clinic, Rochester MN
Department of Neurology

Received May 25, 2021; Accepted for publication July 28, 2021; Published online Nov. 5, 2021
https://doi.org/10.17161/kjm.vol14.15512

ABSTRACT

Introduction. Circulatory-respiratory death declaration is a common duty of physicians, but little is known about the amount of education and physician practice patterns in completing this examination.

Methods. An online survey of physicians was conducted evaluating the rate of formal training and specific examination techniques used in the pronouncement of circulatory-respiratory death. Data, including the level of practice, training received in a formal death declaration, and examination components, were collected.

Results. Respondents were attending physicians (52.4%), residents (30.2%), fellows (10.7%), and interns (6.7%). Most respondents indicated they had received no formal training in death pronouncement; however, most reported self-perceived competence. When comparing examination components used by the study's cohort, 95 different examination combinations were used for death pronouncement.

Conclusions. Formal training in death pronouncement was uncommon and clinical practice varied. Implementation of formal training and standardization of the examination are necessary to improve physician competence and reliability in death declarations.

Kans J Med 2021;14:277-281

INTRODUCTION

Clinicians working in hospitals unfortunately are faced with the declaration of death following circulatory-respiratory arrest. Determination of death following circulatory-respiratory arrest has been practiced for centuries, while formal criteria for the determination of death only recently has been developed. The Uniform Determination of Death Act (UDDA), written in 1981, simply defines death as "total failure of the circulatory-respiratory system or irreversible loss of all brain functions."[1] Currently, only one guideline for the declaration of circulatory-respiratory death exists, and it defines minimal acceptable standards for declaration: cardiopulmonary auscultation, central pulse assessment, pupillary reaction, and responsiveness to stimulation (Table 1).[2] Recently, additional evidence-based declaration standards have been proposed with the introduction of donation after circulatory death (DCD).[3]

Table 1. Recommended minimal acceptable standards for circulatory-respiratory death assessment.

Minimal acceptable clinical standards	Additional testing for consideration
1. Absence of breath sounds 2. Absence of heart sounds 3. Absence of spontaneous respirations and visible chest wall movement 4. Absence of palpable pulse 5. Loss of pulsatile arterial blood pressure through non-invasive measures 6. Coma with fixed and dilated pupils	1. Loss of pulsatile arterial blood pressure through arterial line monitoring 2. Absence of anterograde aortic flow on echocardiography 3. Isoelectric electroencephalogram 4. Absence of pulse by Doppler *Adapted from Shemie et al.*[2]

Autoresuscitation, defined as the spontaneous return of cardiovascular function following death, is an important consideration in death pronouncement.[4] Autoresuscitation can occur both following cardiopulmonary resuscitation (CPR) and in the absence of any resuscitation efforts, but has not been reported to occur beyond 10 minutes after cardiopulmonary arrest. The potential for this phenomenon would suggest that an observation period following apparent circulatory-respiratory arrest prior to a formal declaration of death is reasonable.

Death declarations in academic medical centers are often the responsibility of physicians-in-training, and the degree of formal training these physicians receive is unknown. Additionally, given the paucity of recommendations in a death pronouncement, the exact examination performed to determine death also is unclear. This lack of training and discomfort in completing the examination is illustrated in a recent editorial by a family medicine intern who describes his first encounter in a death pronouncement.[5]

We conducted a survey of physicians to determine the rates of formal training in death declaration and which specific examination techniques are used by physicians to declare a patient deceased. With this information, we aimed to develop an algorithm, based on existing literature and the definition of circulatory-respiratory death, to aid examiners in pronouncing a patient deceased.

METHODS

An electronic survey was developed using REDCap®, an online assessment tool and data repository. Data were collected and stored on the University of Kansas Medical Center site, available through grant support from the Clinical and Translational Science Awards program. The institutional review boards at each institution approved this study.

Participants. Physicians from three academic, tertiary care hospitals (two affiliated with the University of Kansas, one private) were invited via email to participate. Informed consent was waived as accessing the electronic survey was considered implied consent.

Procedure. Potential participants were identified by sending an introductory email with the common survey link to all individual department or division chairs and administrative assistants for distribution through their department email listserv to all attending physicians, fellows, residents, and interns. Participants were asked if and when they received training in a death pronouncement, their perceived competence in death pronouncement, and which examination components they assessed as part of the examination. Specific information requested through this survey is listed in Table 2.

Table 2. Survey tool.

What is your current level of practice?	• Intern • Resident • Fellow • Staff physician
What is your medical specialty?	• [fill in]
What medical facility are you affiliated with?	• Institution A • Institution B • Institution C
Have you ever received formal training in completing a death examination? (Not brain death)	• Yes • No
When did you receive this training?	• Medical school • Internship • Residency • Fellowship • As staff
Do you feel competent in the pronouncement of death (excluding brain death)?	• Yes • No
What components do you assess when completing a death examination? (choose all that apply) (Not brain death)	• Responsiveness to voice • Spontaneous respirations • Heart sounds • Peripheral pulse • Central pulse (i.e., carotid) • Pupillary light response • Corneal response • Oculocephalic response (Doll's Eyes) •Oculovestibular response (cold calorics) • Gag • Cough • Motor response to pain • Peripheral reflexes (i.e., patellar, biceps) • Other _____
Do you announce a time of death while in the patient's room?	• Yes • No
Have you ever pronounced a patient deceased who had not yet passed away?	• Yes • No

Statistical Analysis. A primary interest of the pilot survey was to summarize the clinical practice of determining death. The components assessed by physicians when determining death became the focus of the analysis. Five respondents did not select any exam components and completed less than 25% of the survey, and were not included in the analysis.

Neurologic responsiveness was defined as assessing any one of the following clinical examination components: responsiveness to voice, pupillary light response, corneal response, oculocephalic response, oculovestibular response, cough, gag, motor response to pain, or peripheral reflexes. Chi-square tests were used to compare trained and untrained respondents using particular components when determining death. A significance level of 0.05 was used and no corrections for multiple testing were made. The analysis was completed with SAS software, version 9.4 of the SAS System for Windows.

RESULTS

Overall distribution of the survey included 42 separate division or departmental chairs across the three study institutions, with physicians from 23 different departments/divisions responding, for an overall response rate of 54.8%. The specific number of survey recipients is unknown as individual distribution of the survey was not possible. Five respondents did not respond to any of the physical examination questions and were excluded from the final analysis.

Of the 225 respondents, most were attending physicians (n = 118, 52.4%), followed by residents (n = 68, 30.2%), fellows (n = 23, 10.7%), and interns (n = 15, 6.7%; Figure 1). The departments of neurology and anesthesiology were represented most highly in this study.

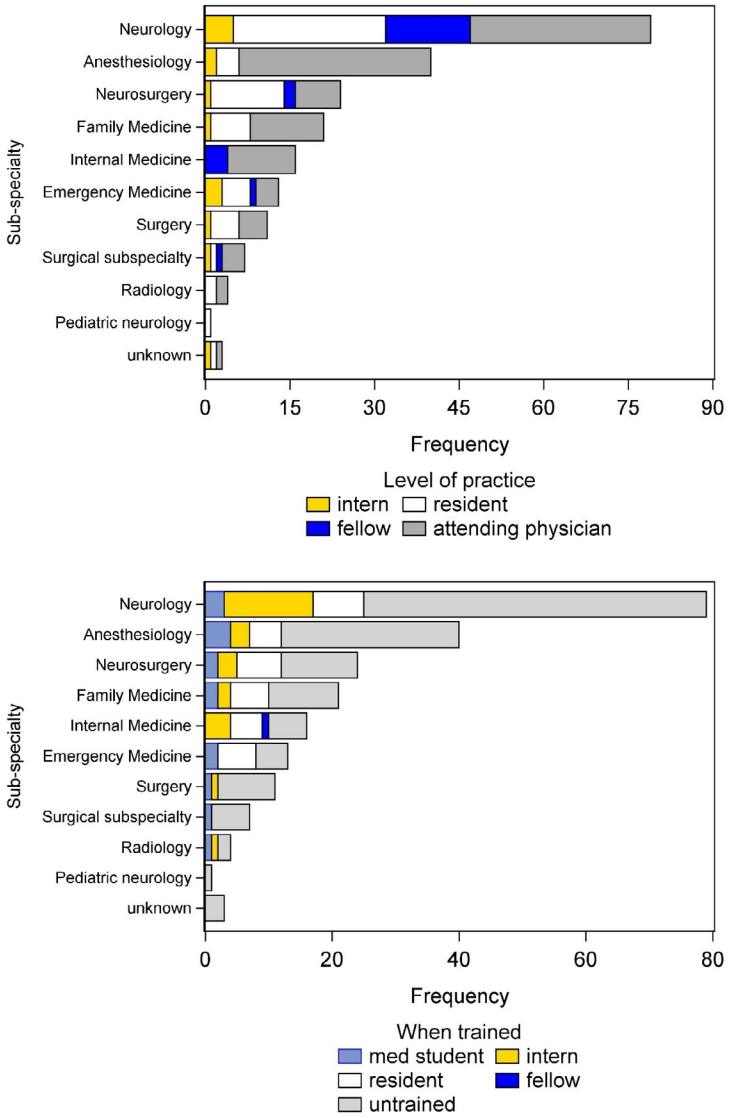


Figure 1. Sub-specialty representation, level of training, and timing of training amongst survey respondents.

Most physicians (62.7%) indicated they had received no formal training in performing a death pronouncement. For those who had formal education, training most often occurred during residency (45.2%) and internship (33.3%). Most respondents (78.7%) reported self-perceived competence in the determination of death. When separated by level of training, only 6.7% of interns (1 of 15 respondents) reported formal training in death declaration with 26% reporting self-competency (4 of 15 respondents). Conversely, 33% of residents and fellows and 36% of attending physicians reported formal training, while 82% and 77% self-reported competency, respectively.

The frequencies of examination techniques used by the study's cohort in the determination of death are listed in Table 3. Most respondents reported assessing breath sounds (97%), listening for heart sounds (90%), and checking central pulses (79%); while the majority of those surveyed reported some assessment of neurological responsiveness, with pupillary response being evaluated most often. Neurologists or neurosurgeons evaluated at least one component of the neurologic examination 85.6% of the time, while non-neurology specialties reported assessing at least one component of the neurologic examination 87.5% of the time. Somewhat surprisingly, there was no statistical difference in the frequency of a single physical examination component between those who were trained in death pronouncement and those who were not (Table 3), as indicated by the overlapping confidence intervals among the two groups. However, 95 different examination combinations were used to declare a patient deceased by the survey cohort.

Table 3. Examination components of circulatory-respiratory death determination.

	Trained in death declaration			
	Not trained, n = 138		Trained, n = 82	
Exam component	n (% of column)	95% CI	n (% of column)	95% CI
Respirations	132 (96%)	(90.8, 98.4)	81 (99%)	(93.4, 100.0)
Heart sounds	123 (89%)	(82.7, 93.8)	75 (91%)	(83.2, 96.5)
Central pulse	106 (77%)	(68.9, 83.6)	68 (83%)	(73.0, 90.3)
Pupils	90 (65%)	(56.6, 73.1)	58 (71%)	(59.6, 80.3)
Voice response	83 (60%)	(51.5, 68.4)	56 (68%)	(57.1, 78.1)
Peripheral pulse	75 (54%)	(45.7, 62.8)	45 (55%)	(43.5, 65.9)
Painful stimulus	65 (47%)	(38.6, 55.8)	41 (50%)	(38.7, 61.3)
Corneal response	57 (41%)	(33.0, 50.0)	34 (41%)	(30.7, 52.9)
Gag	37 (27%)	(19.6, 35.0)	25 (30%)	(20.8, 41.6)
Oculocephalic	36 (26%)	(19.0, 34.2)	16 (20%)	(11.6, 29.7)
Cough	28 (20%)	(13.9, 28.0)	15 (18%)	(10.6, 28.4)
Oculovestibular	22 (16%)	(10.3, 23.1)	10 (12%)	(6.0, 21.3)
Peripheral reflexes	15 (11%)	(6.2, 17.3)	7 (9%)	(3.5, 16.8)
Other finding	15 (11%)	(6.2, 17.3)	8 (10%)	(4.3, 18.3)

Large variation was seen across respondents in the reported use of a neurological examination in their assessment. Examination techniques included assessment of pupillary responses, corneal responses, gag reflex, oculocephalic reflex, cough reflex, and peripheral neurological reflexes. Forty-eight percent of all respondents reported the assessment of central responses to painful stimuli and formal assessment of coma.

When comparing the examination performed based on level of training, 100% of interns reported checking for breath sounds, while only 66.7% assessed heart sounds, and 26.7% checked peripheral pulses. Comparatively, greater than 90% of all other physician groups reported using all three of these examination components.

A substantial majority of respondents (75.2%) announced a time of death while in the patient's room. Two individuals (0.9%) reported incorrectly pronouncing a patient as deceased, but the circumstances of these pronouncements were otherwise unknown. Of interest, 11% of all physicians reported using means other than a clinical examination in death determination, such as ultrasound to confirm cardiac standstill (3.1%), evaluation using cardiac telemetry (3.1%), and absence of vital signs for greater than 15 minutes (0.4%).

DISCUSSION

Performing a complete and accurate examination for death determination is a necessary skill that should be learned early in medical training. Yet, the survey results suggested that formal training often was lacking. Physicians self-reported a variable degree of competence, with interns reporting less competence than more experienced physicians.

In the traditional hierarchy of academic medical education, death declaration has primarily been the responsibility of physicians-in-training at academic medical centers in the U.S. However, only one of the interns in this study reported receiving formal training in death declaration, and a substantial minority felt competent. Additionally, only one-third of all responding physicians reported formal training in death declaration throughout their medical career. Despite such a large gap in training, over two-thirds of respondents reported self-perceived competency when pronouncing death. Over time, competence appears to increase, which is likely a consequence of accumulated experience.

When performing a pronouncement, physicians reported performing many different examination combinations. This result emphasized the lack of standardization in clinical practice, and this inconsistency may indicate an insufficient understanding of the definition of circulatory-respiratory death, further complicating the development of a formal training program for new physicians.

Most of the respondents reported completing an assessment of breath sounds, heart sounds, and central pulses, while about half of those surveyed reported an assessment of the nervous system (i.e., pupillary response, corneal response). Interns were less likely to perform cardiac auscultation as compared to residents, fellows, or attending physicians.

Published acceptable minimum standards for circulatory death recommended assessment of responsiveness to pain and pupillary light reaction in addition to cardio-pulmonary auscultation and palpation of central pulses.[1] Only two-thirds of the cohort reported compliance with the neurological standard in this guideline. In contrast, the

UDDA defined death as either total failure of the circulatory-respiratory system or irreversible loss of all brain functions.[1] One could argue that the assessment of pain after identifying the absence of cardiac and pulmonary function does not make physiologic sense. Additionally, it is fully possible for a patient to have unreactive pupils (due to an upper brainstem, cranial nerve III lesions, or post-surgical pupillary abnormalities) but not be deceased.[6] These latter points may make the neurologic assessment in the setting of cardiopulmonary failure unnecessary to determine death.

Of note, it is important to emphasize that the definition of clinical death may not be documented formally or defined in the same manner in countries outside of the U.S., and these findings cannot be extrapolated to suggest international practice is similar, as no hospitals outside of the U.S. were surveyed.

In the U.S., death may be declared within a protocol for DCD in patients who are not brain dead but have a brain injury that they cannot survive. Discussion related to declaration in DCD was out of the scope of this paper; however, it is important to note that guidelines related to this process include a defined waiting period prior to the death pronouncement.[7] Such a waiting period was developed to account for the possibility of autoresuscitation, which is a rare but important phenomenon that should be considered during formal death declaration. In patients who have undergone CPR, autoresuscitation times have ranged from 30 seconds to 10 minutes.[3,4] In patients who did not receive CPR or underwent withdrawal of life sustaining therapies, times have ranged from seconds to three minutes.[8,9] These data suggested that a defined waiting period prior to death declaration in all patients is reasonable. In this study, two of the respondents indicated that they incorrectly had pronounced a patient deceased. The details behind such situations were not disclosed; however, it is plausible that autoresuscitation or simply an incomplete assessment of circulatory-respiratory function may have played a role.

Of interest, three-quarters of the respondents in this survey announced time of death while in the patient's room. Though time of death is legally necessary for documentation, no formal recommendation regarding an audible pronouncement exists. Calling out the time of death while in a patient's room may lead to unease amongst staff and undue psychological stress on the patient's family. We do not believe that stating the time of death aloud is necessary to complete a formal death pronouncement. On the same token, physicians cannot leave any uncertainty when performing a death pronouncement, and audibly indicating that the patient has died is necessary to prevent confusion by family members that are present for the clinical examination.

Study results indicated wide variability among physicians from multiple specialties in the degree of formal training on death determination and the examination performed. To help fill this gap, we propose an algorithm for circulatory-respiratory death pronouncement, based on the definition provided in the UDDA, existing evidence, and expert opinion, which is detailed in Figure 2. The authors are hopeful that providing a standardized method for death pronouncement, a clear mechanism for training can be developed, improving physician confidence and competence in this examination.

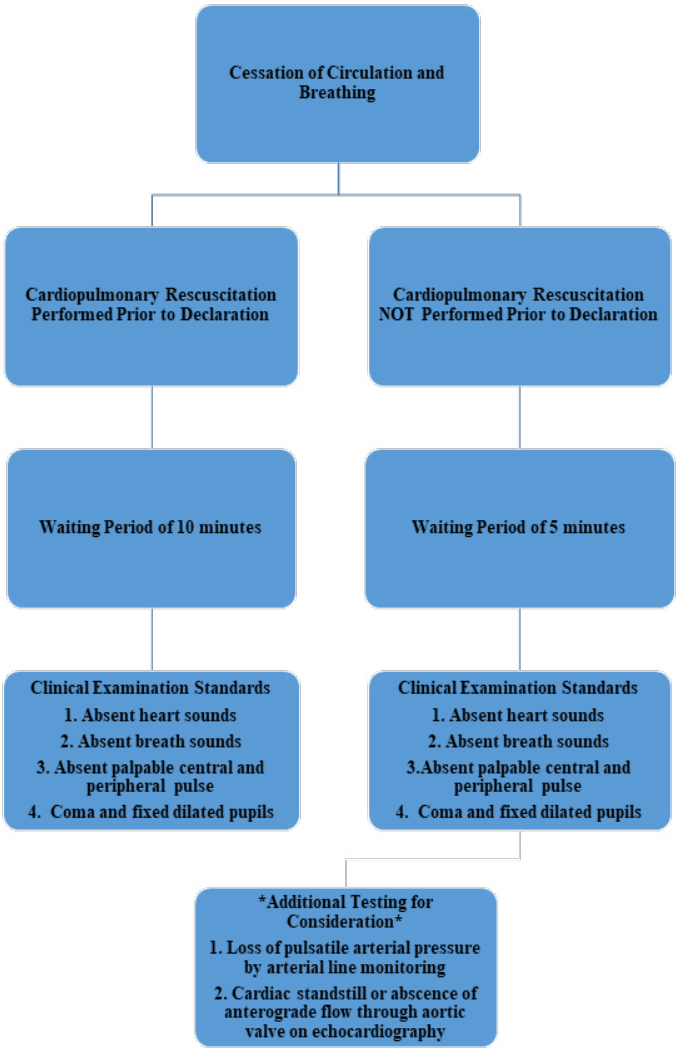


Figure 2. Proposed algorithm for circulatory-respiratory death declaration.

This survey-based study had limitations. The study design was dependent on individual department chairs, division heads, and administrators to distribute the email to the physician members of their department. Consequently, the responses are not from a random sample. As physicians-in-training and practicing physicians in the U.S. may have received some or all of their training outside of the U.S., information regarding differences in training based on location may be lacking, as this was not collected as a part of this survey. A low response rate impaired the ability to evaluate the current clinical practice completely across the study sites. There was the possibility that respondents misread components of the survey and inaccurately answered the questions as a result. Results were limited in the data analysis because not all providers answered every question included in the survey.

CONCLUSIONS

Formal training in death declaration often was missing and clinical practice varied among physicians in academic medical centers. Implementation of formal training in medical school or during internship is necessary to fill this important gap, eliminate discrepancies in practice, and guarantee the reliability of the death declaration.

REFERENCES

[1] President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research. Defining death: A report on the medical, legal, and ethical issues in the determination of death. July 1981. https://repository.library.georgetown.edu/bitstream/handle/10822/559345/defining_death.pdf?sequence=1&isAllowed=y. Accessed May 26, 2021.
[2] Shemie SD, Hornby L, Baker A, et al. International guideline development for the determination of death. Intensive Care Med 2014; 40(6):788-797. PMID: 24664151.
[3] Dhanani S, Hornby L, Ward R, Shemie S. Variability in the determination of death after cardiac arrest: A review of guidelines and statements. J Intensive Care Med 2012; 27(4):238-252. PMID: 21841147.
[4] Hornby L, Dhanani S, Shemie SD. Update of a systematic review of autoresuscitation after cardiac arrest. Crit Care Med 2018; 46(3):e268-e272. PMID: 29286944.
[5] Eberly JB Jr. Words, practices, and pronouncing death. Acad Med 2020; 95(7):978-979. PMID: 32101918.
[6] Biller J. Practical Neurology. 4th Ed. Philadelphia, PA: Wolters Kluwer, 2012. ISBN: 9781451142631.
[7] Hornby K, Hornby L, Shemie SD. A systematic review of autoresuscitation after cardiac arrest. Crit Care Med 2010; 38(5):1246-1253. PMID: 20228683.
[8] Sheth KN, Nutter T, Stein DM, Scalea TM, Bernat JL. Autoresuscitation after asystole in patients being considered for organ donation. Crit Care Med 2012; 40(1):158-161. PMID: 21926577.
[9] Yong SA, D'Souza S, Philpot S, Pilcher DV. The Alfred Hospital experience of resumption of cardiac activity after withdrawal of life-sustaining therapy. Anaesth Intensive Care 2016; 44(5):605-606. PMID: 27608344.

Keywords: determination of death, practice guidelines as topic, medical education, cardiopulmonary arrest, questionnaires and surveys

KANSAS JOURNAL of MEDICINE

Emergency Action Planning in School-Based Athletics: A Systematic Review

Riley Hedberg, B.S.[1], William Messamore, M.D., Ph.D.[1], Tanner Poppe, B.S.[1], Armin Tarakemeh, B.A.[1], Rick Burkholder, M.S., ATC[2], Trent Carter, M.S., ATC[3], Bryan Vopat, M.D.[1], Jean-Philippe Darche, M.D.[1]

[1]University of Kansas Medical Center, Kansas City, KS Department of Orthopedic Surgery, Orthopedic Sports Medicine

[2]Kansas City Chiefs, Kansas City, MO

[3]University of Kansas Health System, Lawrence, KS

Received March 25, 2021; Accepted for publication July 30, 2021; Published online Nov. 5, 2021
https://doi.org/10.17161/kjm.vol14.15299

ABSTRACT

Introduction. A significant number of preventable catastrophic injuries occur in secondary school athletics. Compliance to Emergency Action Plan (EAP) recommendations is not well documented. The purpose of this systematic review was to identify compliance to EAP recommendations, access to an athletic trainer (AT) and automated external defibrillator (AED), and current legislative mandates in school-based athletics.

Methods. Electronic databases were searched to identify articles that met criteria for inclusion. Studies in English that focused on adoption, implementation, or compliance with EAPs or other national guidelines pertaining to athlete health were eligible for inclusion. Quality and validity were examined in each article and data were grouped based on outcome measures.

Results. Of 12,906 studies, 21 met the criteria for inclusion and full text review. Nine studies demonstrated EAP adoption rates ranging from 55% - 100%. Five studies found that EAPs were rehearsed and reviewed annually in 18.2% - 91.6% of schools that have an EAP. At total of 9.9% of schools were compliant with all 12 National Athletic Trainers Association (NATA) EAP guidelines. A total of 2.5% - 27.5% of schools followed NATA exertional heat illness guidelines and 50% - 81% of schools had access to an athletic trainer. In addition, 61% - 94.4% of schools had an AED available at their athletic venues. Four of 51 state high school athletic association member schools were required to meet best practice standards for EAP implementation, 7 of 51 for AED access, 8 of 51 for heat acclimation, and 3 of 51 for concussion management.

