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The relationship of preoperative versus postoperative hyperglycemia on clinical outcomes after elective colorectal surgery

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ABSTRACT

Background: The relationship between preoperative hyperglycemia and complications after surgery is not well defined. We compared the relationship of preoperative versus postoperative hyperglycemia on clinical outcomes and assessed if preoperative hyperglycemia was a predictor for postoperative hyperglycemia in patients undergoing elective colorectal surgery.

Methods: We performed a retrospective review of an institutional database for patients who underwent elective colorectal resection between July 2015 and June 2017. Data regarding patient characteristics, history of diabetes, preoperative and postoperative hyperglycemic events, and postoperative complications were collected. Bivariate and multivariate logistic analyses were used to assess relationships.

Results: Of 755 surgical operations reviewed, preoperative hyperglycemia >180 mg/dL was not significantly associated with adverse outcomes in an adjusted model. Only postoperative hyperglycemia >180 mg/dL was significantly associated with complications, including acute kidney injury (odds ratio 2.58, $P < 0.001$), anastomotic leak (odds ratio 2.64, $P = 0.01$), arrhythmia (odds ratio 2.40, $P = 0.009$), and sepsis (odds ratio 3.86, $P < 0.001$). Preoperative hyperglycemia remained a significant predictor of postoperative hyperglycemia (odds ratio 4.91, $P < 0.001$).

Conclusion: Postoperative hyperglycemia was more significantly associated with adverse clinical outcomes after elective colorectal surgery than was preoperative hyperglycemia. However, preoperative hyperglycemia was associated with postoperative hyperglycemia, suggesting that improved glycemic management preoperatively may help reduce hyperglycemic events after surgery.

Introduction

Hyperglycemia has emerged as a modifiable mediator of adverse events after surgery. Potential mechanisms for these outcomes include the vascular, inflammatory, and hemodynamic derangements that occur as a result of persistently elevated glucose levels, all of which can contribute to the risk of morbidity and mortality after surgery.[1] Retrospective studies spanning multiple surgical specialties, including general surgery,[2] colorectal surgery,[3] cardiac surgery,[4] vascular surgery,[5] and orthopedic surgery,[6] have continued to strengthen the link between hyperglycemia and complications after surgery. Specifically, in general surgery patients, the oft-cited study by Kwon et al[2] utilized the Surgical Care and Outcomes Assessment Program from Washington state and concluded that postoperative hyperglycemia in general surgery patients was significantly associated with infection, operative interventions, and death. Similarly, Kiran et al[3] linked postoperative hyperglycemia to both infectious and noninfectious complications in patients undergoing colorectal surgery.

After these landmark studies, the vast majority of studies have continued to focus on the link between postoperative hyperglycemia and morbidity and mortality after surgery. However, the role preoperative hyperglycemia may have on these same clinical outcomes has not been as thoroughly evaluated, particularly in patients undergoing elective colorectal surgery. Understanding drivers of adverse outcomes in this cohort of patients is especially important because these patients oftentimes present with elevated inflammatory conditions and are potentially more susceptible to worse outcomes after undergoing complex resections and anastomoses. In addition, a better understanding of the relationship between preoperative hyperglycemia and the development of

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postoperative hyperglycemia may offer surgeons the opportunity to intervene and optimize glycemic control in the preoperative phase to improve outcomes. The objective of this study was to assess the clinical significance of preoperative hyperglycemia on patient outcomes after elective colorectal surgery by comparing the relationship of preoperative versus postoperative hyperglycemia with morbidity after surgery and by assessing whether preoperative hyperglycemia was a potential predictor of postoperative hyperglycemia in this population of patients.

Methods

Study design and patient population

We conducted a retrospective cohort study on patients who underwent elective colorectal surgery at Northwestern Memorial Hospital from July 2015 to June 2017. Data were abstracted and deidentified from a query of the institutional electronic medical records for patients undergoing colon or rectal resection, with or without anastomosis. Operations included for study were standard operations and extended right and left colectomy, sigmoid resection, low anterior resection, abdominoperineal resection, total proctocolectomy, total abdominal colectomy, and subtotal colectomy. Open, laparoscopic, open-converted-to-laparoscopic, and laparoscopic-assisted cases were included. We excluded patients aged <18 years, cases coded as emergent, or those performed via a transanal approach or isolated pelvic resection, as has been established previously.[3] These surgeries were excluded owing to differences in patient type, physiological response, and perioperative management when compared with an elective transperitoneal colorectal resection. The data abstraction was part of an ongoing quality-improvement project at our institution and was deemed exempt by the Institutional Review Board. The majority of operations were performed by 3 colorectal fellowship–trained surgeons on a dedicated colorectal surgery service at our institution.