Conclusions. There was a wide range of EAP adoption and a low rate of compliance to EAP guidelines in U.S. schools. Barriers to EAP adoption and compliance were not well documented and additional research should aim to identify impeding and facilitating factors.

Kans J Med 2021;14:282-286

INTRODUCTION

In 2019, nearly 8 million adolescents participated in school-related sporting activities according to the 2018 - 19 High School Athletics Participation Survey conducted by the National Federation of State High School Associations.[1] From 2011 to 2014, the Centers for Disease Control and Prevention reported nearly 5.6 million injuries related to sport or recreation among persons aged 5 - 24.[2] Although the majority of injuries were not life threatening, there were a significant amount of catastrophic and fatal injuries. During the 2017 - 2018 academic year, 99 catastrophic injuries, defined as fatalities, permanent disability injuries, serious injuries (fractured neck or serious head injury) even though the athlete has a full recovery, temporary or transient paralysis, heat stroke due to exercise, or sudden cardiac arrest or sudden cardiac or severe cardiac disruption, occurred in high school and college athletes.[3] Of these, 85 events occurred during or due to sport-related activities, and 66 of 85 sport-related catastrophic injuries were at the high school level.

Implementing emergency action plans (EAPs) likely mitigates athletes' risk of sudden death or catastrophic injury. Professional organizations have published guidelines on emergency preparedness and state high school athletic associations (SHSAA) have issued policies of their own, based on those professional guidelines. Specifically, the National Athletic Trainers' Association (NATA) has published 13 consensus statements endorsed by over 26 organizations on various aspects of emergency health and safety, and sports medicine best practices in collaboration with various inter-association task forces. Most notably, NATA has published a position statement on emergency planning in athletics detailing the 12 best practice guidelines athletic organizations should follow (Table 1).

The American Heart Association (AHA), Sideline Preparedness Collaboration (AAFP, AAOS, ACSM, AMSSM, AOSSM, AOASM), and National Collegiate Athletic Association (NCAA) have published similar documents that align closely with NATA consensus statements.[4-9] It is agreed widely that sports related injuries and medical emergencies are best prevented by implementing and rehearsing a venue specific EAP.[4-9] The goal of this review was to analyze the adoption and compliance of EAP recommendations, access to an athletic trainer (AT) and automated external defibrillator (AED), and current legislative mandates in school based athletics. In addition, we aimed to identify ways to improve compliance to evidence-based guidelines, like those that have been created by the Sideline Preparedness Collaboration, NCAA, AHA, and NATA.

METHODS

A systematic review of the literature was conducted on March 12, 2020, using PubMed, Embase, MEDLINE, Cochrane, CINAHL, and Google Scholar with the following string: Emergency preparedness OR Emergency action plan OR School-based athletics OR Sport injury and illness OR exertional heat illness in sports. After removal of duplicates, articles were screened by abstract and title using our predetermined inclusion and exclusion criteria. Studies were included if the article was written in the English language and focused on adoption and/or compliance with EAPs or other national guidelines pertaining to athlete health. Studies were excluded if they not written in the English language, focused solely on epidemiology in school-based athletics, or did not evaluate adoption or compliance with an EAP or national guideline. The full text of the articles was obtained and evaluated if eligibility could not be assessed from the first screening. Of note, one study included in our results was only available as an abstract.

Article selection was performed by an orthopedic sports medicine fellow (W.M.). In the case of uncertainty regarding inclusion of an article, discrepancies were solved by an experienced sports medicine physician (J.D.). An electronic database search was supplemented by manual search of the reference list of the selected articles.

Table 1. National Athletic Trainers' Association position statement: Best practice recommendations.[4]

1	Each institution or organization that sponsors athletic activities must have a written emergency plan. The emergency plan should be comprehensive and practical, yet flexible enough to adapt to any emergency situation.
2	Emergency plans must be written documents and should be distributed to certified athletic trainers, team and attending physicians, athletic training students, institutional and organizational safety personnel, institutional and organizational administrators, and coaches. The emergency plan should be developed in consultation with local emergency medical services personnel.
3	An emergency plan for athletics identifies the personnel involved in carrying out the emergency plan and outlines the qualifications of those executing the plan. Sports medicine professionals, officials, and coaches should be trained in automatic external defibrillation, cardiopulmonary resuscitation, first aid, and prevention of disease transmission.
4	The emergency plan should specify the equipment needed to carry out the tasks required in the event of an emergency. In addition, the emergency plan should outline the location of the emergency equipment. Further, the equipment available should be appropriate to the level of training of the personnel involved.
5	Establishment of a clear mechanism for communication to appropriate emergency care service providers and identification of the mode of transportation for the injured participant are critical elements of an emergency plan.
6	The emergency plan should be specific to the activity venue. That is, each activity site should have a defined emergency plan that is derived from the overall institutional or organizational policies on emergency planning.
7	Emergency plans should incorporate the emergency care facilities to which the injured individual will be taken. Emergency receiving facilities should be notified in advance of scheduled events and contests. Personnel from the emergency receiving facilities should be included in the development of the emergency plan for the institution or organization.
8	The emergency plan specifies the necessary documentation supporting the implementation and evaluation of the emergency plan. This documentation should identify responsibility for documenting actions taken during the emergency, evaluation of the emergency response, and institutional personnel training.
9	The emergency plan should be reviewed and rehearsed annually, although more frequent review and rehearsal may be necessary. The results of these reviews and rehearsals should be documented and should indicate whether the emergency plan was modified, with further documentation reflecting how the plan was changed.
10	All personnel involved with the organization and sponsorship of athletic activities share a professional responsibility to provide for the emergency care of an injured person, including the development and implementation of an emergency plan.
11	All personnel involved with the organization and sponsorship of athletic activities share a legal duty to develop, implement, and evaluate an emergency plan for all sponsored athletic activities.
12	The emergency plan should be reviewed by the administration and legal counsel of the sponsoring organization or institution.

An electronic form for data extraction was created to analyze the results of the selected articles. Data relating to EAP adoption, compliance with EAP guidelines, access to an AT, access to an AED, or compliance with state mandated guidelines were extracted. Data were grouped into broad categories to account for the wide variety of survey questions in each article. Data were only grouped together if the articles were measuring the same outcome. One limitation of this comparison was the fact that study populations varied between coaches, athletic trainers, and other school staff. We recognized the notable differences between these stakeholders and the fact that this could affect the reliability of comparisons.

RESULTS

A total of 12,906 articles were identified in the initial database search. After duplicates were removed, abstracts were screened for relevance to EAPs based on title and brief summary of abstract. This left 26 articles that were screened using inclusion/exclusion criteria. Five articles were excluded after full text review, these studies focused on epidemiological data. A total of 21 articles remained for full text review, see Figure 1.

Nine studies aimed to identify if schools had adopted a formal EAP and demonstrated EAP adoption rates ranging from 55% - 100% (Figure 2).[10-18]

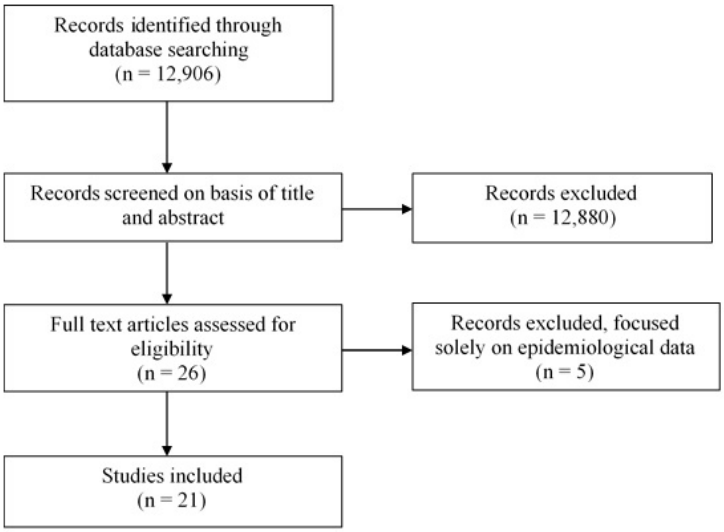


Figure 1. Flow diagram for study selection.

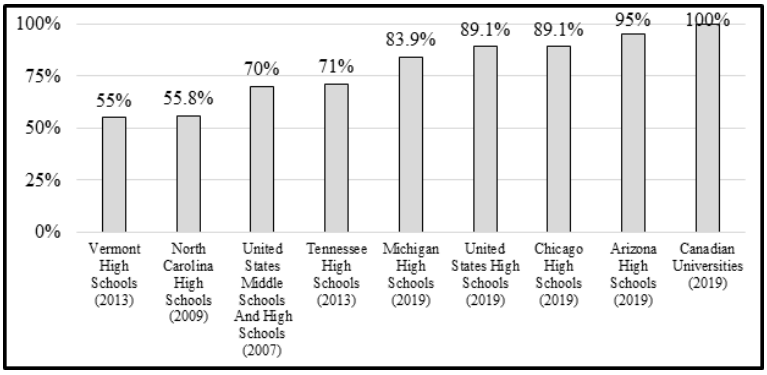


Figure 2. Percentage of schools with a written EAP.[10-18]

One study identified 38% of high schools always having an EAP, while 36% have never had an EAP in place.[19] Five studies found that EAPs were rehearsed and reviewed at least annually in 18.2% - 91.6% of schools that have an EAP.[11,13,15,17,18] Scarneo et al.[16] identified that only 9.9% of schools were compliant with all 12 NATA guidelines, while Meredith et al.[12] found that only 4% of schools were compliant with all three guidelines set forth by the AHA. Two studies identified that 2.5% - 27.5% of schools complied with all Exertional Heat Illness (EHI) guidelines set forth by the NATA.[20,21]

Two studies identified that only 50% - 81% of schools had access to an AT.[11,21] Olympia et al.[13] found that 34% of schools have an AT at all athletic events, while Jones et al.[10] found that only 4.6% of schools had an AT available for medical problems at practices. Nine studies found that 48% - 98% of schools had an AED on campus.[10-12,16-19,23,24] Tennessee had the lowest rate at 48%, while West Virginia high schools had the highest rate of 98% among the states included in the studies.[12,19] Four studies found that 61% - 94.4% of schools had an AED available at all athletic venues.[13-15,19] In 2017, Johnson et al.[22] found that only 56% of Oregon high schools had an AED available for early defibrillation (within four minutes) at all athletic venues. Meredith et al.[12] found that of the 21 sudden cardiac arrest events that occurred in the previous five years in Tennessee high schools, an AED was not available in 10 (48%) and in four cases (19%) the AED was present, but not opened.

A benchmark study was performed in 2018 to identify the extent to which SHSAAs and other state regulations mandate their respective member schools to create health and safety guidelines that align with current best practices.[25] This study showed that only 4 of 51 SHSAA member schools were required to meet best practice standards for EAP adoption, 7 of 51 for AED access, 8 of 51 for heat acclimatization, and 3 of 51 for concussion management.

DISCUSSION

The results of this systematic review supported the hypothesis that there is low EAP adoption (55% - 100%) and compliance (9.9% when using NATA guidelines) with EAP guidelines in schools. This review also identified poor access to ATs (50% - 81%) and AEDs (48% - 98%). Schools with access to ATs were associated with higher rates of EAP adoption and compliance, as well as better access to AEDs and early defibrillation.[11,22] Schools with AEDs were more likely to follow EAP guidelines than those without.[18,24] The EAP adoption rate of schools with at least one AED was 86.5% compared to 47.4% of schools with no AED.[24] This association could indicate that barriers to AED access may be similar to EAP adoption and compliance barriers.

The three most common barriers to AED access were lack of funding, medical-legal reasons (i.e., fear of liability), and lack of certified medical personnel or access to certified medical personnel.[12,17,-19,23,24] AED access is important, but it is also important to have an EAP in place and to have staff trained in first aid and CPR. The barriers to EAP adoption have not been studied, but could include lack of funding, certified medical personnel, appropriate facilities, and continuing education.[19]

Further studies are needed to identify factors that facilitate and impede EAP adoption and compliance, including discussion with ATs, coaches, and other stakeholders. Finally, only 8% of states mandated EAP adoption, 14% mandated AED access, 16% mandated heat acclimation guidelines, and 6% mandated concussion management guidelines.[25] Illinois, Kentucky, Missouri, and North Carolina required all 10 EAP recommendations between SHSAA bylaws and state legislation. The remaining 47 of 51 SHSAAs do not make the EAP recommended guidelines mandatory for participating schools, and there have been a limited number of studies evaluating compliance with the emergency-preparedness best practices.[4,5,9,26] Although states rarely have EAP mandates, Kerr and colleagues[20,21] identified that states with mandated guidelines had better adoption of EHI guidelines than those without. Kerr et al.[27] found that SHSAA mandated heat acclimation guidelines were associated with a 55% reduction in EHI incidence.

Sports related injuries and medical emergencies are best prevented by implementing and rehearsing a venue specific EAP.[4-9] The NATA, AHA, and Sideline Preparedness Collaboration have set forth guidelines and recommendations that athletic organizations should follow to align with sports medicine best practices.

The NATA in conjunction with the Sideline Preparedness Collaboration and the Inter-Association Task Forces advocate for the implementation of EAPs at any institution that sponsors athletic activities.[4,5] These recommendations included having an EAP placed in writing, and that they be distributed to all appropriate personnel, ensured they are incorporated with local emergency medical services, and rehearsed at least annually.[4] The NATA detailed their recommendations for effective EAP implementation in a 12 point explanation and provided evidence-based reasoning to its position statement. This position statement emphasized the importance of implementing EAPs in preventing catastrophic injury and death, and showed that implementation requires three steps: committing an EAP to writing, educating those involved in the plan, and rehearsing the plan.

Most notable of the 13 consensus statements published by NATA are the best practice recommendations for the prevention of sudden cardiac arrest in secondary school athletics programs, and the document on emergency health and safety.[6,7] The former provided detailed information on EAPs, AT services, conditioning sessions, brain and neck injuries, exertional heat stroke, sudden cardiac arrest, and exertional sickling. It emphasized that most deaths in secondary school athletics are avoidable by providing appropriate prevention, recognition, and treatment strategies. This guide also recognized that supervisors of secondary school athletics programs would benefit from AT services to meet the increasing requirements of health policies and mandates.[6] The latter provided the strength of recommendation and level of evidence to each of the policies and guidelines they recommended. This document served as a guide for national governing bodies for youth sports.[7] These consensus statements and an updated list of endorsing organizations can be found at https://www.nata.org/news-publications/pressroom/statements/consensus.

The Sideline Preparedness Collaboration advocated understanding and practicing specific prevention measures for sports related injury/illness and provided guidelines to help team physicians implement

these prevention strategies.[5] In agreement with the NATA and the Sideline Preparedness Collaborations' stance on EAP implementation, the NCAA released its Inter-Association Recommendations in July 2019.[8] These recommendations emphasized that at a minimum, EAPs should be developed for head and neck injury, cardiac arrest, heat illness and heat stroke, exertional rhabdomyolysis, exertional collapse associated with sickle cell trait, any exertional or non-exertional collapse, asthma, diabetic emergency, and mental health emergency. The NCAA also emphasized that EAPs should be consistent with their concussion safety protocol checklist.[8] Overall, most deaths in sports are deemed preventable and the Inter-Association Task Forces' charge was to meet this expectation.[6-8]

The AHA is a leader among these organizations in advocating for the importance of AED availability.[9] Their stance is predicated on AED availability being crucial in the response to sudden cardiac arrest as neurological outcomes are compromised by every minute without appropriate treatment. Although the AHA recommended that state laws and regulations require schools to have a cardiac emergency response plan, including the availability of an AED, only seventeen out of fifty states (34%) had some legislation that require AED installation in schools.[9,26] In addition, only one state required AED installation in all public grade schools, private schools, and colleges.[26]

CONCLUSIONS

Emergency Action Planning is an important preventative measure for high schools to take to protect their athletes from sports related injuries and illness. The results of this study showed that there is a wide range of EAP adoption across U.S. high schools and a low rate of EAP compliance with NATA/AHA guidelines. In addition, there is poor access to athletic trainers and AEDs in high schools, which may hinder EAP implementation and compliance. One common barrier to AED access was due to costs; to address this, states may need to allocate more funding to high schools to allow them to be fully compliant with AHA recommendations. There also seems to be low percentage of states mandating best practice recommendations for the prevention of the leading causes of sudden death and concussion management. Advocating for the implementation of state mandates may improve high school EAP compliance which would improve prevention of sports related injury or illness in high school athletics as well as improvement in outcomes of sudden cardiac arrest in high schools. In conclusion, given the widely accepted recommendations by multiple respected organizations, EAP for sport related injury and illness should be a top priority for all athletic organizations to ensure the utmost safety of our athletes.

REFERENCES

[1] Niehoff KL. 2019-20 NFHS Handbook. Indianapolis: National Federation of State High School Associations, 2019.
[2] Sheu Y, Chen LH, Hedegaard H. Sports-and recreation-related injury episodes in the United States, 2011-2014. Natl Health Stat Report 2016, 99:1-12. PMID: 27906643.
[3] National Center for Catastrophic Sport Injury Research. Catastrophic Sports Injury Research: Thirty-Sixth Annual Report Fall 1982 - Spring 2018. October 3, 2019. https://nccsir.unc.edu/wp-content/uploads/sites/5614/2019/10/2018-Catastrophic-Report-AS-36th-AY2017-2018-FINAL.pdf. Accessed April 6, 2021.
[4] Andersen J, Courson RW, Kleiner DM, McLoda TA. National Athletic Trainers' Association Position Statement: Emergency Planning in Athletics. J Athl Train 2002; 37(1):99-104. PMID: 12937447.
[5] Selected issues in injury and illness prevention and the team physician: A consensus statement. Med Sci Sports Exerc 2016; 48(1):159-171. PMID: 26671311.
[6] Casa DJ, Almquist J, Anderson SA, et al. The inter-association task force for preventing sudden death in secondary school athletics programs: Best-practices recommendations. J Athl Train 2013; 48(4):546-553. PMID: 23742253.
[7] Huggins RA, Scarneo SE, Casa DJ, et al. The inter-association task force document on emergency health and safety: Best-practice recommendations for youth sports leagues. J Athl Train 2017; 52(4):384-400. PMID: 28430552.
[8] Parsons JT, Anderson SA, Casa DJ, Hainline B. Preventing catastrophic injury and death in collegiate athletes: Interassociation recommendations endorsed by 13 medical and sports medicine organisations. Br J Sports Med 2020; 54(4):208-215. PMID: 31537549.
[9] Rose K, Goble MM, Berger S, et al. Cardiac emergency response planning for schools: A policy statement. NASN Sch Nurse 2016; 31(5):263-270. PMID: 27486226.
[10] Jones NS, Wieschhaus K, Martin B, Tonino PM. Medical supervision of high school athletics in Chicago: A follow-up study. Orthop J Sports Med 2019; 7(8):2325967119862503. PMID: 31448300.
[11] McLeod TCV, Cardenas JF. Emergency preparedness of secondary school athletic programs in Arizona. J Athl Train 2019; 54(2):133-141. PMID: 30517023.
[12] Meredith ML, Watson AM, Gregory A, Givens TG, Abramo TJ, Kannankeril PJ. Sudden cardiac arrests, automated external defibrillators, and medical emergency response plans in Tennessee high schools. Pediatr Emerg Care 2013; 29(3):352-356. PMID: 23426252.
[13] Olympia RP, Dixon T, Brady J, Avner JR. Emergency planning in school-based athletics: A national survey of athletic trainers. Pediatr Emerg Care 2007; 23(10):703-708. PMID: 18090101.
[14] Post EG, Schaefer DA, Biese KM, et al. A comparison of emergency preparedness between high school coaches and club sport coaches. J Athl Train 2019; 54(10):1074-1082. PMID: 31633408.
[15] Reagan J, Moulson N, Velghe J, et al. Automated external defibrillator and emergency action plan preparedness amongst Canadian university athletics. Can J Cardiol 2019; 35(1):92-95. PMID: 30595187.
[16] Scarneo SE, DiStefano LJ, Stearns RL, Register-Mihalik JK, Denegar CR, Casa DJ. Emergency action planning in secondary school athletics: A comprehensive evaluation of current adoption of best practice standards. J Athl Train 2019; 54(1):99-105. PMID: 30676786.
[17] Wasilko SM, Lisle DK. Automated external defibrillators and emergency planning for sudden cardiac arrest in Vermont high schools: A rural state's perspective. Sports Health 2013; 5(6):548-552. PMID: 24427431.
[18] Monroe A, Rosenbaum DA, Davis S. Emergency planning for sudden cardiac events in North Carolina high schools. N C Med J 2009; 70(3):198-204. PMID: 19653601.
[19] Schneider K, Meeteer W, Nolan JA, Campbell HD. Health care in high school athletics in West Virginia. Rural Remote Health 2017; 17(1):3879. PMID: 28257612.
[20] Kerr ZY, Marshall SW, Comstock RD, Casa DJ. Implementing exertional heat illness prevention strategies in US high school football. Med Sci Sports Exerc 2014; 46(1):124-130. PMID: 24346190.
[21] Kerr ZY, Scarneo-Miller SE, Yeargin SW, et al. Exertional heat-stroke preparedness in high school football by region and state mandate presence. J Athl Train 2019; 54(9):921-928. PMID: 31454289.
[22] Johnson ST, Norcross MF, Bovbjerg VE, Hoffman MA, Chang E, Koester MC. Sports-related emergency preparedness in Oregon high schools. Sports Health 2017; 9(2):181-184. PMID: 28129072.

[23] Rothmier JD, Drezner JA, Harmon KG. Automated external defibrillators in Washington State high schools. Br J Sports Med 2007; 41(5):301-305; discussion 305. PMID: 17289857.
[24] Toresdahl BG, Harmon KG, Drezner JA. High school automated external defibrillator programs as markers of emergency preparedness for sudden cardiac arrest. J Athl Train 2013; 48(2):242-247. PMID: 23672389.
[25] Adams WM, Scarneo SE, Casa DJ. Assessment of evidence-based health and safety policies on sudden death and concussion management in secondary school athletics: A benchmark study. J Athl Train 2018; 53(8):756-767. PMID: 30212234.
[26] Sherrid MV, Aagaard P, Serrato S, et al. State requirements for automated external defibrillators in American schools: Framing the debate about legislative action. J Am Coll Cardiol 2017; 69(13):1735-1743. PMID: 28359520.
[27] Kerr ZY, Register-Mihalik JK, Pryor RR, et al. The association between mandated preseason heat acclimatization guidelines and exertional heat illness during preseason high school American football practices. Environ Health Perspect 2019; 127(4):47003. PMID: 30969138.

Keywords: sports medicine, athletic injuries, youth sports, team sports

KANSAS JOURNAL of MEDICINE

Clot in Transit and Pulmonary Artery Percutaneous Mechanical Thrombectomy

Scott E. Janus, M.D.[1], Jamal Hajjari, M.D.[1], Tarek Chami, M.D.[1], Mohamad Karnib, M.D.[1], Mohammed Najeeb Osman, M.D.[1,2]
[1]University Hospital Cleveland Medical Center, Cleveland, OH
Harrington Heart and Vascular Institute
[2]Case Western Reserve University, Cleveland, OH
Department of Medicine

Received June 8, 2021; Accepted for publication July 20, 2021; Published online Nov. 5, 2021
https://doi.org/10.17161/kjm.vol14.15601

INTRODUCTION

Despite an abundance of literature supporting percutaneous mechanical thrombectomy of pulmonary embolism (PE), only a limited number of case reports in the literature attest to the utility of percutaneous mechanical thrombectomy for clot in transit.[1,2] With a recent U.S. Food and Drug Administration (FDA) approval for the FlowTriever® system for percutaneous mechanical thrombectomy for clot in transit,[3] we present a dramatic case with recent trimalleolar fracture, having undergone open reduction and internal fixation, post-operative course being complicated by extensive deep vein thrombosis with resultant pulmonary embolism and clot in transit which was extracted successfully using the percutaneous mechanical thrombectomy FlowTriever® system.

CASE REPORT

A 59-year-old male with past medical history of atrial fibrillation on rivaroxaban, hypertension, morbid obesity, and heart failure with preserved ejection fraction presented with shortness of breath after being discharged from a same day surgical facility for a malleolar fracture repair. He had a fall and suffered a trimalleolar ankle fracture. After holding his rivaroxaban for three days prior to surgery, he underwent internal fixation of the left trimalleolar ankle fracture and was discharged the same day.

Upon trying to exit his car at a fast-food restaurant, the patient had severe shortness of breath and was brought to the emergency room. In the emergency room, he was tachycardic with a heart rate of 137 beats per minute, blood pressure of 95/61 mmHg, and respiratory rate of 18 per minute with an oxygen saturation 96% on 4 liters by nasal cannula. His exam was significant for clear lungs bilaterally, but with increased effort for breathing. Heart examination was irregular without any significant murmurs. He had 1+ edema bilaterally. The differential diagnosis included pulmonary embolism, fat embolism, acute coronary syndrome, and aortic dissection.

Electrocardiogram revealed atrial fibrillation with rapid ventricular rate and low voltage (Figure 1). His blood work was significant for a hemoglobin 13.9 g/dL, white blood cell count of 8.2 x 109/L, platelet count of 137 x 109/L, and creatinine of 1.19 mg/dL. Troponin I returned at 0.04 ng/mL along with an elevated whole blood lactate 5.1 mmol/L. Due to concern for pulmonary embolism, he underwent computed tomography angiogram of the chest which demonstrated a large thrombus burden in the right and left pulmonary arteries with extension into the segmental branches of the left upper, left lower, right lower, and right middle lobes (Figure 2, Video 1) along with an impressive clot in transit in the right atrium (Figure 3). The clot in transit was passing in/out of the tricuspid valve and not attached to any intracardiac structure. The pulmonary embolism response (PERT) team was activated. Given the recent surgery and extensive clot in transit, systemic thrombolysis was avoided despite borderline hemodynamics. He was brought to the catheterization lab where he underwent echocardiography-guided (Figure 4, Video 2) extirpation of the clot in transit (Video 3) and from bilateral pulmonary arteries (Figure 5). [Videos are only available on the website: journals.ku.edu/kjm].

A post procedure echocardiogram (Figure 6, Video 4) demonstrated resolution of the clot in transit in the right atrium, along with dramatic improvement in hemodynamics with heart rate of 79 beats per minute, respiratory rate of 15 per minute, saturating 98% without requiring supplemental oxygen, and blood pressure of 122/99 mmHg. He underwent bilateral lower extremity duplex which showed acute occlusive deep vein thrombosis in the right popliteal and posterior tibial veins. He was started on warfarin with heparin bridging following the procedure. He was discharged on day five, and a plan for a vascular medicine follow-up for hypercoagulable workup as an outpatient.

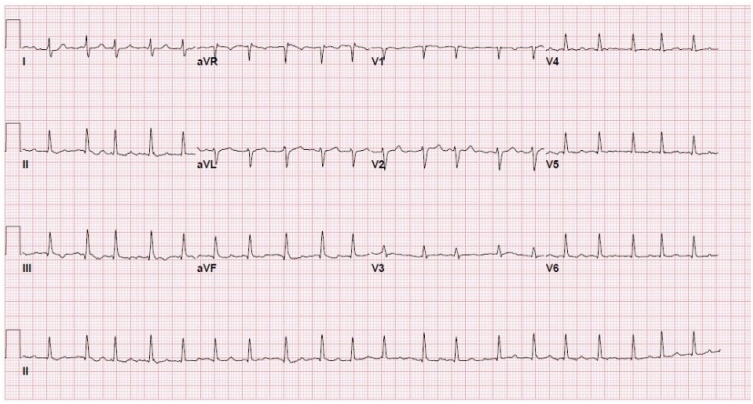


Figure 1. Electrocardiogram demonstrates atrial fibrillation with rapid ventricular rate with S1, T3 inversion.

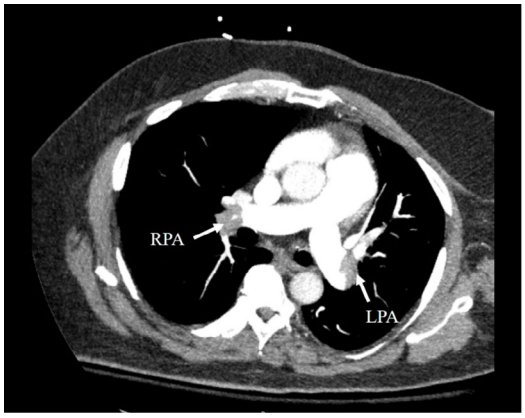


Figure 2. Computed tomography angiogram of chest (pulmonary embolism protocol) demonstrates large bilateral pulmonary artery embolisms (RPA right pulmonary artery; LPA left pulmonary artery).

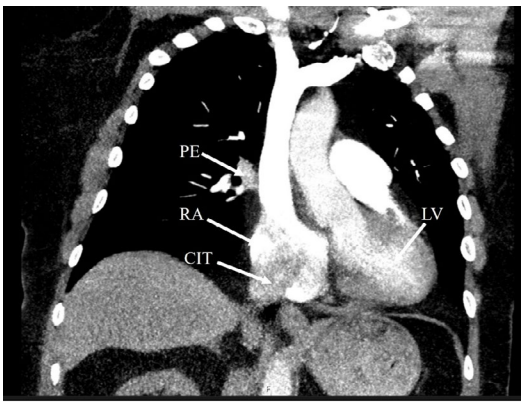


Figure 3. Computed tomography angiogram of chest (pulmonary embolism protocol) demonstrates large clot in transit (CIT), PE (pulmonary embolism), LV (left ventricle), RA (Right atrium).

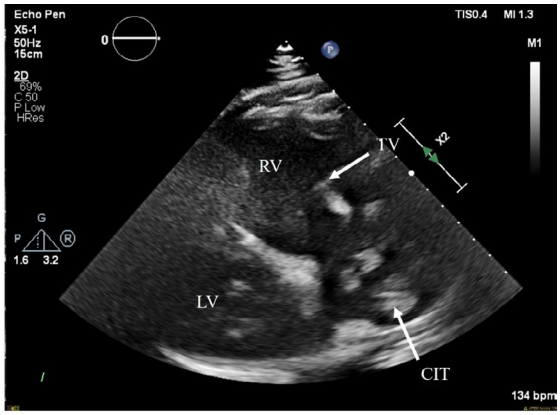


Figure 4. Echocardiogram, right ventricle tilt view demonstrates clot in transit (CIT), TV (tricuspid valve), RV (right ventricle), LV (left ventricle).

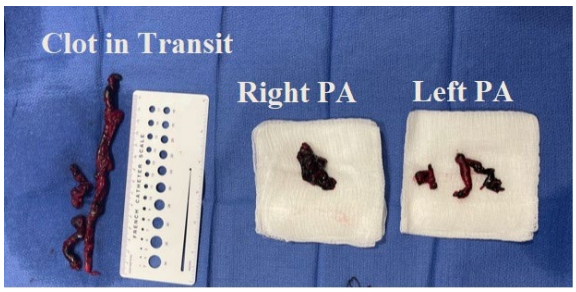


Figure 5. Clot in Transit, Right PA (Pulmonary artery), and Left PA (Pulmonary artery).

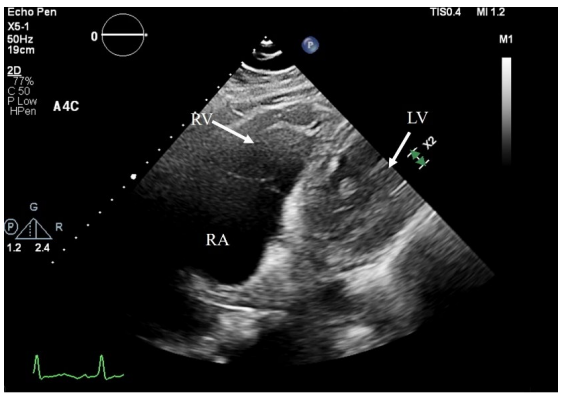


Figure 6. Echocardiogram post procedure demonstrates resolution of the clot in transit, TV (tricuspid valve), RV (right ventricle), and LV (left ventricle).

DISCUSSION

This case demonstrated safe application of percutaneous mechanical thrombectomy in a patient with a clot in transit in the right atrium. While percutaneous mechanical thrombectomy has revolutionized the treatment of pulmonary embolism,[4] relatively little data exist on the safety and efficacy of the utility of percutaneous therapies for clot in transit (CIT).[1] Despite obtaining FDA approval,[3] this application of the FlowTriever® system remains under-described and is vitally important to be recognized.

CIT presents a challenging decision for physicians. While systemic tissue plasminogen activator (TPA) is an option, intracranial hemorrhage and distal embolization of the clot are significant limitations. Percutaneous options avoid cardiopulmonary bypass and the high bleeding risks associated with surgical thrombectomy and systemic TPA.[3] The FLARE (FlowTriever Pulmonary Embolectomy Clinical Study) demonstrated the effectiveness and safety of the percutaneous therapy in pulmonary embolism.[4] This, in combination with utilization of ultrasound guided (radiation free) aspiration of CIT, allows percutaneous mechanical thrombectomy therapies an attractive niche for CIT. This is important especially in the postoperative patient population, where thrombolysis and/or even simple therapeutic anticoagulation compounds the risks.

Similar to our patient, intermediate to higher risk PE patients present diagnostic and therapeutic dilemmas for physicians. While the extremes of acutely unstable patients warrant systemic thrombolytic therapy and low risk patients can be managed safely solely with anticoagulation, these intermediate to higher risk patients require thoughtful consideration and ideally, utilization of a multidisciplinary pulmonary embolism response team.[5] Recent data increasingly support the safety and efficacy of large bore aspiration for acute thromboembolism.[6] Wible et al.[6] found up to a 100% technical success with the device and over 70% of patients required less oxygen following the procedure. They highlighted the low rate of adverse events (3.8%, mainly driven by respiratory deterioration) with zero device related complications, furthering the evidence for the utility of the device for acute thromboembolism.

CONCLUSIONS

Due to the limited literature regarding percutaneous extirpation of clot in transit, this dramatic case of hemodynamic and clinical improvement was presented. Several learning points are notable. Clot in transit creates a challenging therapeutic decision for physicians. Percutaneous mechanical thrombectomy has the potential to revolutionize the treatment of thromboembolism in transit and should continue to gain momentum given the safety and efficacy of the device.

REFERENCES

[1] Verma I, Chang EY, Kumar G, Sachdeva R. Catheter directed embolectomy of right atrial clot in transit-A case series. Catheter Cardiovasc Interv 2021; 97(5):869-873. PMID: 33226187.

[2] Abdel-hafez O, Salih M, Aloka F, Patel K. Intravascular ultrasound-guided mechanical thrombectomy using the INARI ClotTriever device of an iatrogenic deep venous thrombosis. BMJ Case Rep 2020; 13(7):e235464. PMID: 32675124.

[3] Giri J, Sista AK, Weinberg I, et al. Interventional therapies for acute pulmonary embolism: Current status and principles for the development of novel evidence: A scientific statement from the American Heart Association. Circulation 2019: e774-e801. PMID: 31585051.

[4] Tu T, Toma C, Tapson VF, et al. A prospective, single-arm, multicenter trial of catheter-directed mechanical thrombectomy for intermediate-risk acute pulmonary embolism: The FLARE study. JACC Cardiovasc Interv 2019; 12(9):859-869. PMID: 31072507.
[5] Chaudhury P, Gadre SK, Schneider E, et al. Impact of multidisciplinary pulmonary embolism response team availability on management and outcomes. Am J Cardiol 2019; 124(9):1465-1469. PMID: 31495443.
[6] Wible BC, Buckley JR, Cho KH, Bunte MC, Saucier NA, Borsa JJ. Safety and efficacy of acute pulmonary embolism treated via large-bore aspiration mechanical thrombectomy using the Inari FlowTriever device. J Vasc Interv Radiol 2019; 30:1370-1375. PMID: 31375449.

Keywords: percutaneous aspiration thrombectomy, pulmonary embolism, deep vein thrombosis

KANSAS JOURNAL of MEDICINE

Brushing Up on Brush Borders: Intestinal Spirochetosis Diagnosis and Management

Joy E. Fesen, M.D.[1], Ethar K. Al-Husseinawi, MBChB[2], Jessica R. Newman, D.O.[3]
[1]Tulane University School of Medicine, New Orleans, LA
Department of Internal Medicine
University of Kansas Medical Center, Kansas City, KS
[2]Department of Pathology
[3]Department of Internal Medicine, Division of Infectious Diseases

Received May 27, 2021; Accepted for publication July 28, 2021; Published online Nov. 5, 2021
https://doi.org/10.17161/kjm.vol14.15535

INTRODUCTION

Intestinal spirochetosis was first described in 1967.[1] Diagnosis is based on colon biopsy histology where spirochetal microorganisms are found attached to the apical cell membrane of colorectal epithelium as a pseudo-brush border. Higher risk groups include those living in poorly developed nations, persons living with human immunodeficiency virus (HIV), and men who have sex with men.[2] Symptoms most commonly associated with adult cases of intestinal spirochetosis include abdominal pain with watery diarrhea.[3] Adolescent cases of intestinal spirochetosis may present with nausea and failure to thrive, along with diarrhea.[4] Many case patients are asymptomatic.

This case highlighted a patient diagnosed with intestinal spirochetosis after years of nonspecific abdominal symptoms. The diagnosis of this rare condition requires ruling out common etiologies and a detailed inspection of colon biopsy histology.

CASE REPORT

A 46-year-old man with HIV infection and exocrine pancreatic insufficiency was referred for colonoscopy with symptoms of intermittent diffuse abdominal cramping, nausea, and diarrhea of unexplained origin for several years. He had no improvement with lipase-protease-amylase capsules for pancreatic enzyme replacement (taken as two capsules three times daily with meals and one capsule with snacks). His work-up included negative *Clostridium difficile* PCR, *Giardia* and *Cryptosporidium* fecal antigens, stool culture, stool acid fast stain (no cyclospora, cryptosporidium or isospora seen), and syphilis antibody. The patient had a normal complete blood count with differential, thyroid stimulating hormone level and fecal fat percentage on two random collections, tissue transglutaminase antibody level, vitamin B12 level, and vitamin D (25-OH) total. At the time of his planned procedure, the patient denied fever, chills, night sweats, unintentional weight loss, vomiting, hematochezia, and melena. Otherwise, his recent review of systems was unremarkable.

The patient did not use tobacco, alcohol, or recreational drugs. He lived in a house with his son and denied sexual partners for several years, though in the remote past had male and female partners. He had no recent travel history though had been to Iraq and the desert southwest United States in the past. He was not working. He had no animal exposures aside from dogs. He did not consume raw meat or uncooked shellfish. He had not been swimming in the recent past.

On physical examination, the patient was afebrile and in no distress. Cardiac, pulmonary, and abdominal examinations demonstrated no abnormal findings. His most recent absolute CD4+ T-cell count was 140 cells/μL with an HIV viral load of 37,700 copies/mL. Serum white blood cell count was normal. Computed tomography scan of the abdomen and pelvis with contrast demonstrated homogeneous enhancement of the pancreas without mass, ductal dilation, parenchymal calcification, or peripancreatic inflammatory changes. He had normal caliber small bowel and colon, and a normal appendix with no free fluid or mesenteric lymphadenopathy. There was a tiny nonobstructive right renal calculus.

Colonoscopy revealed a normal appearance of the colon. Biopsy of colonic mucosa was performed, demonstrating no active inflammation or architectural distortion. On histologic examination, typical organisms were found adherent to the surface epithelium as a pseudo-brush border (Figure 1). A Warthin-Starry stain highlighted the organisms (Figure 2).

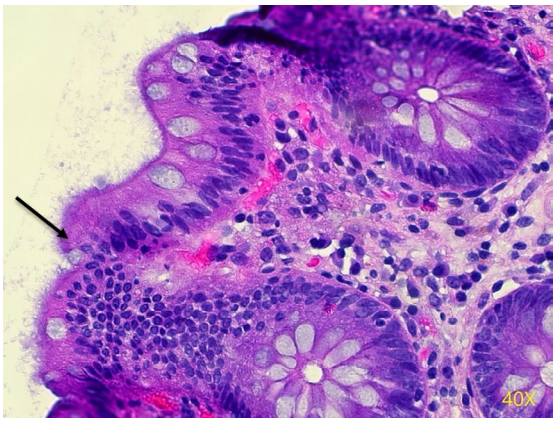


Figure 1. Typical organisms were found adherent to the surface epithelium as a pseudo-brush border.

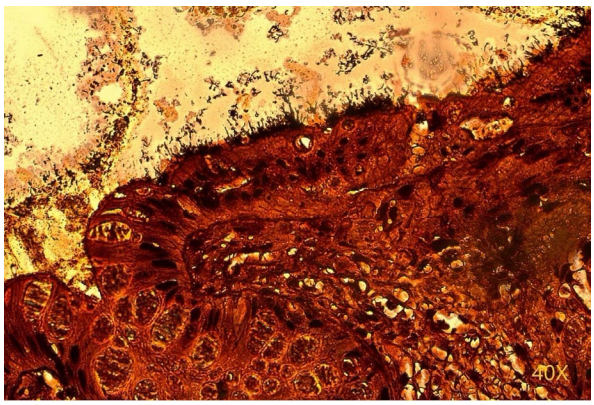


Figure 2. A Warthin-Starry stain highlighted the typical organisms.

This patient with HIV infection, a low CD4+ cell count, a lengthy history of abdominal cramping, nausea, and diarrhea without definitive alternative diagnosis, and normal findings on colonoscopy was found via colonic biopsy to have spirochetal organisms adherent to the surface of the colonic mucosa. These findings were consistent with a diagnosis of intestinal spirochetosis. The patient was prescribed a seven day course of metronidazole. One month following the therapy, he had subjective improvement in cramping abdominal pain as well as improvement in both quantity and consistency of his loose stools.

DISCUSSION

Spirochetes are classified into *Spirochaetaceae*, *Leptospiraceae*, and *Brachyspiraceae* based on morphologic and phylogenetic differences.[2] *Brachyspiraceae* species *Brachyspira pilosicoli* and *Brachyspira aalborgi* are the most commonly identified organisms in human intestinal spirochetosis.[5] These fastidious anaerobes grow between 6 and 14 days at around 38.5°C on artificial culture media and brain heart infusion agar with 10% bovine blood and spectinomycin plus polymyxin B, respectively.[6,7] Their main host species include pigs and chickens, where they can cause diarrhea, failure to thrive, and delayed egg production. The bacteria are shed in feces leading to the proposed mechanism of infection being transmission by the fecal-oral route or exposure to contaminated water with higher colonization rates in developing countries.[8,9] When observed with in vitro antimicrobial susceptibility of *Brachyspira pilosicoli*, the pathogen has been found to be susceptible to metronidazole, ceftriaxone, meropenem, tetracycline, moxifloxacin, and chloramphenicol.[10] Most published case series recommend metronidazole as an initial treatment.[2,11,12]

Some debate exists regarding whether intestinal spirochetosis is a disease process or merely intestinal colonization.[13] One reason for this uncertainty is the high incidence of coinfection with other enteric bacteria.[14] In some case series, risks such as men who have sex with men, HIV virus infection, and co-infection with *Neisseria gonorrhoeae* or *Chlamydia trachomatis* were suggested.[15] In one series looking at 20 cases, 70% had CD4 lymphocyte cells >200/microL.[15] In a large series investigating colorectal biopsies in Japan, there was a slightly higher incidence of intestinal spirochetosis in patient with HIV.[16] Visualization of mucosa with colonoscopy contributed little to diagnosis, as the findings rarely correlated with disease severity, but can be used to rule out other pathologies.

Intestinal spirochetosis has been identified from proximal colon to rectum and within the vermiform appendix.[2] Diagnosis is made with biopsy. Histology findings along the intercryptal epithelial layer show diffuse blue fringe on hematoxylin-eosin stain. Spirochetes subsequently can be visualized on Warthin-Starry or Dieterle silver impregnation stains.[1,2] The proposed pathogenic mechanism for diarrhea associated with this disease is microvillus destruction caused by spirochetal attachment.[17] Furthermore, when a significant population of enterocytes become attached it may lead to a physical restriction of electrolyte and water resorption adding to diarrhea.[8]

In our patient, it was difficult to confirm if the spirochetes were pathogenic. In the months subsequent to the diagnosis, he had recurrent diarrhea that improved without intervention and an additional episode that improved with a repeat short course of metronidazole.

CONCLUSIONS

Diagnosis of intestinal spirochetosis should be considered for a patient with unexplained chronic, watery diarrhea and abdominal pain, particularly in a patient with HIV infection. Work-up should include a thorough review of history, *Clostridium difficile* PCR, *Cryptosporidium* and *Giardia* fecal antigen testing, and colonoscopy to rule out alternative diagnoses. Diagnosis of intestinal spirochetosis can be confirmed with biopsies of colonic mucosa viewed on Warthin-Starry stain which will reveal spirochetal organisms adherent to mucosa surface. Patients with intestinal spirochetosis can be treated with a course of metronidazole, although symptoms may resolve spontaneously.

ACKNOWLEDGEMENTS

Full informed consent was obtained from the patient for the publication of his information and imaging.

We thank Dr. John Bonino in the Division of Gastroenterology, Department of Internal Medicine at the University of Kansas Medical Center for his aid in the clinical care of this patient. We also would like to extend thanks to Dr. Stephanie Wood in the Department of Pathology at the University of Kansas Medical Center for her assistance in the preparation and interpretation of the biopsy specimen.

REFERENCES

1 Harland WA, Lee FD, Krasewski A, Gordon J, McSeveney D. Intestinal spirochaetosis. Gut 1971; 12(2):126-133. PMID: 5548558.
2 Tsinganou E, Gebbers JO. Human intestinal spirochetosis - A review. Ger Med Sci 2010; 8:Doc01. PMID: 20200654.
3 Körner M, Gebbers JO. Clinical significance of human intestinal spirochetosis - A morphologic approach. Infection 2003; 31(5):341-349. PMID: 14556061.
4 Koteish A, Kannangai R, Abraham SC, Torbenson M. Colonic spirochetosis in children and adults. Am J Clin Pathol 2003; 120(6):828-832. PMID: 14671970.
5 Lee JI, Hampson DJ. Genetic characterisation of intestinal spirochaetes and their association with disease. J Med Microbiol 1994; 40(5):365–371. PMID: 8176724.
6 Mikosza AS, La T, de Boer WB, Hampson DJ. Comparative prevalences of Brachyspira aalborgi and Brachyspira (Serpulina) pilosicoli as etiologic agents of histologically identified intestinal spirochetosis in Australia. J Clin Microbiol 2001; 39(1):347-350. PMID: 11136797.
7 Brooke CJ, Riley TV, Hampson DJ. Evaluation of selective media for the isolation of Brachyspira aalborgi from human faeces. J Med Microbiol 2003; 52(Pt 6):509-513. PMID: 12748271.
8 Hampson DJ. The spirochete Brachyspira pilosicoli, enteric pathogen of animals and humans. Clin Microbiol Rev 2017; 31(1):e00087-17. PMID: 29187397.
9 Gebbers JO, Marder HP. Human intestinal spirochetosis: Unusual findings. Microecol Therap 1989; 18:214-252.
10 Brooke CJ, Hampson DJ, Riley TV. In vitro antimicrobial susceptibility of Brachyspira pilosicoli isolates from humans. Antimicrob Agents Chemother 2003; 47(7):2354-2357. PMID: 12821498.
11 Peghini PL, Guccion JG, Sharma A. Improvement of chronic diarrhea after treatment for intestinal spirochetosis. Dig Dis Sci 2000; 45(5):1006-1010. PMID: 10795768.
12 Surawicz CM, Roberts PL, Rompalo A, Quinn TC, Holmes KK, Stamm WE. Intestinal spirochetosis in homosexual men. Am J Med 1987; 82(3 Spec No):587-592. PMID: 3826122.
13 Erikson LA, Torbenson MS. Intestinal spirochetosis. Mayo Clin Proc 2020; 95(2):427-428. PMID: 32029097.
14 Garcia-Hernandez D, Vall-Mayans M, Coll-Estrada S, et al. Human intestinal spirochetosis, a sexually transmissible infection? Review of six cases from two sexually transmitted infection centres in Barcelona. Int J STD AIDS 2021; 32(1):52-58. PMID: 33232216.
15 Ena J, Simón-Aylón A, Pasquau F. Intestinal spirochetosis as a cause of chronic diarrhoea in patients with HIV infection: Case report and review of the literature. Int J STD AIDS 2009; 20(11):803-805. PMID: 19843615.
16 Tateishi Y, Takahashi M, Horiguchi S, et al. Clinicopathologic study of intestinal spirochetosis in Japan with special reference to human immunodeficiency virus infection status and species types: Analysis of 5265 consecutive colorectal biopsies. BMC Infect Dis 2015; 15:13. PMID: 25582884.
17 Rodgers FG, Rodgers C, Shelton AP, Hawkey CJ. Proposed pathogenic mechanism for the diarrhea associated with human intestinal spirochetes. Am J Clin Pathol 1986; 86(5):679-682. PMID: 3776923.