Study variables and statistical analysis

Basic patient demographics, clinical history, and operative details were abstracted from electronic medical records. Data abstracted included age, sex, race, body mass index (BMI) closest to admission, American Society of Anesthesiologist (ASA) classification, indication and type of operation performed, and patient disposition. Indications were classified as benign or malignant neoplasm, inflammatory bowel disease, or other indication (eg, diverticulitis or prolapse).

Diagnosis of diabetes was determined based on whether the patient had the diagnosis documented in his or her chart at the time of preoperative screening. Hyperglycemia was defined as a blood glucose value >180 mg/dL, based on established glycemic targets recommended by multiple organizations, including the American Diabetes Association and the American Association of Clinical Endocrinologists.[7,8] A preoperative hyperglycemic event was then defined as a blood glucose value >180 mg/dL within 90 days before the surgery date. A postoperative hyperglycemic event was defined as a blood glucose level >180 mg/dL during a patient's initial postoperative stay, for up to 90 days, drawn from a point-of-care glucometer check or blood chemistry value.

Complications after surgery were extrapolated from the electronic medical records based on laboratory values and diagnosis codes up to 90 days after surgery. Degree of postoperative kidney injury was stratified based on thresholds from the Acute Kidney Injury Network classification, with a 1.5× increase over baseline creatinine corresponding to stage 1 acute kidney injury, and a 2× increase over baseline creatinine corresponding to stage 2 acute kidney injury.[9] Baseline creatinine was defined as a patient's last known preoperative creatinine. Other studied clinical outcomes included anastomotic leak, arrhythmia, urinary tract infection (UTI), and sepsis. Patients were deemed to have an anastomotic leak if the diagnosis appeared in their chart. Each individual diagnosis of anastomotic leak was determined based on a combination of clinical, biochemical, radiographic, or intraoperative findings. The association of hyperglycemia, either preoperatively or postoperatively, to these complications was first assessed using standard bivariate analysis. Multivariate logistic regression was then utilized to obtain odds ratios (ORs) adjusted for established clinical risk factors, including patient's age, ASA classification, sex, and diagnosis of diabetes.

We then sought to assess potential predictors for postoperative hyperglycemia in our cohort of patients. In addition to preoperative blood glucose, other clinical covariates were chosen based on their potential to be indicators for hyperglycemia or diabetes screening in the preoperative phase. Clinical covariates included age, sex, BMI, diagnosis of diabetes, and race. Predictors were coded as binary or categorical variables. Preoperative blood glucose was assessed at 2 thresholds: mild preoperative hyperglycemia >125 mg/dL or high preoperative hyperglycemia >180 mg/dL. A threshold of 125 mg/dL was chosen based on prior study thresholds for defining and examining mild hyperglycemia in surgical patients.[3,10] Age was categorized as <45 years or ≥45 years, based on recommendations from the American Diabetes Association for initiating screening for type 2 diabetes on patients aged ≥45 years.[11] BMI was categorized as <35 kg/m^2 or ≥35 kg/m^2. Race was categorized based on patient self-reporting as White or Caucasian, Black or African American, other, or declined to answer or unknown. White or Caucasian was used as the baseline group for comparison. These clinical variables were analyzed independently to assess the association with postoperative hyperglycemia using univariate logistic regression. Significantly associated variables in univariate logistic analysis were then added into a multivariate logistic regression model to determine adjusted ORs for the association with postoperative hyperglycemia. P values <0.05 were deemed statistically significant for all analyses. Data analysis was generated using STATA, version 15.1 (StataCorp, LLC, College Station, TX) and SAS software, version 9.4 (SAS Institute, Inc, Cary, NC).