Keywords: infectious disease, gastroenterology, microbiology, brush border, spirochete infection

KANSAS JOURNAL of MEDICINE

KANSAS JOURNAL OF MEDICINE

VOLUME 14 • 2021

Have a manuscript ready to publish?
Visit our website for instructions on submitting a manuscript.

journals.ku.edu/kjm

Office of Research
1010 N. Kansas, Wichita, KS 67214
316-293-2617 • Email: kjm@kumc.edu

VOLUME 14 • 2021

WHAT'S INSIDE: ORIGINAL RESEARCH • CASE REPORT • IMAGES

KANSAS JOURNAL of MEDICINE

TABLE OF CONTENTS

KANSAS JOURNAL of MEDICINE

Rural-Urban Differences in Esophagectomy for Cancer

Joseph G. Brungardt, M.D.[1], Omar A. Almoghrabi, M.D.[2], Carolyn B. Moore, M.D.[2], G. John Chen, M.D., Ph.D., MPH[1], Alykhan S. Nagji, M.D.[2]
University of Kansas Medical Center, Kansas City, KS
[1]Department of Surgery
[3]Department of Cardiothoracic Surgery

Received June 7, 2021; Accepted for publication Aug. 24, 2021; Published online Dec. 2, 2021
https://doi.org/10.17161/kjm.vol14.15597

ABSTRACT

Introduction. Patients who are disadvantaged socioeconomically or live in rural areas may not pursue surgery at high-volume centers where outcomes are better for some complex procedures. The objective of this study was to compare rural and urban patient differences directly by location of residence and outcomes after undergoing esophagectomy for cancer.

Methods. An analysis of the Healthcare Cost and Utilization Project National Inpatient Sample (HCUP-NIS) database was performed, capturing adult patients with esophageal cancer who underwent esophagectomy. Patients were stratified into rural or urban groups by the National Center for Health Statistics Urban-Rural Classification Scheme. Demographics, hospital variables, and outcomes were compared.

Results. A total of 2,877 patients undergoing esophagectomy for esophageal cancer were captured by the database, with 228 (7.92%) rural and 2,575 (89.50%) urban patients. The rural and urban groups had no differences in age, race, and insurance status, and shared many common comorbidities. Major outcomes of mortality (3.95% versus 4.27%, p = 0.815) and length of stay (15.75 ± 13.22 vs. 15.55 ± 14.91 days, p = 0.828) were similar for both rural and urban patients. There was a trend for rural patients to more likely be discharged home (35.96% vs. 29.79%, OR 0.667 [95% CI 0.479 - 0.929]; p = 0.0167).

Conclusions. This retrospective administrative database study indicated that rural and urban patients received equivalent postoperative care after undergoing esophagectomy. The findings were reassuring as there did not appear to be a disparity in major outcomes depending on the location of residence, but further studies are necessary to assure equitable treatment for rural patients. ***Kans J Med 2021;14:292-297***

INTRODUCTION

Multiple studies have captured the differences between patients with surgical problems who reside in rural versus urban environments.[1-5] Unfortunately, there are fewer data on rural-urban differences within the U.S. on the subject of esophageal cancer and esophagectomy outcomes. Substantial evidence supports decreased mortality in those patients undergoing high-risk surgical procedures at high-volume hospitals compared to low-volume hospitals, which would suggest rural patients should receive their complex surgery at high-volume centers.[6] While some worry the centralization of complex surgeries would impact the financial security of rural institutions negatively, this impact may be negligible.[7] Others described this regionalization leading to difficulty in receiving complex cancer care.[8,9] Fuchs et al.[10] studied the Nationwide Inpatient Sample, but did not include an analysis of rural patients, finding mortality elevated among low and intermediate-volume hospitals compared to high-volume hospitals. Schlottmann and colleagues[11] concluded that centralization of care occurred in the U.S., but did not analyze patients residing in rural areas. While increased travel distance has been associated with improved survival, the reason for this is not well defined.[12] Additionally, Song et al.[13] reported on trends in complex cancer operations nationally using the NIS database, but like other studies, it did not dive into the problem of rural-urban outcomes and differences. Instead, they looked at hospital and procedure-based outcomes rather than patient populations.

Direct comparisons of rural and urban patient populations are lacking. A Canadian study found that patients from rural areas had similar outcomes regardless of the volume of the surgical center, but they were more likely to travel farther for esophageal surgery, indicating regionalization.[14] The epidemiologic trends in esophageal cancer in China have been studied, noting rural-urban differences in incidence and mortality.[15,16] Within the U.S., those who are disadvantaged socioeconomically and live in rural areas may not pursue surgery for esophageal cancer at high-volume cancer accredited centers, where outcomes were better for some procedures.[17] While center volume and travel distance have been used as surrogates for rural patient outcomes and to indicate the best treatment pathway for rural patients, little direct comparison of rural and urban patients exists, especially in the esophageal cancer population.

METHODS

Data from 2010 to 2014 from the Health Care Cost and Utilization Project National Inpatient Sample (HCUP-NIS) were used.[18] These were adult patients (at least 18 years of age), undergoing esophagectomy for esophageal cancer, as identified by the International Classification of Diseases (ICD) codes.[19] Patients in a rural setting were compared to patients residing in an urban setting using the National Center for Health Statistics (NCHS) Urban-Rural Classification Scheme, a system stable over the study period, to find differences in outcomes such as mortality, length of stay, and cost of hospital care.[20] Those from non-core counties (not metropolitan or micropolitan counties) were designated as rural patients to create a comparison of very rural patients to those from more metropolitan areas. The rural patients were compared to patients from counties considered micropolitan (counties with a population of 10,000 - 50,000), small metro (counties in metro areas with a population of 50,000 - 249,999), medium metro (counties in metro areas with a population of 250,000 - 999,999), large fringe metro (fringe counties with a population greater than 1,000,000), or large central metro (large central counties with a population greater than 1,000,000); these counties were all considered urban. This created two groups, one from more rural areas and one from the more metropolitan areas based upon the county populations. ICD coding was not used to designate comorbidities or complications as there is no way to define when a code is used for a pre- or postoperative diagnosis.

The NIS data were drawn from all states participating in HCUP, or

about 96% of the U.S. population. It approximated 20% of discharges from U.S. hospitals, excluding long-term acute care and rehabilitation hospitals. State and hospital identifiers were not used. Sample sizes were typically large except for rare diagnoses, uncommon treatments, and unique patient populations. The NIS data were representative of the national population.

Statistical analysis and data management were performed using SAS (SAS Institute, Cary, NC), SPSS (IBM® Corp. Released 2015. IBM SPSS Statistics for Windows®, Version 23.0. Armonk, NY: IBM® Corp.), and Excel® (Microsoft® version 16.32). Significance was indicated by $p < 0.05$. Chi-square tests and Satterthwaite or pooled *t*-tests were used where appropriate. Multivariate regression analysis was carried out using modeling based upon significantly different variables where $p < 0.05$.

RESULTS

From 2010 to 2014, HCUP identified a total of 37,312,324 patients; 2,675,783 (7.17%) were rural and 34,146,602 (91.52%) were urban (Figure 1; Table 1). This was an expected distribution of patients, with more patients within the urban group and less within the rural group. Within these groups, some patients had no NCHS rural-urban code, hence a small portion of non-coded and non-grouped patients were kept out of statistical analysis. Of these, 12,476 patients were captured who had a diagnosis code of esophageal cancer or carcinoma in situ of the esophagus; 982 (7.87%) were rural and 11,275 (90.37%) were urban. Of these, 2,877 patients diagnosed with esophageal cancer underwent esophagectomy; 228 were rural patients (7.92%) and 2,575 were urban (89.50%). Seventy-four (2.57%) patients had no NCHS rural-urban code and were left within the groups but not within statistical sub-group analysis.

In comparing baseline characteristics, rural patients, as compared to urban patients, had no differences in age, sex, or insurance status (Table 1). There were significant differences in income, with rural patients being more likely to fall into a lower income quartile than urban patients (53.07% rural patients in the first quartile compared to 19.26% urban patients, $p < 0.0001$). The urban patients were a more racially diverse population, though rural patients were more likely to be Native American (2.63% compared to 0.39%, $p < 0.0001$).

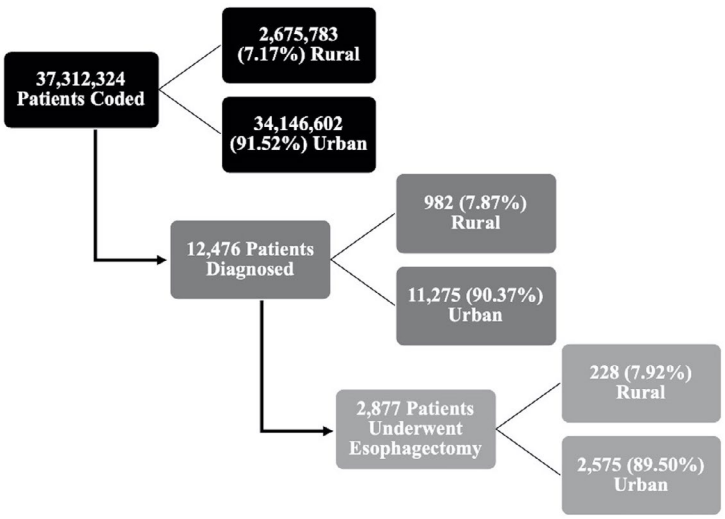


Figure 1. Patient selection was from the Healthcare Cost and Utilization Project database and included all patients coded within the database, those diagnosed with esophageal cancer, and those who underwent esophagectomy for cancer. Only patients who underwent esophagectomy were studied.

Rural patients were more likely than urban patients to have diabetes (24.56% vs. 18.56%, $p = 0.0271$) and fluid and electrolyte disorders (45.61% vs. 35.53%, $p = 0.0024$), while urban patients were more likely to have anemia (13.16% vs. 35.53%, $p = 0.0299$; Table 2). History of drug abuse between rural and urban patient population was not statistically significant ($p = 0.0855$).

There was no difference between rural and urban patients with respect to the treating hospital bed size, urban teaching status, or volume of total hospital discharges (Table 3). While rural patients were more likely to be treated at rural hospitals (4.39% vs. 1.35%, $p = 0.0010$), there was no difference in the percent of rural and urban patients treated at urban teaching hospitals. Rural patients were more likely to live in the Midwest (40.79% vs. 26.37%) and Southern U.S. (39.04% vs. 34.80%), while urban patients were more likely to live in the Northeast (11.40% vs. 23.96%) and Western (8.77% vs. 14.87%) regions ($p < 0.0001$).

A description of major outcomes was carried out and described (Table 4). No difference was found in length of stay between rural and urban patients. No difference existed between in-hospital mortality or total charges. Discharge disposition did not reach statistical significance on univariate analysis, but there was a trend for rural patients to more likely be discharged home compared to urban patients, who were more often discharged home with home health services. Both groups appeared to go home with home health services more often than they were discharged to home. Multivariate analysis showed rural patients may be statistically more likely than urban patients to be discharged home than other dispositions (35.96% vs. 29.79%, OR 0.667 [95% CI 0.479 - 0.929]; $p = 0.0167$).

DISCUSSION

This study showed that within a nationally representative group of patients with esophageal cancer undergoing esophagectomy, living in a rural setting did not portend a higher risk of inpatient mortality, a longer length of stay, discharge to a higher level of care, or higher cost of care. While a minority of patients may be receiving complex esophageal surgery for cancer at rural hospitals, the majority of the rural-urban population received their cancer care at urban teaching institutions. The clinical significance of the rural patient receiving surgery at rural centers was unable to be answered with this study, but other studies attempted to study this problem using travel distance to hospitals, hospital location, or hospital volume as surrogates for rurality of patient and outcome. However, there was a consensus that patients should receive complex operations requiring extended recoveries at high-volume centers with teams experienced in their perioperative care.

Within our study, the urban population was more likely to be more diverse and have a higher income. Urban populations historically have been more diverse than rural populations and our findings concur with this. While rural patients were more likely to receive care at a rural hospital, the majority of patients received care at an urban teaching facility. This was reassuring that complex care is sought at large facilities that are likely tertiary/quaternary referral centers with multiple studies

Table 1. Demographics of patients undergoing esophagectomy for cancer.

	Total	Rural (n; %)	Urban (n; %)	p Value
All HCUP patients 2010 - 2014	37,312,324	2,675,783 (7.17%)	34,146,602 (91.52%)	
Diagnosed with esophageal cancer	12,476	982 (7.87%)	11,275 (90.37%)	
Underwent esophagectomy	**2,877**	**228 (7.92%)**	**2,575 (89.50%)**	0.7858
Mean age, years (± SD)	64 (9.72)	63.11 (10.01)	63.62 (9.70)	0.4511
Male (n; %)	2,351 (81.72%)	192 (84.21%)	2,098 (81.48%)	0.3060
Race (n; %)				
White	2,262 (78.62%)	176 (77.19%)	2,027 (78.72%)	< 0.0001
Black	166 (5.77%)	10 (4.39%)	148 (5.75%)	
Hispanic	111 (3.86%)	3 (1.32%)	104 (4.04%)	
Asian or Pacific Islander	25 (0.87%)	0 (0.00%)	25 (0.97%)	
Native American	16 (0.56%)	6 (2.63%)	10 (0.39%)	
Other	60 (2.09%)	2 (0.88%)	55 (2.14%)	
Insurance status (n; %)				
Medicare	1,336 (46.44%)	110 (48.25%)	1,194 (46.37%)	0.4667
Medicaid	221 (7.68%)	23 (10.09%)	194 (7.53%)	
Private insurance	1,203 (41.81%)	87 (38.16%)	1,080 (41.94%)	
Self-pay	34 (1.18%)	1 (0.44%)	32 (1.24%)	
No charge	6 (0.21%)	0 (0.00%)	6 (0.23%)	
Other	72 (2.50%)	7 (3.07%)	64 (2.49%)	
Income quartile (n; %)				
0 to 25th percentile	626 (21.76%)	121 (53.07%)	496 (19.26%)	< 0.0001
26th to 50th percentile	740 (25.72%)	68 (29.82%)	663 (25.75%)	
51st to 75th percentile	743 (25.83%)	31 (13.60%)	693 (26.91%)	
76th to 100th percentile	710 (24.68%)	1 (0.44%)	683 (26.52%)	

HCUP: Healthcare Cost and Utilization Project

Table 2. Comorbidities of population undergoing esophagectomy for cancer.

	Total 2,877	Rural (n; %) 228 (7.92%)	Urban (n; %) 2,575 (89.50%)	p Value
AHRQ comorbidities (n; %)				
Fluid and electrolyte disorders	1,048 (36.43%)	104 (45.61%)	915 (35.53%)	0.0024
Anemia	542 (18.84%)	30 (13.16%)	497 (19.30%)	0.0229
Diabetes, uncomplicated	554 (19.26%)	56 (24.56%)	478 (18.56%)	0.0271
Drug abuse	35 (1.22%)	0 (0.00%)	33 (1.28%)	0.0855
Acquired immunodeficiency syndrome	5 (0.17%)	0 (0.00%)	3 (0.12%)	0.6061
Alcohol abuse	145 (5.04%)	12 (5.26%)	125 (4.85%)	0.7838
Rheumatoid arthritis	45 (1.56%)	6 (2.63%)	39 (1.51%)	0.1984
Chronic blood loss anemia	49 (1.70%)	4 (1.75%)	45 (1.75%)	0.9940
Congestive heart failure	145 (5.04%)	15 (6.58%)	126 (4.89%)	0.2643
Chronic pulmonary disease	640 (22.25%)	58 (25.44%)	575 (22.33%)	0.2820
Coagulopathy	214 (7.44%)	21 (9.21%)	187 (7.26%)	0.2820
Depression	231 (8.03%)	18 (7.89%)	207 (8.04%)	0.9388
Diabetes, with chronic complications	65 (2.26%)	5 (2.19%)	58 (2.25%)	0.9537
Hypertension	1,613 (56.07%)	134 (58.77%)	1,434 (55.69%)	0.3689
Hypothyroidism	218 (7.58%)	12 (5.26%)	201 (7.81%)	0.1649
Liver disease	83 (2.88%)	5 (2.19%)	72 (2.80%)	0.5933

Table 2. Comorbidities of population undergoing esophagectomy for cancer. *continued.*

	Total 2,877	Rural (n; %) 228 (7.92%)	Urban (n; %) 2,575 (89.50%)	p Value
AHRQ comorbidities (n; %)				
Lymphoma	16 (0.56%)	2 (0.88%)	14 (0.54%)	0.5217
Metastatic cancer	487 (16.93%)	45 (19.74%)	424 (16.47%)	0.2047
Neurological disorders	90 (3.13%)	12 (5.26%)	78 (3.03%)	0.0666
Obesity	279 (9.70%)	25 (10.96%)	246 (9.55%)	0.4894
Peripheral vascular disorders	145 (5.04%)	13 (5.70%)	131 (5.09%)	0.6871
Psychoses	80 (2.78%)	5 (2.19%)	73 (2.83%)	0.5722
Pulmonary circulation disorders	68 (2.36%)	3 (1.32%)	64 (2.49%)	0.2678
Renal failure	154 (5.35%)	8 (3.51%)	143 (5.55%)	0.1900
Valvular heart disease	106 (3.68%)	7 (3.07%)	96 (3.73%)	0.6128
Weight loss	662 (23.01%)	47 (20.61%)	591 (22.95%)	0.4198
APR DRG risk of mortality (n; %)				
Minor likelihood of dying	854 (29.68%)	59 (25.88%)	782 (30.37%)	0.4312
Moderate likelihood of dying	807 (28.05%)	73 (32.02%)	716 (27.81%)	
Major likelihood of dying	762 (26.49%)	59 (25.88%)	670 (26.02%)	
Extreme likelihood of dying	454 (15.78%)	37 (16.23%)	407 (15.81%)	
APR DRG severity of illness (n; %)				
Moderate loss of function	510 (17.73%)	39 (17.11%)	466 (18.10%)	0.8815
Major loss of function	1,602 (55.68%)	126 (55.26%)	1,431 (55.57%)	
Extreme loss of function	765 (26.59%)	63 (27.63%)	678 (26.33%)	
Elective admission (n; %)	2,690 (93.50%)	207 (90.79%)	2,413 (93.71%)	0.0698

AHRQ: Agency for Healthcare Research and Quality; APR DRG: All Patients Refined Diagnosis Related Group

Table 3. Hospital variables of patients undergoing esophagectomy for cancer.

	Total 2,877	Rural (n; %) 228 (7.92%)	Urban (n; %) 2,575 (89.50%)	p Value
Hospital size, beds (n; %)				
Small	259 (9.00%)	23 (10.09%)	236 (9.17%)	0.8473
Medium	400 (13.90%)	32 (14.04%)	368 (14.29%)	
Large	2,126 (73.90%)	167 (73.25%)	1,959 (76.08%)	
Location/teaching status of hospital (n; %)				
Rural	45 (1.56%)	10 (4.39%)	35 (1.36%)	0.0010
Urban non-teaching	337 (11.71%)	21 (9.21%)	314 (12.19%)	
Urban teaching	2,477 (86.10%)	191 (83.77%)	2,214 (85.98%)	0.3598
Urban-rural classification of county (n; %)				
"Central" counties of metro areas ≥ 1 million population	654 (22.73%)	0 (0.00%)	654 (25.40%)	< 0.0001
"Fringe" counties of metro areas ≥ 1 million population	756 (26.28%)	0 (0.00%)	756 (29.36%)	
Counties in metro areas of 250,000 - 999,999 population	561 (19.50%)	0 (0.00%)	561 (21.79%)	
Counties in metro areas of 50,000 - 249,999 population	282 (9.80%)	0 (0.00%)	282 (10.95%)	
Micropolitan counties	322 (11.19%)	0 (0.00%)	322 (12.50%)	
Not metropolitan or micropolitan counties	228 (7.92%)	228 (100.00%)	0 (0.00%)	
Hospital region (n; %)				
Northeast	711 (24.71%)	26 (11.40%)	617 (23.96%)	< 0.0001
Midwest	774 (26.90%)	93 (40.79%)	679 (26.37%)	
South	989 (34.38%)	89 (39.04%)	896 (34.80%)	
West	403 (14.01%)	20 (8.77%)	383 (14.87%)	
Total hospital discharges (mean; SD)	1,9143.44 (21,011.52)	1,7692.6 (17,764.30)	18,553.60 (20,990.50)	0.4905

Table 4. Outcomes of patients undergoing esophagectomy for cancer with regression analysis.

	Total 2,877	Rural (n; %) 228 (7.92%)	Urban (n; %) 2,575 (89.50%)	p Value	Odds ratio	95% CI	p Value
Mean length of stay, days (± SD)	15.62 (14.82)	15.75 (13.22)	15.55 (14.91)	0.8278	N/A	(-7.39 - 2.28)	0.3650
Died during hospitalization (n; %)	119 (4.14%)	9 (3.95%)	110 (4.27%)	0.8149	1.64	(0.694 - 3.887)	0.2995
Disposition							
Short-term hospital for inpatient care	855 (29.72%)	82 (35.96%)	767 (29.79%)	0.4911	0.667	(0.479 - 0.929)	0.0167
Discharged to designated cancer center	42 (1.46%)	4 (1.75%)	28 (1.09%)				
Home health service	493 (17.14%)	38 (16.67%)	446 (17.32%)				
Left against medical advice or discontinued care	1,362 (47.34%)	95 (41.67%)	1,218 (47.30%)				
Expired	4 (0.14%)	0 (0.00%)	4 (0.16%)				
Discharged alive	119 (4.14%)	9 (3.95%)	110 (4.27%)				
Destination unknown	1 (0.03%)	0 (0.00%)	1 (0.04%)				
Total charges, dollars (± SD)	194,606.02 (218,991.47)	179,462.28 (203,208.39)	194,581.40 (221,433.01)	0.3214	N/A	(-66,708 - 75,990)	0.8980

describing improved outcomes at these high-volume centers.[6,7,9,10] A multivariate regression analysis showed rural patients may be more likely than urban patients to be discharged home. This was difficult to describe further and may be an excellent area of research; why are patients from rural areas undergoing complex surgery discharged home more often urban patients? Possible theories are that if they are at an urban facility a half-day or days drive from their home, then they might stay slightly longer to rehabilitate before a direct discharge to home compared to discharge to a local rehabilitation facility. More research in this area is needed. Unsurprisingly, rural patients were more likely to be from the south and Midwest regions compared to urban patients from the west and northeast regions of the U.S.

Patients in rural areas with cancer diagnoses may face multiple challenges in obtaining the same care as urban patients. This includes barriers to transportation, finance issues, limited trials, and even access to oncologists, as only 3% of the nation's oncologists work in rural areas.[21,22] Solutions often include telemedicine (i.e., consultation, tumor boards), outreach clinics, incentivizing work or education in these areas, and traveling screening options. For cancer screening, some advocate imaging or laboratory-based screening over procedure-based screening, when possible, for example in colorectal cancer screening.[23]

Few epidemiologic data existed on the rural-urban differences in esophageal cancer in North America. Wang et al.[24] studied the Surveillance, Epidemiology, and End Results (SEER) Program, finding similar incidence of esophageal cancer in metropolitan, urban, and rural patients, as well as similar survival and late-stage diagnosis. Disagreement on whether SEER was generalizable to populations of certain geographic locations and caution must be used in interpreting such results.[25] Studies from China and other countries described the differences in the rate of esophageal cancer incidence and presentation stage depending on rural status or region of residence.[15,16,26] Location data were not available for other large databases such as the National Surgical Quality Improvement Program or Society of Thoracic Surgeons, limiting our comparison to other large databases using procedures.[1] An epidemiologic study of esophageal cancer using this database was outside the scope of our study. While esophageal cancer is typically squamous cell subtype in these regions compared to adenocarcinoma subtype in Western populations, this observation of epidemiologic rural-urban difference is important.

Treatment of the rural and urban esophageal cancer populations varies and may lead to different outcomes. Wasif and colleagues[17] used the National Cancer Database to find a correlation between the decreased use of high-volume centers for esophagectomy in populations of African American patients, the uninsured, and patients residing in low educational zip codes. High-volume was defined by some as greater than 20 cases per year.[12] Cushman and colleagues[27] used the same database to study the T4b esophageal cancer population, finding rural patients significantly more likely to undergo surgery, possibly due to travel distance or surgeon concern that surveillance would be difficult. Lin et al.[28] found rural patients possibly may use radiation therapy less than urban patients, but this result did not reach statistical significance.

The findings of this study showed minimal differences in outcomes between rural and urban patient populations and should be interpreted cautiously considering the limitations of its retrospective analysis of administrative data. Our level of evidence was inferior to a prospective study that would enroll rural and urban patients. The administrative nature of the data created possible misclassification and was subject to recall bias. With cancer diagnoses within the NIS, it was difficult to study the stage and severity of oncologic burden. Furthermore, the database lacked the ability to study conditions that were comorbidities versus diagnoses that arose or were discovered during hospitalization (complications). Along these same lines, the database lacked granular clinical data, such as that which existed in other surgical databases or oncologic databases.

Additionally, there was the limitation of the ICD system, which changed in 2015 to its tenth edition.[18,20] This created major issues for

those who would want to look at trends over time, specifically those looking at procedure codes. The NIS database also changed in 2012 to include a sample of all hospital discharges, instead of a sample of hospitals and all their discharges.[18] This change primarily affected those looking at trends over time and should not have affected this study. Finally, while the database was large enough to detect small differences in a population, the question often was raised whether it was clinically relevant for the thoracic surgeon or oncologist. Within our own study, a 5 - 10% difference in anemia, electrolyte disorders, or diabetes likely had little effect on outcomes after surgery and treatment between the rural and urban populations.

The advantages and strengths of this study were inherent in the direct comparison of the two populations of patients, rather than using hospitals or distance to describe rurality. The NIS database allowed for a large sample size, giving the study more power. Since the database was representative of all inpatient hospitalizations in the U.S., it was useful in describing costs, observing trends over time, and creating basic descriptive studies and estimates. The database was an acceptable representation of a national population.

CONCLUSIONS

This study was unique in its direct comparison of rural and urban patients undergoing esophagectomy for esophageal cancer. While it lacked in the ability to provide granular data, oncologic staging, or long-term outcomes, it was novel in that it demonstrated a difference in two populations of patients with respect to their income, race, and nationwide region of residence, and was reassuring in demonstrating what appeared to be little difference in outcomes between rural and urban patients. Within the rural population, further research is necessary to understand access to esophageal cancer treatment and surgery as well as epidemiologic disparities and long-term follow up and surveillance. The study findings should provide motivation to understand differences in populations of patients undergoing complex surgery and multidisciplinary treatment for cancer. Specific research questions should look at disposition after complex oncologic surgery and access to care for rural and remote populations.

REFERENCES

[1] Chaudhary MA, Shah AA, Zogg CK, et al. Differences in rural and urban outcomes: A national inspection of emergency general surgery patients. J Surg Res 2017; 218:277-284. PMID: 28985861.
[2] Ross KH, Patzer RE, Goldberg D, Osborne NH, Lynch RJ. Rural-urban differences in in-hospital mortality among admissions for end-stage liver disease in the United States. Liver Transpl 2019; 25(9):1321-1332. PMID: 31206223.
[3] Thomas AA, Pearce A, O'Neill C, Molcho M, Sharp L. Urban-rural differences in cancer-directed surgery and survival of patients with non-small cell lung cancer. J Epidemiol Community Health 2017; 71(5):468-474. PMID: 27913615.
[4] Poulose BK, Phillips S, Nealon W, et al. Choledocholithiasis management in rural America: Health disparity or health opportunity? J Surg Res 2011; 170(2):214-219. PMID: 21571311.
[5] Shelton J, Kummerow K, Phillips S, et al. An urban-rural blight? Choledocholithiasis presentation and treatment. J Surg Res 2012; 173(2):193-197. PMID: 21737099.
[6] Birkmeyer JD, Finlayson EVA, Birkmeyer CM. Volume standards for high-risk surgical procedures: Potential benefits of the Leapfrog initiative. Surgery 2001; 130(3):415-422. PMID: 11562662.
[7] Chappel AR, Zuckerman RS, Finlayson SRG. Small rural hospitals and high-risk operations: How would regionalization affect surgical volume and hospital revenue? J Am Coll Surg 2006; 203(5):599-604. PMID: 17084319.
[8] Clark JM, Boffa DJ, Meguid RA, Brown LM, Cooke DT. Regionalization of esophagectomy: Where are we now? J Thorac Dis 2019; 11(Suppl 12):S1633-S1642. PMID: 31489231.
[9] Gabriel E, Narayanan S, Attwood K, Hochwald S, Kukar M, Nurkin S. Disparities in major surgery for esophagogastric cancer among hospitals by case volume. J Gastrointest Oncol 2018; 9(3):503-516. PMID: 29998016.
[10] Fuchs HF, Harnsberger CR, Broderick RC, et al. Mortality after esophagectomy is heavily impacted by center volume: Retrospective analysis of the Nationwide Inpatient Sample. Surg Endosc 2017; 31(6):2491-2497. PMID: 27660245.
[11] Schlottmann F, Strassle PD, Charles AG, et al. Esophageal cancer surgery: Spontaneous centralization in the US contributed to reduce mortality without causing health disparities. Ann Surg Oncol 2018; 25(6):1580-1587. PMID: 29349529.
[12] Speicher PJ, Englum BR, Ganapathi AM, et al. Traveling to a high-volume center is associated with improved survival for patients with esophageal cancer. Ann Surg 2017; 265(4):743-749. PMID: 28266965.
[13] Song Y, Tieniber AD, Roses RE, Fraker DL, Kelz RR, Karakousis GC. National trends in centralization and perioperative outcomes of complex operations for cancer. Surgery 2019; 166(5):800-811. PMID: 31230839.
[14] Simunovic M, Rempel E, Thériault M, et al. Influence of hospital characteristics on operative death and survival of patients after major cancer surgery in Ontario. Can J Surg 2006; 49(4):251-258. PMID: 16948883.
[15] Zhao P, Dai M, Chen W, Li N. Cancer trends in China. Jpn J Clin Oncol 2010; 40(4):281-285. PMID: 20085904.
[16] Lin Y, Totsuka Y, Shan B, et al. Esophageal cancer in high-risk areas of China: Research progress and challenges. Ann Epidemiol 2017; 27(3):215-221. PMID: 28007352.
[17] Wasif N, Etzioni D, Habermann EB, et al. Racial and socioeconomic differences in the use of high-volume commission on cancer-accredited hospitals for cancer surgery in the United States. Ann Surg Oncol 2018; 25(5):1116-1125. PMID: 29450752.
[18] U.S. Agency for Healthcare Research and Quality. Healthcare Cost and Utilization Project (HCUP). May 2, 2021. https://www.hcup-us.ahrq.gov/. Accessed June 9, 2021.
[19] World Health Organization. International Statistical Classification of Diseases and Related Health Problems (ICD). Ninth Edition. Geneva: World Health Organization, 1978. ISBN: 9241541334.
[20] U.S. Centers for Disease Control and Prevention. National Center for Health Statistics. NCHS Urban-Rural Classification Scheme for Counties. June 1, 2017. https://www.cdc.gov/nchs/data_access/urban_rural.htm. Accessed June 9, 2021.
[21] Unger JM, Moseley A, Symington B, Chavez-MacGregor M, Ramsey SD, Hershman DL. Geographic distribution and survival outcomes for rural patients with cancer treated in clinical trials. JAMA Netw Open 2018; 1(4):e181235. PMID: 30646114.
[22] Charlton M, Schlichting J, Chioreso C, Ward M, Vikas P. Challenges of rural cancer care in the United States. Oncology (Williston Park) 2015; 20(9):633-640. PMID: 26384798
[23] Woodall M, Deletter M. Colorectal cancer: A collaborative approach to improve education and screening in a rural population. Clin J Oncol Nurs 2018; 22(1):E69-E75. PMID: 29350693.
[24] Wang Z, Goodman M, Saba N, El-Rayes F. Incidence and prognosis of gastroesophageal cancer in rural, urban, and metropolitan areas of the United States. Cancer 2013; 119(22):4020-4027. PMID: 23963864.
[25] Kuo TM, Mobley LR. How generalizable are the SEER registries to the cancer populations of the USA? Cancer Causes Control 2016; 27(9):1117-1126. PMID: 27443170.
[26] Chen W, Zheng R, Baade PD, et al. Cancer statistics in China, 2015. CA Cancer J Clin 2016; 66(2):115-132. PMID: 26808342.
[27] Cushman TR, Shaaban SG, Moreno AC, Lin C, Verma V. Management of unresectable T4B esophageal cancer. Am J Clin Oncol Cancer Clin Trials 2019; 42(2):154-159. PMID: 30499838.
[28] Lin SH, Zhang N, Godby J, et al. Radiation modality use and cardiopulmonary mortality risk in elderly patients with esophageal cancer. Cancer 2016; 122(6):917-928. PMID: 26716915.

Keywords: esophageal cancer, rural health services, urban health, health care disparities, geography

KANSAS JOURNAL of MEDICINE

Invisible Spread and Perceived Stress Amidst COVID-19

Emily B. K. Thomas, Ph.D.[1], Jessica Hamilton, Ph.D.[2], Carrie L. Francis, M.D.[3], Kevin J. Sykes, Ph.D., MPH[3]
[1]University of Iowa, Iowa City, IA
Department of Psychological and Brain Sciences
University of Kansas Medical Center, Kansas City, KS
[2]Department of Psychiatry and Behavioral Sciences
[3]Department of Otolaryngology-Head and Neck Surgery

Received June 14, 2021; Accepted for publication Aug. 31, 2021; Published online Dec. 2, 2021
https://doi.org/10.17161/kjm.vol14.15612

ABSTRACT

Introduction. There are limited reports on the mental health toll associated with the fear of spreading coronavirus disease 2019 (COVID-19) and the associated stay-at-home orders. The goal of the present study was to characterize the self-reported stress of participants from the Kansas City Metropolitan Area (KCMA) and to examine the relation between potential for asymptomatic spread and perceived stress.

Methods. This prospective convenience sample study enrolled 461 participants from May 4 to May 22, 2020. Participants were consented and surveyed prior to free SARS-CoV-2 testing. Measures employed included the Perceived Stress Scale-10 and a comprehensive COVID-19 questionnaire. During the study period, testing resources were limited. In the community, only symptomatic individuals or close contacts of known positives could be tested. Our program aimed to reach those who were unable to access testing resources due to their asymptomatic status or other barriers to care.

Results. Worry about asymptomatic spread was associated significantly with greater perceived stress ($p < 0.001$). Higher stress was reported among women ($p < 0.001$), Hispanic/Latinx ($p = 0.001$), non-Black/African American individuals ($p < 0.001$), and those reporting the presence of COVID-19 symptoms ($p = 0.001$).

Conclusions. The COVID-19 pandemic has caused significant economic, social, and health disruptions around the world. Distress is significantly related to concern over unintentionally contributing to the spread of SARS-CoV-2 through asymptomatic transmission. In addition to examining outcomes like distress, future research should characterize the modifiable psychotherapeutic processes that might be targeted through intervention among those experiencing distress.

Kans J Med 2021;14:298-301

INTRODUCTION

Kansas and Missouri leaders issued statewide stay-at-home orders on March 30 and April 4, 2020, respectively, to mitigate the spread of COVID-19. Stay-at-home orders resulted in significant growth in unemployment claims across the country and have been associated with loneliness and social isolation.[1,2] Reopening hinged on case detection and isolation, but the limited availability of testing resources created the need for monitoring a series of predictive symptoms.

Asymptomatic infections brought about the potential for unknowingly spreading the virus, even with careful symptom monitoring, and represent a potential source of anxiety and fear. There are limited reports on the mental health toll associated with the fear of spreading COVID-19 and the associated stay-at-home orders.[3,4] The goal of the present study was to characterize the self-reported stress of participants from the Kansas City Metropolitan Area (KCMA) and to examine the relation between potential for asymptomatic spread and perceived stress. It was hypothesized that individuals who were concerned about asymptomatic spread would report elevated perceived stress.

METHODS

Procedures. Enrollment began for this prospective convenience sample study on May 4, 2020, and all data collection ended before both Kansas and Missouri re-opened following governmental stay-at-home orders (May 22, 2020). The Institutional Review Board approved this study. Data collection and consent were completed via Research Electronic Database Capture (REDCap®), a secure, web-based software platform designed for research.[5] Participants received a link either via email, social media, or QR codes on promotional flyers to a consent and survey, or were given tablet devices to complete consents prior to testing. Demographic data are required by health departments for reporting, and 461 people electronically consented to provide this information and were tested.

Participants. Non-profit community-based organizations recruited adults from the communities they serve through outreach flyers, social media, and local media coverage. Eligible participants included anyone interested in free testing for SARS-CoV-2; all associated costs were grant funded. Symptom status (symptomatic, pre-symptomatic, or asymptomatic) was not part of the selection criteria, and the sample ultimately included both those with symptoms and those without. At the time of data collection, SARS-CoV-2 testing in the KCMA was limited to symptomatic individuals or close contacts of known positives, so this program was unique in that it welcomed asymptomatic individuals. As Table 1 shows, the average age of participants was 44.94 (SD = 14.56); the majority, 70% (321 of 461), were women; and 67% (310 of 461) identified as White.

Measures. The Perceived Stress Scale-10 (PSS-10) is a reliable and valid 10-item, 5-point Likert-type scale format instrument (0 = never to 4 = very often), and the total score ranges from 0 to 40.6. Higher scores indicated greater perceived stress.[7] Internal consistency in this sample was adequate (alpha = 0.88). Item-level missing data were imputed if 80% or more of the items were complete (n = 11).

Participants completed a comprehensive questionnaire, including self-reported demographics. As concerns about the impact of the pandemic grew, researchers and government agencies created publicly available survey question banks. Specifically, the National Institutes of Health Office of Behavioral and Social Sciences Research compiled lists of questions with the hopes of creating more consistent data collection across clinical and population research programs (https://www.niehs.nih.gov/research/programs/disaster/index.cfm). The questions used in our study were selected from these resources. Specific questions regarding amount of information ("How much information do you feel you have about COVID-19?") and worry about

asymptomatic spread ("During the past two weeks, how worried have you been about friends or family being infected because you accidently brought it home?") were included (see Appendix A). Comparisons were conducted using independent samples *t*-tests or analyses of variance, and continuous associations were examined using bivariate correlations.

Table 1. Sample demographics and characteristics (N = 461).

	N	%*
State of residence		
Kansas	218	47.3
Missouri	243	52.7
Age, M (SD)	44.94	14.56
Gender		
Women	321	69.6
Men	137	29.7
Other	3	0.7
Racial background**		
White	310	67.2
African American or Black	98	21.3
Asian	7	1.5
Native American/Alaska Native	9	2.0
Native Hawaiian/Pacific Islander	1	0.2
Other	57	12.4
Ethnicity		
Hispanic/Latinx	92	20
Non-Hispanic/Latinx	365	79.2
Missing	4	0.9
Educational background		
Some grade school	3	0.7
Some high school	18	3.9
High school diploma/GED	39	8.5
Some college or two-year degree	104	22.6
Four-year college degree	113	24.5
Post-college education	32	6.9
Graduate or professional degree	147	31.9
Missing	5	1.1

*Except for Age (SD).
**Participants endorsed multiple races.

RESULTS

Of the 461 participants in the study, 448 (97.2%) began the survey portion of the study, and 445 (96.5%) completed the survey.

Perceived stress was related to age (r = - 0.44, p < .001), such that greater stress was related to younger age. Perceived stress differed by gender (t (443) = -4.8, p < 0.001), with women ((n = 311): M = 16.2, SD = 6.7) reporting greater perceived stress than men ((n = 134): M = 12.8, SD = 6.9). Perceived stress also differed by ethnicity (t (145.8) = -3.5, p = 0.001), with Hispanic or Latinx individuals (M = 17.4, SD = 6.3) reporting more perceived stress than non-Hispanic or Latinx individuals (M = 14.7, SD = 7.0). Individuals identifying as African American or Black reported significantly (t (446) = 3.8, p < 0.001) less perceived stress (M = 12.9, SD = 6.8) than non-African American or Black individuals (M = 15.9, SD = 6.8).

Worry about asymptomatic spread was recoded to reflect individuals who were not at all or slightly worried, as compared to those who reported moderate to extreme worry. Individuals reporting significant worry also reported greater perceived stress ((n = 266): M = 16.5, SD = 6.3) than individuals reporting minimal or no worry ((n = 181): M = 13.4, SD = 7.4), and this difference was significant between groups (t (342.1) = -4.7, p < 0.001). The amount of information individuals felt they knew regarding COVID-19 was not associated with perceived stress (t (446) = 1.4, p = 0.16; Figure 1).

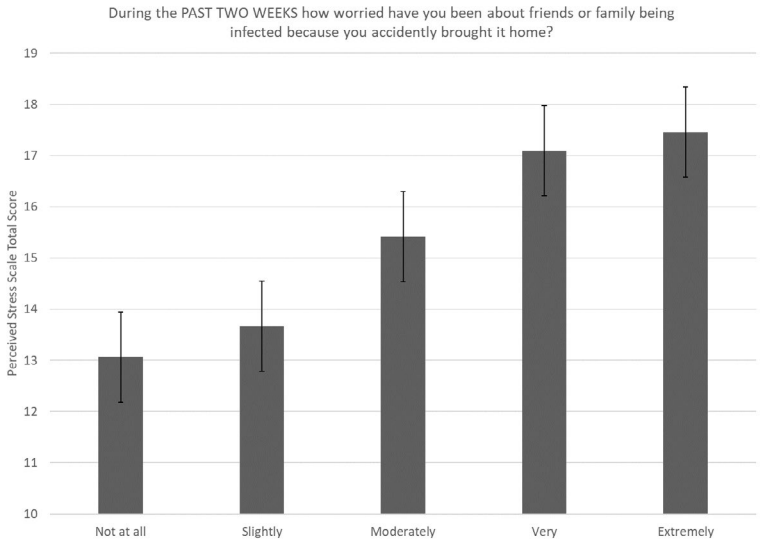


Figure 1. The relation between overall perceived stress and worry about asymptomatic spread.

When comparing those reporting symptoms of COVID-19, as defined by U.S. Centers for Disease Control and Prevention case definitions, to those who were not, significant differences were observed (t (446) = -3.2, p = 0.001). Symptomatic individuals reported higher perceived stress ((n = 81); M = 17.4, SD = 6.5) than asymptomatic individuals ((n = 367); M = 14.8, SD = 6.9). The number of COVID-related symptoms reported related to increased perceived stress (r = 0.14, p = 0.003).

DISCUSSION

We sought to provide insights into the correlates of perceived stress amidst the COVID-19 pandemic. Higher stress was reported among individuals who were female, Hispanic or Latinx, and non-Black or African American. Worry about asymptomatic spread (accidentally infecting family or friends) was associated with greater perceived stress. Perceived stress also was associated with the presence of COVID-19 symptoms.

Our findings aligned with prior research on women reporting higher levels of depression and anxiety symptoms during the pandemic.[8] Higher levels of stress among individuals identifying as Hispanic or Latinx aligned with one study indicating higher fear of COVID-19 in a similar group.[9] As reported in prior research, the presence of physical symptoms of COVID-19 also was associated with higher stress.[10]

Our findings represented a unique view of perceived stress among individuals testing for SARS-CoV-2 during government mandated stay-at-home orders. Even in the early stages of the pandemic, information about the risk of asymptomatic spread was growing in the scientific and lay press.[11] To our knowledge, no previous reports existed regarding concern about asymptomatic spread as they relate to distress, anxiety, or other mental health outcomes. It may not be possible or reasonable to reduce worry about asymptomatic spread, particularly given that such worry may promote prosocial and community-oriented behaviors. The impact of this worry on general distress, however, is a potential target for intervention, especially among individuals moving about communities more widely and concerned about propensity for asymptomatic spread.

Limitations. The current study examined self-reported variables, introducing potential social desirability, selection bias, or bias resulting from variability in health literacy. The data were cross-sectional, so no causal conclusions can be drawn. The convenience sampling design may overestimate concerns about COVID-19. Those seeking testing opportunities were likely to be more concerned and aware of the disease, and their opinions may not represent broader community concerns.

Prior to the lifting of the stay-at-home orders, the cases of COVID-19 were relatively low in the KCMA, at approximately 80 incident diagnoses per day.[12] This could underestimate the presence of stress as the influence of COVID-19 incidence on stress was unclear. Our findings may not generalize to higher incidence communities that may have been more disrupted by control measures.

CONCLUSIONS

The COVID-19 pandemic has not only taken hundreds of thousands of human lives, but it has caused significant economic, social, and health disruptions around the world. Distress was related significantly to concern over unintentionally contributing to the spread of SARS-CoV-2 through asymptomatic transmission. In addition to examining outcomes like distress, future research should characterize the modifiable psychotherapeutic processes that might be targeted through intervention among those experiencing distress.

REFERENCES

[1] Gaeta L, Brydges CR. Coronavirus-related anxiety, social isolation, and loneliness in older adults in northern California during the stay-at-home order. J Aging Soc Policy 2020;1-12. PMID: 33016253.
[2] Baek C, McCrory PB, Messer T, Mui P. Unemployment effects of stay-at-home orders: Evidence from high frequency claims data. April 29, 2020. https://irle.berkeley.edu/unemployment-effects-of-stay-at-home-orders-evidence-from-high-frequency-claims-data/. Accessed June 17, 2021.
[3] Kronbichler A, Kresse D, Yoon S, Lee KH, Effenberger M, Shin JI. Asymptomatic patients as a source of COVID-19 infections: A systematic review and meta-analysis. Int J Infect Dis 2020; 98:180-186. PMID: 32562846.
[4] Ren Y, Feng C, Rasubala L, Malmstrom H, Eliav E. Risk for dental healthcare professionals during the COVID-19 global pandemic: An evidence-based assessment. J Dent 2020; 101:103434. PMID: 32693111.
[5] Harris PA, Taylor R, Minor BL, et al. The REDCap consortium: Building an international community of software platform partners. J Biomed Inform 2019; 95:103208. PMID: 31078660.
[6] Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. J Health Soc Behav 1983; 24(4):385-396. PMID: 6668417.
[7] Cohen S, Williamson, G. Perceived stress in a probability sample of the United States. In: S. Spacapan, S. Oskamp (Eds). The Social Psychology of Health: Claremont Symposium on Applied Social Psychology. Thousand Oaks,CA: Sage Publications, 1988. ISBN: 0803931638.
[8] Barzilay R, Moore TM, Greenberg DM, et al. Resilience, COVID-19-related stress, anxiety and depression during the pandemic in a large population enriched for healthcare providers. Transl Psychiatry 2020; 10(1):291. PMID: 32820171.
[9] Fitzpatrick KM, Harris C, Drawve G. Fear of COVID-19 and the mental health consequences in America. Psychol Trauma 2020; 12(S1):S17-S21. PMID: 32496100.
[10] Chew NWS, Lee GKH, Tan BYQ, et al. A multinational, multicentre study on the psychological outcomes and associated physical symptoms amongst healthcare workers during COVID-19 outbreak. Brain Behav Immun 2020; 88:559-565. PMID: 32330593.
[11] Hu Z, Song C, Xu C, et al. Clinical characteristics of 24 asymptomatic infections with COVID-19 screened among close contacts in Nanjing, China. Sci China Life Sci 2020; 63(5):706-711. PMID: 32146694.
[12] Mid-America Regional Council. Kansas City Region COVID-19 Data Hub. 2020. https://marc2.org/covidhub/. Accessed February 4, 2021.