Results

Patient demographics and incidence of hyperglycemia

After exclusion criteria were applied, 755 patients were included from within the study period. The study population was 50% male (n = 378) and 50% female (n = 377), with a median age of 57 years (interquartile range 45–67). Mean BMI was 27.1 ± 6.6 kg/m^2, and 17% (n = 127) of patients were diagnosed with diabetes. Distribution of operations performed included 32% (n = 242) right or extended right colectomies; 23% (n = 174) left, extended left, or sigmoid colectomies; 24% (n = 181) low anterior resections or abdominoperineal resections; and 21% (n = 158) subtotal or total colectomies. A laparoscopic or laparoscopic-assisted approach was utilized in 41% (n = 310) of cases. Conversely, an open or laparoscopic-converted-to-open approach was utilized in 59% (n = 445) of operations. Indications for surgery were 43% (n = 325) for benign or malignant neoplasm, 21% (n = 158) for inflammatory bowel disease, and 36% (n = 272) for diverticulitis or other indication. A total of 33% (n = 252) of patients had mild preoperative hyperglycemia, with a blood glucose

value >125 mg/dL, and 11% ($n = 85$) of patients had high preoperative hyperglycemia, with a blood glucose value >180 mg/dL. Postoperative hyperglycemia >180 mg/dL occurred in 23% ($n = 175$) of patients. The overall incidence of specific complications was 11% ($n = 81$) for a 1.5× increase over baseline creatinine, 4% ($n = 32$) for a 2× increase over baseline creatinine, 5% ($n = 35$) for anastomotic leak, 6% ($n = 44$) for arrhythmia, 5% ($n = 41$) for UTI, and 4% ($n = 32$) for sepsis. A summary of the study cohort is provided in Table I.

Association of preoperative hyperglycemia with adverse outcomes

Preoperative hyperglycemia >180 mg/dL was independently associated with postoperative complications. On unadjusted bivariate analysis, preoperative hyperglycemia >180 mg/dL was independently associated with a 1.5× increase in baseline creatinine (OR 2.16, 95% confidence interval [CI] 1.18–3.94, $P = 0.01$) and with a 2× increase in baseline creatinine (OR 3.33, 95% CI 1.49–7.46, $P = 0.003$). Preoperative hyperglycemia was also independently associated with arrhythmia (OR 2.87, 95% CI 1.39–5.92, $P = 0.004$) and UTI (OR 2.36, 95% CI 1.09–5.13, $P = 0.03$). Preoperative hyperglycemia was not significantly associated with anastomotic leak (OR 1.33, 95% CI 0.50–3.54, $P = 0.6$) or with sepsis (OR 2.32, 95% CI 0.97–5.53, $P = 0.06$). After adjustment for age, ASA classification, sex, and diagnosis of diabetes, preoperative hyperglycemia was no longer significantly associated with increased odds for postoperative complications (Table II).

Table I
Cohort characteristics

Total patients	755
Age, median (interquartile range)	57 (45–67)
Sex	
Male	378 (50%)
Female	377 (50%)
Diagnosis of diabetes	127 (17%)
BMI (kg/m^2), means (SD)	27.1 (6.6)
Race	
White	573 (77%)
Black	81 (11%)
Other	64 (9%)
Declined to answer/unknown	37 (5%)
ASA classification	
I–II	430 (57%)
III–IV	325 (43%)
Indication for operation	
Neoplasm	325 (43%)
Inflammatory bowel disease	158 (21%)
Diverticulitis/other	272 (36%)
Resection type	
Right/extended right	242 (32%)
Left/extended left/sigmoid	174 (23%)
LAR/APR	181 (24%)
Subtotal/total colectomy	158 (21%)
Surgical approach	
Laparoscopic or laparoscopic assisted	310 (41%)
Open or converted to open	445 (59%)
Complications	
1.5 times baseline serum creatinine	81 (11%)
2.0 times baseline serum creatinine	32 (4%)
Anastomotic leak	35 (5%)
Arrhythmia	44 (6%)
UTI	41 (5%)
Sepsis	32 (4%)
Blood glucose value (mg/dL)	
Preoperative blood glucose >125	252 (33%)
Preoperative hyperglycemia >180 mg/dL	85 (11%)
Postoperative hyperglycemia >180 mg/dL	175 (23%)
HbA_{1c} within 3 months, *n* (% of values)	
<6.5%	55 (58%)
6.5%–7.9%	25 (26%)
>8.0%	15 (16%)

Data are *n* (%), unless otherwise indicated.
APR, abdominoperineal resections; *HbA_{1c}*, hemoglobin A1c; *LAR*, low anterior resections.