Keywords: COVID-19, psychological distress, asymptomatic viral shedding, pandemics, public health practice

APPENDIX A

Self-Report Questions and Response Options

Domain	Specific Question	Response Options
COVID-19 Symptom Checklist	During the PAST TWO WEEKS have you had any of the following symptoms?	• Cough • Fever (101°F or greater) • Shortness of breath • Fatigue or feeling significantly tired from illness • Loss of sense of taste • Loss of sense of smell • Gastrointestinal symptoms (nausea, loss of appetite, diarrhea) • I don't have any symptoms
COVID-19 Knowledge	How much information do you feel you have about COVID-19?	• A lot • Some • A little • Nothing
Worry about Asymptomatic Spread	During the past two weeks, how worried have you been about friends or family being infected because you accidently brought it home?	• Not at all • Slightly • Moderately • Very • Extremely

KANSAS JOURNAL of MEDICINE

Incidental Leriche Syndrome in Horseshoe Kidney Disease: A Non-Classic Couple

Adrián Valverde M.[1], Richard G. Vaca, M.D.[2], Kevin Orellana, M.D.[1], Fabian Delgado, M.D., FACP[3]
[1]Universidad de Guayaquil, School of Medicine, Guayaquil, Ecuador
[2]Universidad Católica de Santiago de Guayaquil, School of Medicine, Guayaquil, Ecuador
[3]Vantage Healthcare, Canton, MA, USA

Received July 11, 2021; Accepted for publication Sept. 17, 2021; Published online Dec. 2, 2021
https://doi.org/10.17161/kjm.vol14.15670

INTRODUCTION

Atherosclerotic disease is the leading cause of death in the U.S.[1] Leriche syndrome (LS) is a rare variant of the atherosclerotic occlusive disease, also known as aortoiliac occlusive disease, because it commonly produces total occlusion of the aorta, below renal arteries, and/or both iliac arteries.[2] LS was first mentioned by Robert Graham of London in 1814 and named by René Leriche, a famous French surgeon in 1923.[3]

LS risk factors are hypertension, hyperlipidemia, smoking, and diabetes.[4] It usually presents as a late atherosclerotic disease due to reduced blood flow to the renal artery, producing significant stenosis with accelerated hypertension or acute renal injury.[5] It also could affect the iliac vessels producing a wide range of manifestations including: sexual dysfunction, intermittent claudication of lower limbs, bilateral buttock claudication, and absent femoral arterial pulses,[6] especially when the occlusion is greater than 50% of the arterial lumen.[7]

Horseshoe kidney disease (HSK) is defined as a fused renal parenchyma with uncrossed ureteral systems,[8] and even though it is mostly benign, abnormal urine drainage predisposes to urologic diseases,[9] including hydronephrosis, nephrolithiasis, urinary tract infections, chronic abdominal pain, and urogenital cancer.[10,11] HSK has an incidence of 1/600 and male predominance 2:1.[12]

Both conditions, although rare causes of acute abdominal pain, are potentially fatal and should be suspected due to the concomitant risk factors in this scenario. We present a case report describing a patient with abdominal pain and progressive intermittent claudication. Due to the physical findings, altered blood-urine panel, and antecedent of horseshoe kidney disease, hospital admission and imaging were ordered.

CASE REPORT

A 61-year-old Latin American man presented to the emergency room complaining of progressively severe abdominal pain. His medical history included poorly controlled hypertension (HTN), type 2 diabetes mellitus, recurrent urinary tract infections, and horseshoe kidney. He also reported a 40 pack-year smoking history. The patient also complained of dysuria, and two months progressive lower limb pain walking short distances.

Vital signs included: blood pressure 120/80 mmHg, heart rate 116 bpm, temperature 36° C, oxygen saturation 98%, respiratory rate 26 rpm, and capillary refill 2 seconds. Physical examination revealed pallor skin, hypogastric tenderness but no guarding or rebound sign, and percussion elicited pain over the left flank; no lower limb edema was found. Initial blood workup showed: hemoglobin 14.9 g/dl, hematocrit 44.9%, glucose 149 mg/dl, creatinine 1.6 mg/dL, urea 34 mg/dl, total cholesterol 185 mg/dl (LDL 135.5 mg/dl), elevated transaminases (ALT 134 U/L, AST 207 U/L), and potassium 5.3 mEq/L. Urinalysis revealed abundant bacteria and leukocytes. Abdominal x-rays showed bilateral kidney stones (Figure 1).

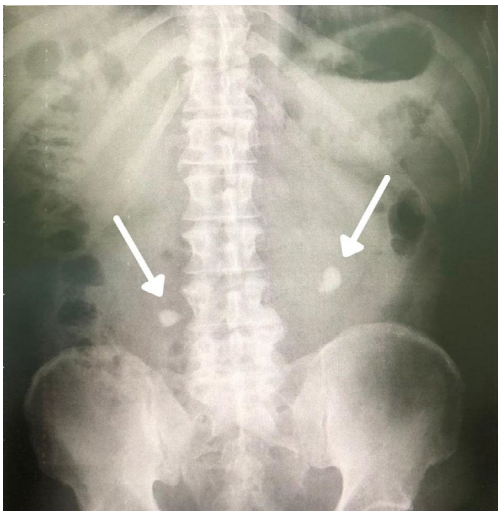


Figure 1. Abdominal x-ray showing bilateral kidney stones.

The patient was admitted for hospitalization under the clinical suspicion of acute pyelonephritis. Treatment with broad spectrum antibiotics was started. Bedside electrocardiogram showed atrial fibrillation and images suggestive of prior myocardial infarction. Amiodarone 200 mg/day for rhythm control and aspirin 100 mg/day as antiplatelet therapy were started.

The urology service was consulted due to nephrolithiasis and a possible lithotripsy procedure. Contrast abdominal computed tomography (CT) and a renal angiography were ordered, and horseshoe kidney and atherosclerotic plaques occluding arterial lumen were found (Figures 2, 3, and 4).

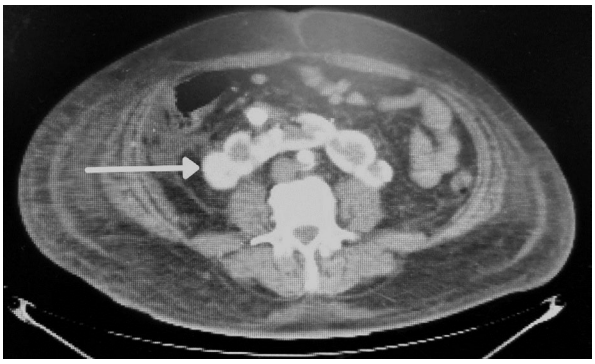


Figure 2. Contrast abdominal CT showing the horseshoe kidney disease.

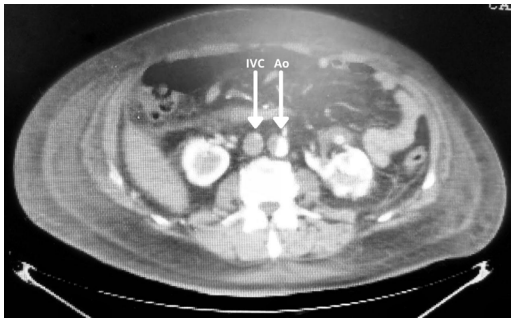


Figure 3. Contrast abdominal CT showing 50% occlusion of abdominal aorta below the renal arteries. IVC: inferior vena cava, Ao: Aorta.

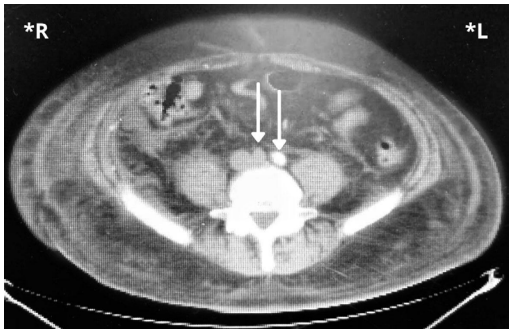


Figure 4. Contrast abdominal CT showing full occlusion of right common iliac artery (right side arrow) and the presence of a minor plaque within the left common iliac artery (left side arrow). R: right, L: left.

Later, the patient developed shortness of breath, fever, and productive cough. RT-PCR for SARS-CoV-2 and blood cultures were negative. Chest CT demonstrated alveolar infiltrates, pleural effusion, and a thrombus allocated in the right pulmonary artery. Transthoracic echocardiography revealed left ventricular ejection fraction of 27%, left-sided dilation, and pulmonary hypertension (43 mmHg). Low-molecular-weight heparin was started.

During the following days, the patient's respiratory symptoms markedly improved, but he frequently complained of nocturnal right leg pain. We identified edema in the right leg and no peripheral pulses. The patient died shortly after due to a massive aortic thromboembolic event.

DISCUSSION

Our patient complained of intermittent claudication for months but sought no medical opinion, and 24 hours prior to his death, physical examination revealed absent arterial pulses in the lower limbs. Both findings were a consequence of complete arterial obstruction caused by LS.

Mortality risk was considered in the patient, since 63% of intermittent claudication cases have a 10-year mortality trend.[13] Death has been reported as a consequence of thrombosis of the ascending aorta.[14] Other systemic complications following systemic embolization included sudden vision loss due to acute retinal artery occlusion,[7] ischemic stroke, and skin necrosis,[15] which our patient did not present during hospitalization.

Although conventional angiography is considered the gold standard for evaluating LS, noninvasive imaging techniques can identify vascular anatomy with great accuracy and increasingly have become the first choice technique, especially computed tomography angiography (CTA) with three-dimensional (3D) reconstruction which provides more information about distal permeability.[16] In our case, a contrast abdominal CT was clear enough to demonstrate the vascular occlusion, even though it was accidental. Regarding LS treatment, aortobifemoral bypass has shown better long-term results but in the short-term endovascular reperfusion may be more advantageous,[17] which our patient could not undergo due to his hemodynamic-respiratory instability.

HSK often presents with nephrolithiasis, urinary tract infections, and chronic abdominal pain,[10,11] such as in our patient. Among the pediatric population, abdominal pain and urinary tract infections are also the most common manifestations.[18] Renovascular HTN in the setting of HSK is unusual,[19] but HTN might accelerate atherosclerotic disease, since it is a risk factor for vasculopathy and our patient had controlled poorly.

As a part of the approach for horseshoe kidney, imaging to analyze kidney anatomy and its vessels were made for our patient, showing the classic presentation of fusion of the kidney's inferior poles,[10] and nephrolithiasis bilaterally. Diagnosis usually is made accidentally when performing noninvasive imaging for another reason.[10] Surgical treatment has been used in these patients, such as shockwave lithotripsy, ureteroscopy, percutaneous nephrolithotomy, and laparoscopy.[20] Lithotripsy was a possible plan due to nephrolithiasis, but aortoiliac atherosclerotic plaque came across in imaging studies.

CONCLUSIONS

Patients' comorbidities and cardiovascular risk factors may accelerate the development of atherosclerotic disease.[21] Intermittent claudication is a first indicator of peripheral occlusive arterial disease, but it may be overlooked during anamnesis. In our case, the use of contrast abdominal computed tomography was useful to diagnose Leriche Syndrome. HSK, despite being a rare condition, predisposes nephrolithiasis and urinary tract infections,[10] which are common diseases.[22,23] Imaging studies in a patient with acute abdominal pain should be analyzed thoroughly, focusing not only on solid organs but also in small vascular details to avoid missing rare and potentially deadly syndromes.

ACKNOWLEDGEMENTS

We are grateful to Yan Carlos Duarte Vera, M.D., Miguel Intriago, M.D., Adriana Ramirez Ibarra, M.D., and Jenny Marcillo Gavilanez, M.D. for the great support behind this manuscript.

REFERENCES

[1] U.S. Centers for Disease Control and Prevention. Leading Causes of Death. March 1, 2021. https://www.cdc.gov/nchs/fastats/leading-causes-of-death.htm. Accessed July 9, 2021.
[2] An X, Fu R, Zhao Z, et al. Leriche syndrome in a patient with acute pulmonary embolism and acute myocardial infarction: a case report and review of literature. BMC Cardiovasc Disord 2020; 20(1):26. PMID: 31952498.
[3] Leriche R, Morel A. The syndrome of thrombotic obliteration of the aortic bifurcation. Ann Surg 1948; 127(2):193-206. PMID: 17859070.
[4] Wilson PWF. Overview of established risk factors for cardiovascular disease. 2021. https://www.uptodate.com/contents/overview-of-established-risk-factors-for-cardiovascular-disease?search=cardiovascular%20risk%20factors&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1. Accessed July 17, 2021.
[5] Ryoo SR, Hong YS, Kim J, Park I. Renal artery stenosis in a patient with Leriche syndrome. Postgrad Med J 2019; 95(1119):51. PMID: 29909399.
[6] Lee W-J, Cheng Y-Z, Lin H-J. Leriche syndrome. Int J Emerg Med 2008; 1(3):223. PMID: 19384523.

[7] Venkatesh R, Gupta I, Jain K, et al. Multiple retinal vascular occlusions in Leriche syndrome. Indian J Ophthalmol 2020; 68(6):1171-1173. PMID: 32461464.
[8] Cook WA, Stephens FD. Fused kidneys: Morphologic study and theory of embryogenesis. Birth Defects Orig Artic Ser 1977; 13(5):327-340. PMID: 588702.
[9] Kirkpatrick JJ, Leslie SW. Horseshoe Kidney. April 19, 2021. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021. PMID: 28613757.
[10] Natsis K, Piagkou M, Skotsimara A, Protogerou V, Tsitouridis I, Skandalakis P. Horseshoe kidney: A review of anatomy and pathology. Surg Radiol Anat 2014; 36(6):517-526. PMID: 24178305.
[11] Kang M, Kim YC, Lee H, et al. Renal outcomes in adult patients with horseshoe kidney. Nephrol Dial Transplant 2021; 36(3):498-503. PMID: 31697372.
[12] Weizer AZ, Silverstein AD, Auge BK, et al. Determining the incidence of horseshoe kidney from radiographic data at a single institution. J Urol 2003; 170(5):1722-1726. PMID: 14532762.
[13] Sartipy F, Sigvant B, Lundin F, Wahlberg E. Ten year mortality in different peripheral arterial disease stages: A population based observational study on outcome. Eur J Vasc Endovasc Surg 2018; 55(4):529-536. PMID: 29478910.
[14] Johnson JK. Ascending thrombosis of abdominal aorta as fatal complication of Leriche's syndrome. AMA Arch Surg 1954; 69(5):663-668. PMID: 13206556.
[15] Kobayashi Y, Takamatsu R, Watanabe R, Sato S. Cerebral infarction with Leriche syndrome. Intern Med Tokyo Jpn 2018; 57(13):1953-1954. PMID: 29491301.
[16] Ahmed S, Raman SP, Fishman EK. CT angiography and 3D imaging in aortoiliac occlusive disease: Collateral pathways in Leriche syndrome. Abdom Radiol 2017; 42(9):2346-2357. PMID: 28401281.
[17] Liang H-L, Li M-F, Hsiao C-C, Wu C-J, Wu T-H. Endovascular management of aorto-iliac occlusive disease (Leriche syndrome). J Formos Med Assoc 2020; 120(7):1485-1492. PMID: 33189506.
[18] Bhandarkar KP, Kittur DH, Patil SV, Jadhav SS. Horseshoe kidney and associated anomalies: Single institutional review of 20 cases. Afr J Paediatr Surg 2018; 15(2):104-107. PMID: 31290474.
[19] Bozić B, Persec Z, Persec J, Borković Z, Galesić K. Diagnostic and treatment of renovascular hypertension in the patient with horseshoe kidney. [Croatian] Acta Medica Croat Cas Hravatske Akad Med Znan 2005; 59(2):137-142. PMID: 15909888.
[20] Stein RJ, Desai MM. Management of urolithiasis in the congenitally abnormal kidney (horseshoe and ectopic). Curr Opin Urol 2007; 17(2):125-131. PMID: 17285023.
[21] Mundi S, Massaro M, Scoditti E, et al. Endothelial permeability, LDL deposition, and cardiovascular risk factors-a review. Cardiovasc Res 2018; 114(1):35-52. PMID: 29228169.
[22] Pearle MS, Goldfarb DS, Assimos DG, etal. Medical management of kidney stones: AUA Guideline. J Urol 2014; 192(2):316-324. PMID: 24857648.
[23] Gupta K, Grigoryan L, Trautner B. Urinary tract infection. Ann Intern Med 2017; 167(7):ITC49-ITC64. PMID: 28973215.

Keywords: Leriche syndrome, arterial occlusive disease, kidney diseases

KANSAS JOURNAL of MEDICINE

Prolonged Asthma Exacerbation as an Initial Presentation in Hereditary Hemorrhagic Telangiectasia

Jacob Umscheid, M.D.[1,2], Joshua Albright, D.O.[1,2], John Chazhoor, MS-4[1], Rhythm Vasudeva, M.D., M.S.[1,3]
[1]University of Kansas School of Medicine-Wichita, Wichita, KS
[2]Department of Pediatrics
[3]Internal Medicine/Pediatrics Residency Program

Received Aug. 4, 2021; Accepted for publication Nov. 21, 2021; Published online Dec. 2, 2021
https://doi.org/10.17161/kjm.vol14.15752

INTRODUCTION

Hereditary hemorrhagic telangiectasia (HHT), also known as Rendu-Osler-Weber syndrome, is an autosomal dominant disease of multiple pathological arteriovenous malformations (AVM) throughout the body.[1] The malformations of HHT are fragile in nature and directly connect arterial blood flow to the venous vasculature, bypassing normally present capillary beds. Disease presentation is dependent on the location of these malformations in the body. Although typically seen as telangiectasias or small AVMs on the skin and mucosa, large AVMs and complications secondary to AVMs can present with symptoms involving the brain, lungs, and liver. As mentioned, the fragility of these vascular malformations lends a hand to deleterious consequences such as hemorrhage, vascular shunting, and passage of venous emboli to the brain.[2]

Initially thought to be a very rare disease, genetic testing has shown the prevalence of HHT to be greater than previously believed.[1] Prevalence for HHT is estimated to be 1/5,000 to 1/10,000 with equal distribution between gender and race.[3-5] Initial symptoms, such as petechiae and epistaxis, may be mild in presentation, and the actual prevalence may be greater than what can be measured. Severe features of HHT, such as pulmonary AVMs, can be the presenting features of HHT and have been observed in 15 to 35% of cases.[6]

In this article, a case of a young female is presented with prolonged acute asthma exacerbation discovered to have large pulmonary AVMs who showed improvement after endovascular coiling and eventual diagnosis of HHT.

CASE REPORT

A 17-year-old female with a past medical history of mild intermittent asthma presented to the pediatric emergency department with a chief complaint of cough, congestion, and wheezing that was unresponsive to albuterol. Her wheezing had started one day prior. Her past medical history included multiple episodes of community acquired pneumonia not requiring hospital admission and recurrent epistaxis. Family history was not available as her parents were not available at the time of presentation.

Initial vital signs included temperature of 37.4°C, pulse of 128 bpm, respiratory rate of 20 breaths per minute, blood pressure of 139/81 mmHg, and oxygen saturation of 85%. Physical examination was significant for respiratory distress with suprasternal retractions and inspiratory and expiratory wheezing. Chest x-ray showed faint patchy airspace opacities in the right midlung (Figure 1). Viral respiratory PCR indicated infection from rhinovirus and enterovirus. Hypoxia improved with 4L via nasal canula and the patient was transferred to the pediatric intensive care unit for management of acute asthma exacerbation triggered by a viral infection. She was initiated on scheduled albuterol for bronchodilation and corticosteroids for anti-inflammation and showed rapid improvement. On day two of hospitalization, she was maintaining an oxygen saturation above 90% on 2L and was transferred to the pediatric floor for continued hypoxia management.

On day three of hospitalization, the patient developed worsening oxygenation and ventilation and a repeat chest X-ray revealed a persistent right middle lobe opacity, prompting initiation of amoxicillin-clavulanate for presumed community acquired pneumonia. She also developed epistaxis that resolved spontaneously and was switched to a high flow face mask due to presumed nasal mucosa irritation from nasal canula. The patient showed minimal improvement and persistent hypoxia despite prolonged treatment course. On day 10 of hospitalization, the patient's mother revealed a personal history of HHT and concern for a pulmonary arteriovenous malformation was investigated with computerized tomography angiogram (CTA). CTA revealed multifocal filling branches extending to the periphery of the right middle lobe with at least three major feeding AVMs present, expanding from directly adjacent to the bifurcation of the right middle lobe and right lower lobe bronchial arteries extending to the periphery (Figure 2). Echocardiogram demonstrated agitated saline contrast in the left atrium, indicating a right to left shunt consistent with a pulmonary AVM. Interventional radiology was consulted for correction of the pulmonary AVMs with three separate locations requiring coil and plug placement (Figure 3). Her hypoxia resolved immediately after this intervention.

An investigation for other AVMs was initiated with a CTA of the head and liver ultrasound, both with negative results. No telangiectasias were observed on the skin of the patient or on the oral mucosa. The genetics service was consulted and a presumptive diagnosis of HHT was made. Genetic testing was offered to confirm the diagnosis but was denied by family.

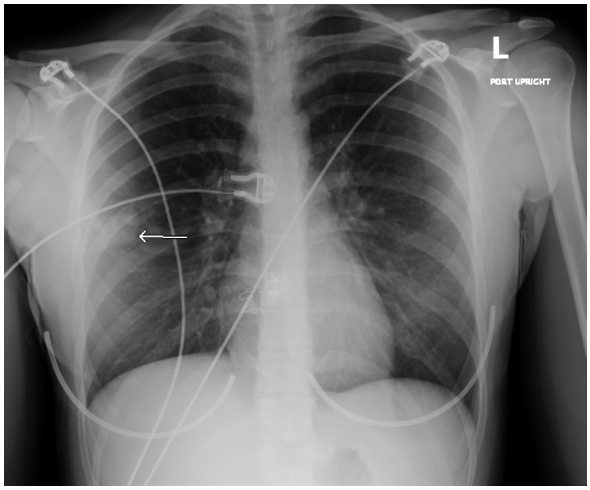


Figure 1. Admission AP chest X-ray showing right mid-lobe air space opacity.

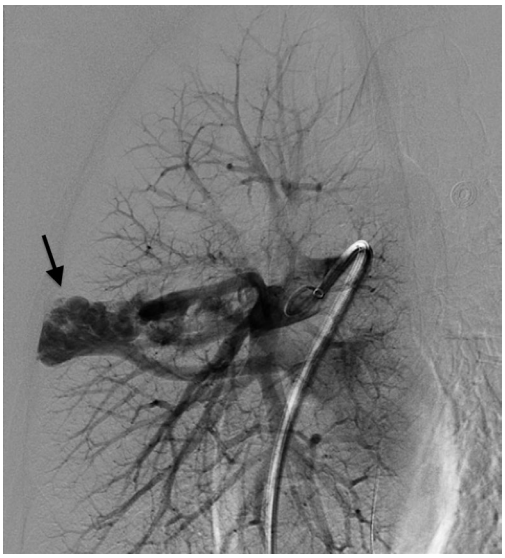


Figure 2. Pre-correction angiography imaging displaying large, complex pulmonary arteriovenous malformations of the right middle lobe.