Association of postoperative hyperglycemia with adverse outcomes

Postoperative hyperglycemia >180 mg/dL after elective colorectal surgery was more significantly associated with adverse outcomes than was preoperative hyperglycemia. Patients with postoperative hyperglycemia >180 mg/dL had a significantly higher incidence of studied complications than patients with blood glucose values ≤180 mg/dL (Fig 1). On unadjusted bivariate analysis, postoperative hyperglycemia >180 mg/dL was significantly associated with increased odds for postoperative complications, including a 1.5× increase in baseline creatinine (OR 2.58, 95% CI 1.59–4.16, $P < 0.001$), a 2× increase in baseline creatinine (OR 4.05, 95% CI 1.98–8.30, $P < 0.001$), arrhythmia (OR 4.03, 95% CI 2.17–7.47, $P < 0.001$), UTI (OR 2.23, 95% CI 1.16–4.29, $P = 0.02$), and sepsis (OR 4.05, 95% CI 1.98–8.30, $P < 0.001$). Postoperative hyperglycemia was independently associated with increased odds for anastomotic leak at the threshold for statistical significance (OR 2.03, 95% CI 1.00–4.13, $P = 0.05$). After adjustment for patient's age, ASA classification, sex, and diagnosis of diabetes, postoperative hyperglycemia >180 mg/dL remained significantly associated with a 1.5× increase in baseline creatinine (OR 2.16, 95% CI 1.31–3.57, $P = 0.003$) and a 2× increase in baseline creatinine (OR 3.38, 95% CI 1.57–7.25, $P = 0.002$), anastomotic leak (OR 2.64, 95% CI 1.25–5.65, $P = 0.01$), arrhythmia (OR 2.40, 95% CI 1.25–4.63, $P = 0.009$), and sepsis (OR 3.86, 95% CI 1.82–8.22, $P < 0.001$). In the adjusted model, postoperative hyperglycemia >180 mg/dL was associated with UTI at the threshold for significance (OR 2.01, 95% CI 1.01–4.00, $P = 0.05$) (Table III).

Clinical predictors of postoperative hyperglycemia

Both mild preoperative hyperglycemia >125 mg/dL (OR 5.95, 95% CI 4.10–8.64, $P < 0.001$) and high preoperative hyperglycemia >180 mg/dL (OR 13.95, 95% CI 8.04–24.21, $P < 0.001$) were independently associated with postoperative hyperglycemia >180 mg/dL. Other significant independent clinical covariates with an association to postoperative hyperglycemia included diagnosis of diabetes (OR 18.57, 95% CI 11.61–29.70, $P < 0.001$), age ≥45 years (OR 2.34, 95% CI 1.44–3.80, $P = 0.001$), ASA classification III/IV (OR 3.44, 95% CI 2.38–4.97, $P < 0.001$), and BMI ≥35 kg/m^2 (OR 2.09, 95% CI 1.34–3.28, $P = 0.001$). Sex and race were not independently associated with increased odds for postoperative hyperglycemia in our study population. After adjustment for significant covariates in a multivariate regression model, mild preoperative hyperglycemia >125 mg/dL (OR 3.28, 95% CI 2.12–5.07, $P < 0.001$) and high preoperative hyperglycemia >180 mg/dL (OR 4.91, 95% CI 2.55–9.42, $P < 0.001$) remained significantly associated with postoperative hyperglycemia. In the multivariate logistic regression model incorporating high preoperative hyperglycemia >180 mg/dL, other significant clinical covariates associated with postoperative hyperglycemia included diagnosis of diabetes (OR 10.73, 95% CI 6.39–18.01, $P < 0.001$) and ASA classification III/IV (OR 1.97, 95% CI 1.25–3.09, $P = 0.003$) (Table IV).

Discussion

In a population of patients undergoing elective colorectal surgery, postoperative hyperglycemia was more strongly associated

Table II
Association of preoperative hyperglycemia >180 mg/dL with adverse outcomes

Complication	Unadjusted			Adjusted*		
	OR	95% CI	*P*	OR	95% CI	*P*
Stage 1 acute kidney injury (1.5× baseline serum creatinine)	2.16	(1.18–3.94)	**.01**	1.61	(0.85–3.07)	.1
Stage 2 acute kidney injury (2× baseline serum creatinine)	3.33	(1.49–7.46)	**.003**	2.45	(0.92–5.47)	.07
Anastomotic leak	1.33	(0.50–3.54)	.6	1.70	(0.61–4.69)	.3
Arrhythmia	2.87	(1.39–5.92)	**.004**	1.60	(0.73–3.52)	.2
UTI	2.36	(1.09–5.13)	**.03**	2.33	(1.00–5.38)	.05
Sepsis	2.32	(0.97–5.53)	.06	2.00	(0.80–5.01)	.1

P values marked in bold indicate significant differences, $P < .05$.
* Clinical covariates included in adjusted model: age, ASA classification, sex, diagnosis of diabetes.