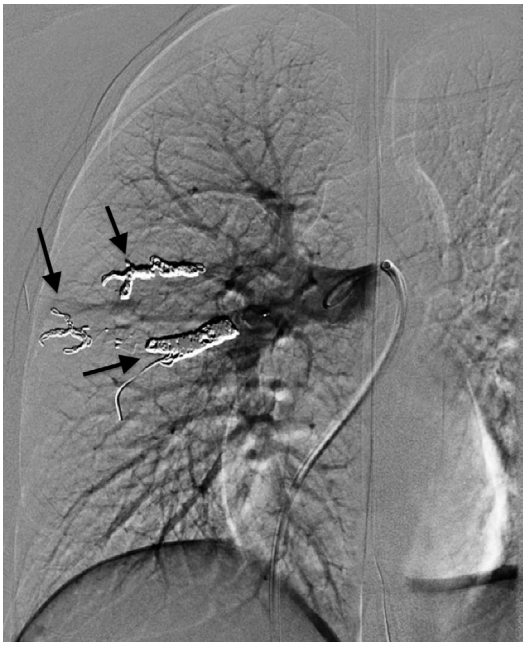


Figure 3. Post-correction angiography imaging showing coil and plug placement with satisfactory exlusion of the AVM with no appreciable residual filling.

DISCUSSION

This case demonstrated a presentation of a pulmonary AVM secondary to HHT resulting in prolonged recovery of an acute asthma exacerbation. Although epistaxis secondary to telangiectasias and involvement of the nasal mucosa is the most common presentation of HHT, these diagnoses can go unrecognized and dismissed as benign.[5] When epistaxis is combined with a prolonged course of respiratory illness, investigation into HHT is warranted. Diagnosis of HHT in adolescents can be difficult, as severity and recurrence increase with age and initial episodes of epistaxis could be relatively mild and result in the underdiagnosis of HHT.[7] The presentation of epistaxis often precedes other manifestations of HHT by 20 to 30 years, making it imperative to carry a low index of suspicion in patients presenting with recurrent epistaxis.[8]

In addition to telangiectasias, much larger AVMs in the pulmonary vasculature can contribute to significant morbidity of individuals with HHT.[6] These consist of a direct connection between a branch of the pulmonary artery and a branch of the pulmonary vein with potential aneurysm at the point of convergence. Patients with HHT tend to present with multiple AVMs and are found most commonly bilaterally in the lower lobes of the lungs.[9] Depending on the method of investigation, 60 to 90% of individuals with pulmonary AVMs have an underlying diagnosis of HHT.[6,10] Detection of these underlying AVMs increases when utilizing tools such as high-resolution computed tomography (CT) and transthoracic contrast CT with saline contrast.[1] Clinical manifestations, such as dyspnea, fatigue, or cyanosis, from pulmonary AVMs stem from the right-to-left shunt created and likely increase in severity depending on the number of AVMs.

Other concerning features of HHT include neurological and hepatic manifestations. Paradoxical emboli resulting in cerebral vascular accidents or abscesses can occur secondary to pulmonary shunting.[11,12] Cerebral vascular malformations also can result in dural fistulas, cavernomas, and aneurysms.[11] Because of this risk, guidelines recommended angio-magnetic resonance imaging screening to investigate cerebral vascular malformations in patients with definite HHT.[5] The prevalence of cerebral AVMs in HHT was approximated to be 10% based on computed tomography, however, this is considered as an underestimate as there are more sensitive methods of investigation available.[13] Akin to both pulmonary and central nervous system vasculature, hepatic vasculature in individuals with HHT also can be found to have AVMs. According to studies utilizing both CT and ultrasounds, frequency of hepatic vascular abnormalities were 74% when using CT and 41% when investigated using ultrasound.[13,14] Only 8% of those studied were symptomatic prior to investigation.[14] Complications of hepatic AVMs include the potential of inducing heart failure secondary to high cardiac output caused by left-to-right shunting within the hepatic vasculature, but also biliary disease and portosystemic encephalopathy.[13,15]

Until 2000, there were no standardized clinical diagnostic criteria for the diagnosis of HHT. A consensus statement on four criteria with an interpretation on the number of positive results and subsequent chances of positive diagnosis, named the Curaçao criteria, was made in 2000.[5,16] These criteria are described in Table 1. Three of the four criteria can be seen with history and physical exam alone. Since its initial release, studies have looked to verify the proposed Curaçao criteria. One study of 263 first-degree relatives who were carriers of disease-causing mutations used genetic testing as a gold standard and found that the Curaçao criteria had a sensitivity of 90.3% of the 186 with HHT causing mutations, 100% positive predictive value of first-degree relatives, and negative predictive value of unlikely diagnosis with 97.7%.[12] In 2020, McDonald et al.[17] reviewed the genetic testing results of 152 individuals who were diagnosed clinically using the Curaçao criteria and concluded approximate 97% presence of causative mutations of either *ENG*, *ACVRL1*, or *SMAD4*.

Table 1. Curaçao criteria for the diagnosis of HHT.

Epistaxis: Spontaneous and recurrent
Telangiectasias: Multiple; at characteristic sites including lips, oral cavity, fingers, and nose
Internal lesions: Such as GI telangiectasia, pulmonary AVM, hepatic AVM, cerebral AVM, and spinal AVM
Family history: A first-degree relative with HHT according to these criteria
The HHT diagnosis is definite if three or more criteria are present, possible or suspected if two are met, and unlikely if fewer than two criteria are present.

CONCLUSIONS

The diagnosis of HHT remains a clinical diagnosis through thorough medical history, family history, and physical examination. When the diagnosis is made, a multisystem investigation is required to investigate potential AVMs. It is also important to investigate family members for HHT due to its autosomal dominant inheritance pattern. Unexplained presentation, such as a prolonged asthma exacerbation in this case presentation, with significant family history should make one suspicious of the diagnosis. Since AVMs can be present in multiple organ systems, a multidisciplinary approach involving specialists in hematology, pulmonology, gastroenterology, interventional radiology, cardiology, neurology, and genetics may be required to provide optimal care for affected patients.

REFERENCES

[1] McDonald J, Bayrak-Toydemir P, Pyeritz RE. Hereditary hemorrhagic telangiectasia: An overview of diagnosis, management, and pathogenesis. Genet Med 2011; 13(7):607-616. PMID: 21546842.
[2] Kim YH, Vu PN, Choe SW, et al. Overexpression of activin receptor-like kinase 1 in endothelial cells suppresses development of arteriovenous malformations in mouse models of hereditary hemorrhagic telangiectasia. Circ Res 2020; 127(9):1122-1137. PMID: 32762495.
[3] Kühnel T, Wirsching K, Wohlgemuth W, Chavan A, Evert K, Vielsmeier V. Hereditary hemorrhagic telangiectasia. Otolaryngol Clin North Am 2018; 51(1):237-254. PMID: 29217066.
[4] Donaldson JW, McKeever TM, Hall IP, Hubbard RB, Fogarty AW. The UK prevalence of hereditary haemorrhagic telangiectasia and its association with sex, socioeconomic status and region of residence: A population-based study. Thorax 2014; 69(2):161-167. PMID: 24188926.
[5] Faughnan ME, Palda VA, Garcia-Tsao G, et al. International guidelines for the diagnosis and management of hereditary haemorrhagic telangiectasia. J Med Genet 2011; 48(2):73-87. PMID: 19553198.
[6] Lacombe P, Lacout A, Marcy PY, et al. Diagnosis and treatment of pulmonary arteriovenous malformations in hereditary hemorrhagic telangiectasia: An overview. Diagn Interv Imaging 2013; 94(9):835-848. PMID 23763987.
[7] Guttmacher AE, Marchuk DA, White RI Jr. Hereditary hemorrhagic telangiectasia. N Engl J Med 1995; 333(14):918-924. PMID: 7666879.
[8] Plauchu H, de Chadarévian JP, Bideau A, Robert JM. Age-related clinical profile of hereditary hemorrhagic telangiectasia in an epidemiologically recruited population. Am J Med Genet 1989; 32(3):291-297. PMID: 2729347.
[9] Khurshid I, Downie GH. Pulmonary arteriovenous malformation. Postgrad Med J 2002; 78(918):191-197. PMID: 11930021.
[10] Dines DE, Arms RA, Bernatz PE, Gomes MR. Pulmonary arteriovenous fistulas. Mayo Clin Proc 1974; 49(7):460-465. PMID: 4834927.
[11] Labeyrie PE, Courthéoux P, Babin E, Bergot E, Touzé E, Pelage JP. Neurological involvement in hereditary hemorrhagic telangiectasia. J Neuroradiol 2016; 43(4):236-245. PMID: 27059009.
[12] van Gent MWF, Velthuis S, Post MC, et al. Hereditary hemorrhagic telangiectasia: How accurate are the clinical criteria? Am J Med Genet A 2013; 161A(3):461-466. PMID: 23401183.
[13] Bayrak-Toydemir P, Mao R, Lewin S, McDonald J. Hereditary hemorrhagic telangiectasia: An overview of diagnosis and management in the molecular era for clinicians. Genet Med 2004; 6(4):175-191. PMID: 15266205.
[14] Ianora AAS, Memeo M, Sabba C, Cirulli A, Rotondo A, Angelelli G. Hereditary hemorrhagic telangiectasia: Multi-detector row helical CT assessment of hepatic involvement. Radiology 2004; 230(1):250-259. PMID: 14645886.
[15] Bernard G, Mion F, Henry L, Plauchu H, Paliard P. Hepatic involvement in hereditary hemorrhagic telangiectasia: Clinical, radiological, and hemodynamic studies of 11 cases. Gastroenterology 1993; 105(2):482-487. PMID: 8335203.
[16] Shovlin CL, Guttmacher AE, Buscarini E, et al. Diagnostic criteria for hereditary hemorrhagic telangiectasia (Rendu-Osler-Weber syndrome). Am J Med Genet 2000; 91(1):66-67. PMID: 10751092.
[17] McDonald J, Bayrak-Toydemir P, DeMille D, Wooderchak-Donahue W, Whitehead K. Curaçao diagnostic criteria for hereditary hemorrhagic telangiectasia is highly predictive of a pathogenic variant in ENG or ACVRL1 (HHT1 and HHT2). Genet Med 2020; 22(7):1201-1205. PMID: 32300199.

Keywords: hereditary hemorrhagic telangiectasia, asthma exacerbation, arteriovenous malformations

KANSAS JOURNAL of MEDICINE

Acute Psychosis Associated with Phenibut Ingestion

Eric Acosta, M.D., Cyrus Munguti, M.D.
University of Kansas School of Medicine-Wichita, Wichita, KS
Department of Internal Medicine

Received May 31, 2021; Accepted for publication Oct. 22, 2021; Published online Dec. 2, 2021
https://doi.org/10.17161/kjm.vol14.15550

INTRODUCTION

β-Phenyl-γ-aminobutyric acid (phenibut) is a glutamic acid analog that acts on the γ-aminobutyric acid receptors ($GABA_A$ and $GABA_B$) and B-phenethylamine receptors.[1] It has been used for anxiety, post-traumatic stress disorder, and insomnia, but it has not been approved by the U.S. Food Drug Administration (FDA) for use. Phenibut is advertised as a supplement and easily purchased from online retailers and has high abuse potential. Common adverse effects occur on abrupt withdrawal and may mimic neuroleptic malignant syndrome or serotonin syndrome.

We present a case of a man who presented with hallucinations and acute psychosis following ingestion of phenibut in combination with his usual prescriptions. This case highlighted the need for clinicians to become aware of potent pharmaceutical substances masquerading as supplements.

CASE REPORT

A 40-year-old man with a past medical history of anxiety, depression, hypertension, and substance abuse presented to the hospital via emergency medical services for agitation, auditory and visual hallucinations, and one episode of seizure-like activity. His mother provided most of the initial history due to the patient's altered mental status. She reported her son had experienced auditory and visual hallucinations for three to five days after taking phenibut, which he had ordered online. The patient also was taking hydroxyzine, gabapentin, and trazodone. Urine drug screen and alcohol level were negative on admission.

The patient became increasingly agitated and paranoid in the days leading up to the presentation. In the emergency department (ED), he became agitated and belligerent to a degree requiring intravenous lorazepam and physical restraints as re-orientation was ineffective. His speech was incoherent. He was shaking, profusely sweating, and tachycardic, with a pulse rate above 140 beats per minute. Due to a decreased Glasgow Coma Scale score, he required intubation in the emergency department for airway protection and sedation. He was placed on multiple sedative medications and was admitted to the intensive care unit (ICU).

Laboratory tests revealed elevated lactic acid of 9.1 mmol/L, creatine phosphokinase at 5,422 U/L, serum creatinine of 2.03 mg/dL, white blood cell count of 15,000/μL, which peaked on day two at 23,700/μL, and mildly elevated transaminase levels. His urinalysis on admission was positive for 3+ ketones and 2+ blood. The patient had no history of diabetes mellitus and did not have hyperglycemia. He was given empiric antibiotics in the emergency department and blood cultures were ordered. The patient was rehydrated, and his renal function was monitored. He remained sedated and on mechanical ventilation for two days in the ICU. He was agitated whenever sedation was weaned for sedation holiday each morning.

The patient was extubated on the third day of hospitalization as he was calm enough to cooperate with spontaneous breathing trials but continued to have intermittent episodes of agitation, which responded to scheduled quetiapine, as needed lorazepam, and dexmedetomidine. His mental status slowly normalized, and he was discharged on day six of hospitalization.

DISCUSSION

The U.S. Centers for Disease Control and Prevention reported a rapid increase in the use of phenibut from 2009 to 2019, and most of this use was driven by unregulated online sales.[1] This case highlighted some of the dangers of co-ingestion of phenibut with other pharmacologically similar drugs that potentially can enhance its effects. Our patient had co-ingestion of gabapentin and phenibut, which have very similar mechanisms of action, potentially enhancing the toxicity of phenibut. Like other reported cases,[2] our patient experienced significant agitation. As in this case, standard urine drug screens do not detect phenibut.

Phenibut was synthesized in St. Petersburg, Russia, in the 1960s.[3] The compound's effects on $GABA_A$, $GABA_B$, dopaminergic, and benzodiazepine receptors were compared to diazepam and a related compound, piracetam. The chemical structure of phenibut results from combining GABA with a phenyl ring with the expectation that this would facilitate blood-brain barrier permeability. Though chemically similar to GABA, phenibut has no activity at the $GABA_A$ receptors and has a lower affinity to $GABA_B$ than the related compound baclofen.

In addition to binding $GABA_B$ receptors, phenibut also has activity on α2δ1 voltage-dependent calcium channels (VDCC), like gabapentin. The R isomer of phenibut acts on $GABA_B$ receptors with a lower affinity than baclofen, while the S isomer has no activity at the $GABA_B$ receptors.[4] Both R and S isomers of phenibut bind with similar affinities to the α2δ1 VDCC. R phenibut binds to the α2δ1 VDCC with a higher affinity than the $GABA_B$ receptor.[5] Though it has a similar mechanism of action as gabapentin, it does not possess anticonvulsant activity. This may be due to gabapentin having activity on α2δ2 VDCC while phenibut does not.[6,7]

Phenibut has a half-life of approximately 5.3 hours, is not metabolized, and is excreted unchanged in the urine.[2] Clinical trials in Russia have reported phenibut activates intellectual functions, improves physical strength, motivates activity, and reduces asthenia and tiredness. Phenibut is an anxiolytic and a nootropic agent and is used to treat neurologic and psychiatric disorders.[3,8]

Phenibut is a widely available pharmaceutical that has generated other case reports due to its toxidrome.[9,10] The U.S. FDA does not regulate phenibut, and its abuse appears to be rising. Cases reported to poison control centers became significant around 2015 and peaked in 2018. There are 56 reported exposures in the U.S., 48 of which occurred in the last five years.[11]

Commonly reported adverse effects include lethargy, agitation, tachycardia, confusion, and coma, and several phenibut-related deaths

have been reported.[1] Acute intoxication results in central nervous system depression, decreased muscle tone, and stupor. Paradoxically, this may present as hallucinations, seizures, and agitation.[2] Chronic use of phenibut causes downregulation of $GABA_B$ receptors, and discontinuation would explain the toxidrome noted in our patient case. Acute withdrawal may be difficult to differentiate from serotonin or neuroleptic malignant syndrome, however, hyperreflexia has not been reported to be a symptom of phenibut intoxication or withdrawal. There are cases where a baclofen taper was used to treat withdrawal in those who develop a substance abuse disorder.[12] Phenibut is excreted in the urine, thus it may be possible to treat intoxication with hemodialysis. However, studies would have to be done to prove efficacy.

CONCLUSIONS

Though clinical trials reported benefits of phenibut, therapeutic doses are unknown. Toxicity from phenibut is treated with supportive care or a baclofen taper until symptoms resolve. The patient was safely discharged home after six days of hospitalization without any sequelae. With an increase in cases in recent years, ingestion of unregulated psychotropic agents needs to be high in the differential diagnosis in cases of psychosis or other psychiatric concerns. Phenibut is advertised as a supplement and easily purchased from online retailers. This case highlighted the need for clinicians to become aware of pharmaceuticals masquerading as supplements.

REFERENCES

[1] Graves JM, Dilley J, Kubsad S, Liebelt E. Notes from the field: Phenibut exposures reported to poison centers - United States, 2009-2019. MMWR Morb Mortal Wkly Rep 2020; 69(35):1227-1228. PMID: 32881852.
[2] Hardman MI, Sprung J, Weingarten TN. Acute phenibut withdrawal: A comprehensive literature review and illustrative case report. Bosn J Basic Med Sci 2019; 19(2):125-129. PMID: 30501608.
[3] Lapin I. Phenibut (beta-phenyl-GABA): A tranquilizer and nootropic drug. CNS Drug Rev 2001; 7(4):471-481. PMID: 11830761.
[4] Blackburn T. (Ed.) GABAb Receptor Pharmacology: A Tribute to Norman Bowery. San Diego: Academic Press, 2010. ISBN: 9780123786470.
[5] Zvejniece L, Vavers E, Svalbe B, et al. R-phenibut binds to the α2-δ subunit of voltage-dependent calcium channels and exerts gabapentin-like antinociceptive effects. Pharmacol Biochem Behav 2015; 137:23-29. PMID: 26234470.
[6] Sills GJ. The mechanisms of action of gabapentin and pregabalin. Curr Opin Pharmacol 2006; 6(1):108-113. PMID: 16376147.
[7] Taylor CP. The biology and pharmacology of calcium channel alpha2-delta proteins Pfizer Satellite Symposium to the 2003 Society for Neuroscience Meeting. Sheraton New Orleans Hotel, New Orleans, LA November 10, 2003. CNS Drug Rev 2004; 10(2):183-188. PMID: 15317151.
[8] Gol'dblat IuV, Lapin IP. [Phenibut potentiation of the therapeutic action of antiparkinson agents.] [Russian] Zh Nevropatol Psikhiatr Im S S Korsakova 1986; 86(8):1146-1148. PMID: 3776387.
[9] Sankary S, Canino P, Jackson J. Phenibut overdose. Am J Emerg Med. 2017; 35(3):516.e1-516.e2. PMID: 27666756.
[10] Downes MA, Berling IL, Mostafa A, Grice J, Roberts MS, Isbister GK. Acute behavioural disturbance associated with phenibut purchased via an internet supplier. Clin Toxicol (Phila) 2015; 53(7):636-638. PMID: 26114346.
[11] McCabe DJ, Bangh SA, Arens AM, Cole JB. Phenibut exposures and clinical effects reported to a regional poison center. Am J Emerg Med 2019; 37(11):2066-2071. PMID: 30878413.
[12] Ahuja T, Mgbako O, Katzman C, Grossman A. Phenibut (β-phenyl-γ-aminobutyric acid) dependence and management of withdrawal: Emerging nootropics of abuse. Case Rep Psychiatry 2018; 2018:9864285. PMID: 2985431.

Keywords: phenibut, pharmacology, nootropic agents, substance-related disorders

KANSAS JOURNAL of MEDICINE

Atypical Presentation of Anti-MOG Ab Disease

Sanjeev K. Bhoi, M.D., D.M.[1], Menka Jha, M.D., D.M.[1], Suprava Naik, M.D.[2], Arijit Bag, M.D.[1], Binaya Jaiswal, M.D.[1], Rajesh Kumar, M.D.[3]
All India Institute of Medical Sciences, Bhubaneswar, Odisha, India
[1]Department of Neurology
[2]Department of Radiodiagnosis
[3]Department of Medicine

Received May 20, 2021; Accepted for publication Nov. 28, 2021; Published online Dec. 2, 2021
https://doi.org/10.17161/kjm.vol14.15494

INTRODUCTION

Myelin oligodendrocyte glycoprotein antibodies (MOG-IgG) associated diseases are a spectrum of central nervous system demyelinating disorders. Clinical differentiations from multiple sclerosis, neuromyelitis spectrum disorder (NMOSD) with or without Aquaporin antibody (AQP4-Ab), are very narrow.[1,2] Recurrence of illness, specific antibody positivity, and response to immunotherapy favors diagnosis. NMOSD and MOG associated diseases share common involvement pattern of optic nerve and cervico-dorsal myelitis.[2,3] MOG involves rhombencephalon especially pontine white matter tract, while NMOSD has predilection around the periventricular Aquaporin channels.[4] Involvement of conus and caudal nerve roots are rare involvement in MOG antibody associated diseases.[5]

We present three cases of MOG-IgG positive patients with bilateral optic neuritis, conus cauda syndrome, and pontine demyelination mimicking Chronic Lymphocytic Inflammation with Pontine Perivascular Enhancement Responsive to Steroids (CLIPPERS).

CASE REPORT

Case 1. A 20-year-old male student presented with acute onset progressive painless asymmetric vision loss of five days. He had no prior comorbidities or addictions. He never experienced any focal neurological symptoms earlier. His general and neurological examinations were normal (Table 1). His intraocular pressure was normal. Maximal visual acuity in the right eye was finger counting at 1-meter; left eye was perception of light. Fundus examination revealed blurred disc margin bilaterally. Ophthalmological evaluation, including retina, anterior chamber, and posterior chamber, was unremarkable.

Routine blood parameters, including complete hemogram, liver function test, renal function test, and serum blood glucose level, were normal. Cerebrospinal fluid (CSF) examination revealed protein level (27 mg/dl) with mild lymphocytic pleocytosis (seven total cells, 86% mononuclear and 14% polymorphonuclear). HbsAg, Anti HCV Ab, and HIV Ab status were negative. Pattern visual evoked potential (VEP) was not recordable on the left eye; right eye P100 latency was prolonged 154.2 ms (amplitude 4.46 µV).

Table 1. Clinical and laboratory findings of MOG Ab positive patients.

Parameters	Case 1	Case 2	Case 3
Age (in years)	20	37	29
Gender	Male	Female	Female
Duration of illness	5 days	30 days	7 days
Symptoms	Bilateral vision loss	Bilateral lower limb weakness, bladder and bowel involvement	Gait ataxia, slurred speech, horizontal diplopia (bilateral)
Preceding illness	Nil	Undergone caesarian section at term for fetal distress under spinal anesthesia, postoperative day one noticed paraplegia	Fever for six days one week prior to neurological deficit
Onset and progression	Acute, right followed by left. Nadir at five days	Acute, maximal at onset	Acute, progression for one week
Past or chronic illness	No	No	No
Treatment received before admission to our Institute	Nil	IV Methyl prednisolone 500 mg x five days	Nil
General examinations and vitals	Normal	Normal	Normal
Neurological examination (abnormal findings)	VA: Right eye: finger counting from 1 meter Left eye: PL+/ PR+ Bilateral optic disc margin blurred	Bilateral lower limb motor power (MRC) 1/5 with weakness of lower truncal muscles. Sensation loss below umbilical level, bladder catheterized and stool incontinence	Higher mental function- normal Bilateral optic disc margin: blurred. Bilateral 6th cranial nerve palsy, left LMN facial palsy, hand incoordination +, gait: ataxic
Biochemical parameters	Urea: 25 mg/dl Creatinine: 0.8 mg/dl LFT: Normal Na+: 134 meq/l K+: 4.5 meq/l Hb%: 14.5 gm% TLC: 8500/cumm N: 52%,L 37% TPC: 232000/ cumm Urine R/E: normal. HIV: NR HbsAg: NR Anti HCV Ab: NR ANA: Neg ANCA: Neg TFT: N CRP: Neg	Urea: 18 mg/dl Creatinine: 0.7 mg/dl LFT: Normal Na+: 136 meq/l K+: 4.3 meq/l Hb%: - 12.5 gm% TLC: 7500/cumm N: 55%,L 45% TPC: 260000/ cumm Urine R/E: normal. HIV: NR HbsAg: NR Anti HCV Ab: NR ANA: Neg ANCA: Neg TFT: N CRP: Neg	Urea: 19 mg/dl Creatinine: 0.6 mg/dl LFT: Normal Na+: 139 meq/l K+: 4.2 meq/l Hb%: 12.9 gm% TLC: 11590/cumm N: 75%,L 18% TPC: 274000/ cumm Urine R/E: normal. HIV: NR HbsAg: NR Anti HCV Ab: NR ANA: Neg ANCA: Neg TFT: N CRP: Neg
CSF Examination	Total cells: 7 85% MNC, 15% PMNC Glucose: 93 mg/dl Protein: 27 mg/dl	Total cells: 8 68% MNC, 32% PMNC Glucose: 98 mg/dl Protein: 104 mg/dl	Total cells: 52 88% MNC, 12% PMNC Glucose: 144 mg/dl Protein: 45 mg/dl
Pattern VEP (P100)	Left: no wave Right: 154.2 ms Amp: 4.46 µV	Prolonged	Left: 129.9 ms Amp: 4.19 µV Right: 123.9 ms Amp: 3.29µV
SSEP (tibial)	Bilateral prolonged CSCT	Bilateral prolonged CSCT	Bilateral prolonged CSCT

Table 1. Clinical and laboratory findings of MOG Ab positive patients. *continued.*

Parameters	Case 1	Case 2	Case 3
BAER	Normal	Normal	Normal
MRI Brain/spine	Normal	Swelling of cord at conus, T2 hyperintense signal in most of cross section of cord up to 3 cm, patchy enhancement on post contrast. Cauda equina nerve roots are thickened and enhancement on post contrast. Brain normal	Multiple T2 & FLAIR hyperintense and contrast enhancing lesion in pons, medulla, cerebellum and left frontal white matter region. Spine normal
Serum IgG Anti-NMO Ab (cell-based assay)	Negative	Negative	Negative
Serum IgG Anti -MOG Ab (cell-based assay)	Positive	Positive	Positive
Treatment	IV methylprednisolone 1 gm daily for five days followed by oral prednisolone 40 mg daily	IV methylprednisolone 1 gm daily for five days followed by oral prednisolone 40 mg/day	IV methylprednisolone 1 gm daily for five days followed by oral prednisolone 30 mg daily
Response to treatment after two weeks	Vision improved in both eye- finger counting from 3 meters distance bilaterally	Both lower limbs having antigravity movement	Walking without support, hand incoordination improved, able to maintain daily life activities with minimal help, diplopia improved.
Last follow- up	1 month: VA 6/18	3 months: Walk with walker aid, urine incontinent	3 months: Improved, mild spasticity of limbs

VA: visual acuity, CSF: cerebrospinal fluid, VEP: visual evoked potential, SSEP: somato sensory evoked potential, BAER: brain stem auditory response, MOG: myelin oligodendrocyte glycoprotein, NMO: neuromyelitis optica, CSCT: central sensory conduction time; LFT: liver function tests

Contrast enhanced magnetic resonance imaging (MRI) of the brain and spine were done to look for any demyelinating lesions in central neuroaxis which was unremarkable (Figure 1). Evaluation for underlying autoimmune pathology included serum anti-nuclear antibody, anti-neutrophilic cytoplasmic antibody; C-reactive protein (CRP) level was negative. Serum IgG anti-MOG Ab was positive by cell-based assay and simultaneous anti-aquaporin-4 antibody status was negative. CSF oligo-clonal band was negative. Tibial somato-sensory evoked potential (SSEP) showed bilaterally prolonged central sensory conduction time (CSCT), which also favored the background demyelinating pathology. Brainstem auditory evoked potential was normal bilaterally.

The patient was managed with intravenous methyl prednisolone 1 gram daily for five days followed by oral prednisolone 40 mg daily which was tapered over the next six months. At one-month follow-up, his visual acuity improved to 6/18 bilaterally.

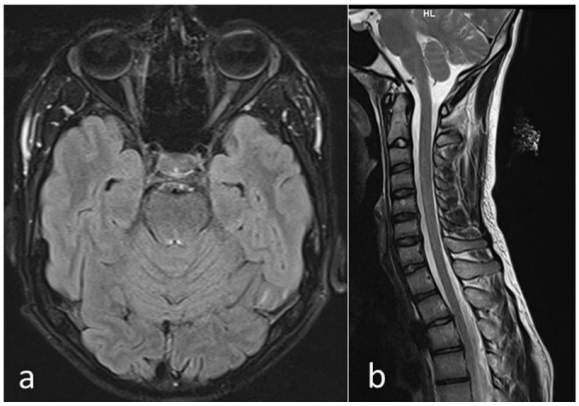


Figure 1. Axial FLAIR image (a) at the orbit level shows normal signal of both optic nerves. Sagittal T2WI (b) of cervical spine shows normal cord signal.

Case 2. A 30-year-old female presented with acute onset paraplegia with bladder and bowel involvement following caesarean section under spinal anesthesia. On post-operative day one, she developed weakness of lower limb, associated truncal weakness, and sensory level below umbilicus. This patient had no prior comorbidity and did not suffer from any focal neurological symptoms earlier. General examination was unremarkable. Neurological examination revealed power (Medical Research Council scale) 1/5 in bilateral lower limbs, diminished tendon reflexes in lower limbs, and sensory impairment below D10 level. She developed urinary retention on day two of her weakness and again re-catheterized after removal during recovery from post-spinal anaesthesia period. Before reaching our clinic, she received intravenous methyl prednisolone pulse therapy of 1 gm for five days, though no significant improvement was noted in form recovery of power in lower limbs and she was in bed bound state (Modified Rankin Scale - 5).

Routine blood parameters, including complete hemogram, liver function test, renal function test, thyroid function test, and serum blood glucose level, were normal (Table 1). Her HbsAg, Anti HCV Ab, and HIV Ab status were negative. Cerebrospinal fluid (CSF) examination revealed elevated protein level 104 mg/dl with mild lymphocytic pleocytosis (eight total cells, 62.8% mononuclear and 37.2% polymorphonuclear cells). MRI of the spine showed swelling of spinal cord at conus level with increased T2 signal and patchy contrast enhancement (Figure 2), the rest of spinal cord and brain was normal. Pattern VEP done was prolonged bilaterally, and tibial SSEP also was prolonged bilaterally. Serum IgG anti-MOG Ab done by cell-based assay was positive. Her brainstem auditory evoked response (BAER) was normal bilaterally. Serum anti-aquaporin-4 antibody status was negative and CSF oligo-clonal band was not detected. Routine urine examination revealed no proteinuria or hematuria. Evaluation of secondary central nervous system (CNS) demyelinating etiologies was non-contributory. Serum ANA antibody, anti-neutrophilic antibody, and CRP were negative. CT scan of thorax and abdomen to evaluate organ involvement in background of inflammatory diseases and rule out infective aetiology was non-contributory.

The patient was managed with IV methylprednisolone 1 gm daily for five days followed by oral prednisolone 40 mg daily which was tapered over the next year with overlapping therapy with azathioprine. At discharge after 15 days, her lower limb motor power improved to MRC grade 3 bilaterally. Follow-up at three months, she was ambulatory with minimal support, though urine and stool were incontinent.

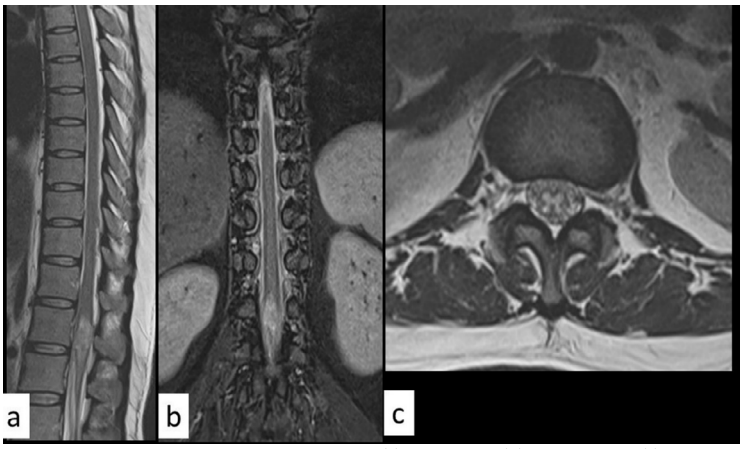


Figure 2. MRI of dorsal spine sagittal (a), coronal (b), and axial (c). T2WI shows focal cord expansion at the conus with increased cord signal intensity predominantly at the center.

Case 3. A 29-year-old female was admitted with acute onset gait ataxia, slurred speech, and bilateral horizontal diplopia that progressed over seven days. She had self-limiting fever one-week prior onset of neurological symptoms. General examination was normal. Neurological evaluation revealed bilateral optic disc edema, left 6th cranial nerve palsy, and left facial lower motor type palsy. Power of lower limb was grade 4/5 with brisk reflexes and positive cerebellar signs. She had no prior comorbidity and no history suggestive of any prior connective tissue disease.

Routine blood parameters, including complete hemogram, liver function test, renal function test, thyroid function test, and serum blood glucose level, were normal. Her HbsAg, anti HCV Ab, and HIV Ab status were negative. Erythrocyte sedimentation rate was 30 mm in the first hour. CSF examination revealed lymphocytic pleocytosis (52 total cells, 88% mononuclear cells and 12% polymorphonuclear cells) with normal protein 45 mg/dl and sugar level. Pattern VEP revealed prolonged P100 latency bilaterally (left: 129.9 ms; right: 123.9 ms) with preserved amplitude. Serum IgG anti-MOG Ab (done by cell-based assay) was positive and anti-NMO Ab was negative (Table 1). MRI of the brain revealed multiple discrete T2 and FLAIR hyperintense lesions in pons, medulla, middle cerebellar peduncles, and left frontal white matter showing patchy contrast enhancement. Her tibial SSEP was prolonged bilaterally though BAER was normal. CSF oligo-clonal band was not detected, and IgG Index was negative. Routine urine examination revealed no proteinuria or hematuria. Evaluation for secondary CNS demyelinating etiologies was non-contributory. Serum ANA antibody, anti-neutrophilic antibody, and CRP were negative. CT scan of the thorax and abdomen to evaluate organ involvement in background of inflammatory diseases and rule out infective etiology was normal.

The patient was managed with IV methylprednisolone 1 gram daily for five days followed by oral prednisolone 30 mg daily. At discharge after 28 days, she was able to walk independently. A repeat MRI of the brain showed significant decrease in lesion size and enhancement (Figure 3). At a three-month follow-up, mild residual spasticity in lower limbs were noted though cranial nerve features and cerebellar deficits were resolved.

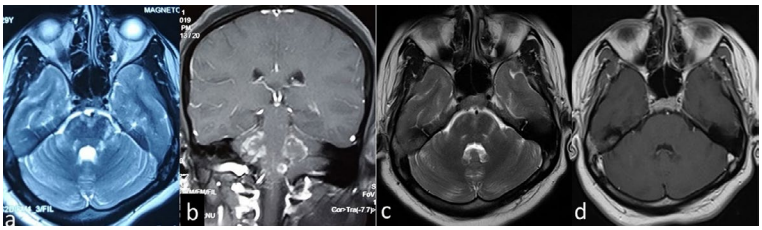


Figure 3. Axial T2WI brain MRI (a) shows multiple hyperintense lesions in pons and middle cerebellar peduncle. Post contrast coronal T1WI (b) shows patchy and curvilinear enhancement mimicking CLIPPERS. Follow up MRI: Axial T2WI (c) and post contrast T1WI (d) shows reduced size and number of the lesions and no enhancement.

DISCUSSION

The three cases highlighted the CNS spectrum of MOG Ab disease. Case 1 was a classic case of bilateral optic neuritis. However, cases 2 and 3 were atypical presentations of MOG disease spectrum. In adults, MOG disease usually is associated with optic neuritis and myelitis in more than 80% of cases.[1,2] In a study, 31 (18.7%) out of 166 episodes had bilateral optic neuritis, myelitis in 32 (19.3%), and brain and stem involvement in 44 (26.5%).[3] MOG Ab associated spinal cord lesions are longitudinally extensive transverse myelitis of cervico-dorsal spinal cord similar to NMOSD (AQP4-Ab+) lesions. Involvement of lower spinal cord and sacral roots are rare but pathognomonic of MOG disease.[4-6] The second case developed paraplegia following caesarean section under spinal anesthesia, which concerns clinicians about operative and other differentials. Recovery of motor power is brisk, however, bladder and bowel control showed poor recovery, as also seen in case 2.[7]

CLIPPERS are a radiological diagnosis of an inflammatory brain stem syndrome of uncertain etiology and T-cell-predominant CSF leukocytosis. CLIPPERS associated with MOG Ab are diagnosed increasingly.[8,9] Clinically, they present with subacute onset brain stem dysfunction. Imaging revealed T2 hyperintense lesions with ill-defined margins in posterior fossa predominantly involving pons and measuring more than 2 cm. Multiple punctate and curvilinear post contrast enhancement in the pons with or without extension to cerebellum and cerebellar peduncle is characteristic of the syndrome. The lesions may extend caudally to the medulla and cervical spinal cord, cranially to the midbrain and supratentorial parenchyma. Enhancement decreases after treatment as the patients respond to corticosteroids.

CLIPPERS responds to corticosteroids both clinically and radiologically and have fair chance to relapse on stopping steroids.[10] Our cases have subclinical involvement of the optic nerve and myelitis as evidenced by VEP latency prolongation and prolong central sensory conduction time in tibial SSEP. MOG Ab is expressed specifically in the central nervous system on the surface of myelin sheaths and oligodendrocyte processes.[11] In humans, presence of MOG Ab are debated

as pathogenic themselves or an epiphenomenon secondary to immune upregulation following prior demyelination or infection. In our series, cases 2 and 3 had preceding illness prior to neurological presentation.

Human MOG Ab might play a minor role in the pathophysiology of inflammatory demyelination, however, there are highly specific markers in specific clinical settings.[12] However, recent developments have established its plausible role in human MOG Ab associated CNS demyelination and its varying clinical spectrum. The exact pathophysiologic effect of human MOG Ab needs further critical evaluation in CNS and PNS demyelination.

CONCLUSIONS

The present case series highlighted the importance to test for anti-MOG antibodies in patients presenting with conus cauda syndrome and CLIPPERS, especially when MRI shows demyelinating features.

REFERENCES

[1] Cobo-Calvo A, Ruiz A, Maillart E, et al. OFSEP and NOMADMUS Study Group. Clinical spectrum and prognostic value of CNS MOG autoimmunity in adults: The MOGADOR study. Neurology 2018; 90(21):e1858-e1869. PMID: 29695592.

[2] Jurynczyk M, Messina S, Woodhall MR, et al. Clinical presentation and prognosis in MOG-antibody disease: A UK study. Brain 2017; 140(12):3128-3138. PMID:29136091.

[3] Akaishi T, Sato DK, Takahashi T, Nakashima I. Clinical spectrum of inflammatory central nervous system demyelinating disorders associated with antibodies against myelin oligodendrocyte glycoprotein. Neurochem Int 2019; 130:104319. PMID:30365980.

[4] Vazquez Do Campo R, Stephens A, Marin Collazo IV, Rubin DI. MOG antibodies in combined central and peripheral demyelination syndromes. Neurol Neuroimmunol Neuroinflamm 2018; 5(6):e503. PMID: 30246057.

[5] Sundaram S, Nair SS, Jaganmohan D, Unnikrishnan G, Nair M. Relapsing lumbosacral myeloradiculitis: An unusual presentation of MOG antibody disease. Mult Scler 2020; 26(4):509-511. PMID: 30931808.

[6] Sato DK, Callegaro D, Lana-Peixoto MA, et al. Distinction between MOG antibody-positive and AQP4 antibody-positive NMO spectrum disorders. Neurology 2014; 82(6):474-481. PMID: 24415568.

[7] Juryńczyk M, Jacob A, Fujihara K, Palace J. Myelin oligodendrocyte glycoprotein (MOG) antibody-associated disease: Practical considerations. Pract Neurol 2019; 19(3):187-195. PMID: 30530724.

[8] Symmonds M, Waters PJ, Küker W, Leite MI, Schulz UG. Anti-MOG antibodies with longitudinally extensive transverse myelitis preceded by CLIPPERS. Neurology 2015; 84(11):1177-1179. PMID: 25681455.

[9] Berzero G, Taieb G, Marignier R, et al. CLIPPERS mimickers: Relapsing brainstem encephalitis associated with anti-MOG antibodies. Eur J Neurol 2018; 25(2):e16-e17. PMID: 29356261.

[10] Matesanz S, Kotch C, Perrone C, Waanders AJ, Hill B, Narula S. Expanding the MOG phenotype: Brainstem encephalitis with punctate and curvilinear enhancement. Neurol Neuroimmunol Neuroinflamm 2019; 6(6):e619. PMID: 31519713.

[11] Delarasse C, Della Gaspera B, Lu CW, et al. Complex alternative splicing of the myelin oligodendrocyte glycoprotein gene is unique to human and non-human primates. J Neurochem 2006; 98(6):1707-1717. PMID: 16903876.

[12] Peschl P, Bradl M, Höftberger R, Berger T, Reindl M. Myelin oligodendrocyte glycoprotein: Deciphering a target in inflammatory demyelinating diseases. Front Immunol 2017; 8:529. PMID: 28533781.

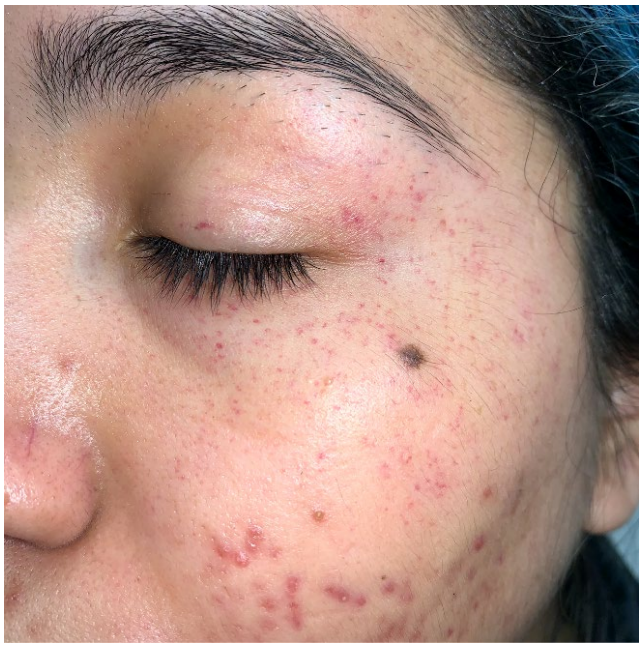
Keywords: myelin-oligodendrocyte glycoprotein, optic neuritis, myelitis, demyelinating diseases

KANSAS JOURNAL of MEDICINE

Mask Phenomenon: Facial Petechiae in a COVID-19 "Long Hauler" Patient

Bao Vincent K. Ho, B.S.[1,2], Manal Hassan, B.S.[1], Malia Downing, M.D.[2], Anand Rajpara, M.D.[2]
[1]University of Kansas School of Medicine, Kansas City, KS
[2]University of Kansas Medical Center, Kansas City, KS
Department of Internal Medicine, Division of Dermatology

Received July 15, 2021; Accepted for publication Aug. 11, 2021; Published online Dec. 2, 2021
https://doi.org/10.17161/kjm.vol14.15680



CASE PRESENTATION

A healthy 18-year-old female presented to the clinic because of an eruption on her face. She tested positive for COVID-19 a few months prior and had headaches, muscle weakness, and severe paroxysms of nonproductive cough since that time. She noticed that her face was covered by asymptomatic small red macules that appeared suddenly.

Physical examination revealed extensive macules in the periorbital area, 1 to 2 mm in diameter, that were non-blanching. These findings were consistent with a diagnosis of petechiae (see Figure); however, it was not present on her arms, legs, or trunk. Other physical examinations revealed unremarkable findings. No laboratory testing or skin biopsy was performed.

A clinical diagnosis of post-emetic petechia, a form of the "mask phenomenon" was suspected. Within 48-hours, the eruption began to fade and had disappeared completely after two weeks without treatment.

DISCUSSION

Facial petechiae, a form of the "mask phenomenon," is often an unrecognized cause of facial rash in the ambulatory setting.[1] Petechiae, purpura, and ecchymoses are non-blanching lesions that occur due to extravasation of blood into the dermis. In the acute setting, the presence of petechiae and purpura can be an alarming sign to general practitioners and dermatologists, as many life-threatening etiologies can present in this manner. Other differential diagnoses of facial purpura to consider include vasculitidies, thrombocytopenic purpura, amyloidosis, autoimmune connective tissues diseases such as systemic lupus erythematous, and drug eruptions.[2]

Post-emetic petechiae occur secondarily to an increase in intravascular pressure such as after prolonged coughing or vomiting, but can appear after any other exertion that raises intrathoracic pressure.[1-3] Distinguishing this cause of petechiae from other etiologies relies upon identification of the location of the lesion, as it classically manifests around the periorbital area given the high vascularity and thus propensity for blood extravasation into the relatively loose tissues of the face.

The history in this case was important in ascertaining the cause of petechiae. Notably, the clinical presentation suggested that the mask phenomenon can be a post-acute sequela of SARS-CoV-2 infection.[4] An estimated 10% of COVID-19 survivors continue to experience symptoms several weeks to months after the appearance of initial symptoms, also called "long-haulers". Twenty percent of suspected cases were in healthy adults ages 18 to 34. Recognizing post-emetic petechiae can help to avoid misdiagnoses that lead to ordering unnecessary tests, as work-up for coagulopathies or thrombocytopenia is not required.

The physician can reassure the patient that the mask phenomenon is transient. Spontaneous resolution of the eruption occurs within several days.[1-3] Further evaluation of the condition of this otherwise healthy patient thus was avoided. Physicians should consider the possibility of a mask phenomenon when COVID-19 long-hauler patients present with facial petechiae.

REFERENCES

[1] Alcalay J, Ingber A, Sandbank M. Mask phenomenon: Postemesis facial purpura. Cutis 1986; 38(1):28. PMID: 3731865.
[2] Ono R, Takahashi H, Fukushima K. Emesis-induced facial purpura as a mask phenomenon. BMJ Case Rep 2021; 14(2):e241456. PMID: 33568416.
[3] Ibraheim MK, Gavvala S. Problematic purpura. Cureus 2021; 13(2):e13473. PMID: 33777561.
[4] Vehar S, Boushra M, Ntiamoah P, Biehl M. Post-acute sequelae of SARS-CoV-2 infection: Caring for the 'long-haulers'. Cleve Clin J Med 2021; 88(5):267-272. PMID: 33941600.

Keywords: purpura, COVID-19, facial dermatoses, sequelae, case study

KANSAS JOURNAL of MEDICINE

KANSAS JOURNAL OF MEDICINE

VOLUME 14 • 2021

Have a manuscript ready to publish?
Visit our website for instructions on submitting a manuscript.

journals.ku.edu/kjm

Office of Research
1010 N. Kansas, Wichita, KS 67214
316-293-2617 • Email: kjm@kumc.edu