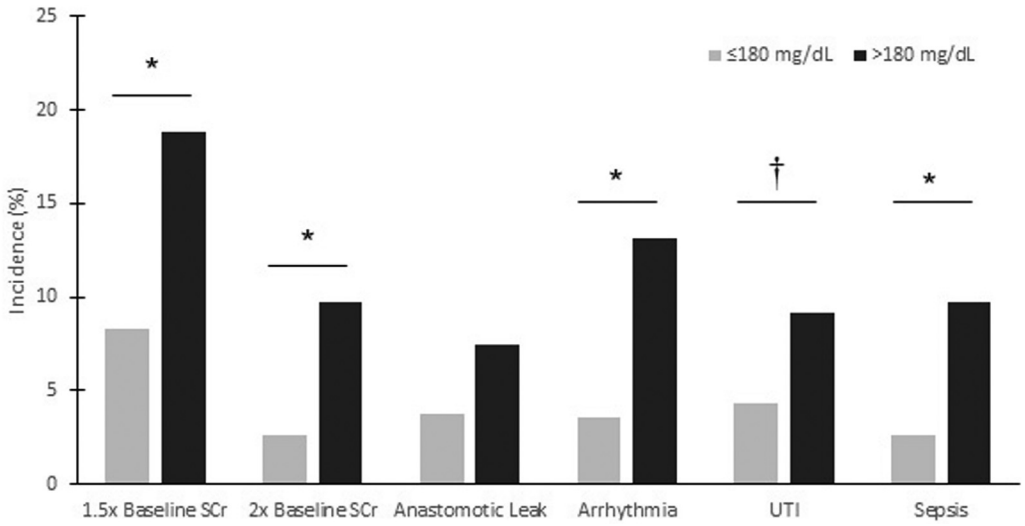

Fig 1. Unadjusted incidence rates of postoperative complications in patients with postoperative hyperglycemia >180 mg/dL versus patients with blood glucose ≤180 mg/dL (*$P < 0.001$, †$P < 0.05$).

with adverse clinical outcomes than was preoperative hyperglycemia. In this patient population, preoperative hyperglycemia >180 mg/dL was not significantly associated with a decline in renal function, anastomotic leak, arrhythmia, UTI, or sepsis after adjustment for confounding clinical variables. In contrast, postoperative hyperglycemia >180 mg/dL was significantly associated with these studied complications, conveying a 2-fold to nearly 4-fold increased odds for morbidity after colorectal surgery. Demonstrating the clinical significance of preoperative glucose control, patients with preoperative hyperglycemia were more likely to be hyperglycemic postoperatively, with preoperative hyperglycemia >180 mg/dL conveying approximately a 5-fold increased odds for postoperative hyperglycemia after adjustment for clinical covariates.

The link between postoperative hyperglycemia and complications after surgery has been demonstrated previously, including with large-scale, retrospective cohort studies.[2,3,12] Whether preoperative hyperglycemia has a similar relationship with these surgical complications has been less well studied because preoperative blood glucose values are not routinely included in the databases that have been utilized in these prior studies. To begin to address this issue, Ata et al[13] independently abstracted preoperative blood glucose values from a review of their institutional electronic medical records. Their study concluded that in a cohort of 1,561 general surgery patients and in a subgroup analysis of 226 colorectal surgery patients, preoperative hyperglycemia was not significantly associated with surgical site infection.[13] Building upon these results, we have expanded the group of colorectal surgery patients studied to 755 patients and were able to examine the potential association of preoperative hyperglycemia to additional complications other than surgical site infection. Similarly to the results of Ata et al, we also found that preoperative hyperglycemia was not significantly associated with adverse outcomes after surgery. We did not observe a significant relationship between preoperative hyperglycemia and a decline in renal function, anastomotic leak, arrhythmia, UTI, or sepsis after adjustment for clinical covariates. The absence of increased clinical morbidity, as seen by both Ata et al and our study, contrasts with the results of a study performed by Davis et al, [14] which did demonstrate a link between preoperative hyperglycemia and adverse outcomes in a cohort of neurosurgery patients. These conflicting findings likely allude to the major differences in baseline patient characteristics, types of operations performed, perioperative management, and clinical outcomes between neurosurgery patients and elective colorectal surgery patients.

Given the breadth of observational evidence linking postoperative hyperglycemia with adverse outcomes after surgery, the American Diabetes Association and the American Association of Clinical Endocrinologists have released a consensus statement recommending 180 mg/dL as the upper threshold for blood glucose in both critically and noncritically ill patients.[8] Therefore, identifying and quantifying patient risk factors for postoperative hyperglycemia offers the possibility of targeting interventions on

Table III
Association of postoperative hyperglycemia >180 mg/dL with adverse outcomes

Complication	Unadjusted			Adjusted*		
	OR	95% CI	*P*	OR	95% CI	*P*
Stage 1 acute kidney injury (1.5× baseline serum creatinine)	2.58	(1.59–4.16)	**<.001**	2.16	(1.31–3.57)	**.003**
Stage 2 acute kidney injury (2× baseline serum creatinine)	4.05	(1.98–8.30)	**<.001**	3.38	(1.57–7.24)	**.002**
Anastomotic leak	2.03	(1.00–4.13)	.05	2.64	(1.25–5.65)	**.01**
Arrhythmia	4.03	(2.17–7.47)	**<.001**	2.40	(1.25–4.63)	**.009**
UTI	2.23	(1.16–4.29)	**.02**	2.01	(1.01–4.00)	.05
Sepsis	4.05	(1.98–8.30)	**<.001**	3.86	(1.82–8.22)	**<.001**

P values marked in bold indicate significant differences, $P < .05$.
* Clinical covariates included in adjusted model: age, ASA classification, sex, diagnosis of diabetes.

Table IV
Predictors of postoperative hyperglycemia >180 mg/dL

Variable	Unadjusted			Adjusted*		
	OR	95% CI	*P*	OR	95% CI	*P*
Mild preoperative hyperglycemia						
≤125 mg/dL	†			†		
>125 mg/dL	5.95	(4.10–8.64)	**<.001**	3.28	(2.12–5.07)	**<.001**
High preoperative hyperglycemia						
≤180mg/dL	†			†		
>180 mg/dL	13.95	(8.04–24.21)	**<.001**	4.91	(2.55–9.42)	**<.001**
Diabetes						
No	†			†		
Yes	18.57	(11.61–29.70)	**<.001**	10.73	(6.39–18.01)	**<.001**
Age (y)						
<45	†			†		
≥45	2.34	(1.44–3.80)	**.001**	1.32	(0.74–2.34)	.35
Sex						
Male	†					
Female	0.93	(0.66–1.31)	.67			
ASA classification						
I–II	†			†		
III–IV	3.44	(2.38–4.97)	**<.001**	1.97	(1.25–3.09)	**.003**
BMI						
<35 mg/kg^2	†			†		
≥35 mg/kg^2	2.09	(1.34–3.28)	**.001**	0.90	(0.49–1.64)	.73
Race						
White or Caucasian	†					
Black or African American	1.60	(0.96–2.70)	.07			
Other	1.76	(0.86–3.59)	.12			
Declined to answer/unknown	0.93	(0.45–1.91)	.84			

P values marked in bold indicate significant differences, $P < .05$.
* Significant independent clinical covariates included in adjusted model: diabetes, age, ASA classification, and BMI.
† Reference category.

these at-risk patients and optimizing their blood glucose before surgery. In patients undergoing cardiac surgery, Garg et al[15] identified preoperative patient characteristics that were associated with postoperative hyperglycemia, including age, BMI, male sex, and comorbidities, such as hypertension and hypercholesteremia. Notably, in their cohort of cardiac surgery patients, the authors found no significant difference in mean preoperative blood glucose values between postoperative normoglycemic and hyperglycemic patients.[15] Conversely, in our cohort of colorectal surgery patients, we found that preoperative hyperglycemia was a predictor for postoperative hyperglycemia and that the degree of association increased in a dose-response relationship with the severity of hyperglycemia. After adjustment for significant clinical covariates, mild preoperative hyperglycemia >125 mg/dL conveyed a 3-fold–increased odds for postoperative hyperglycemia. Comparatively, high preoperative hyperglycemia >180 mg/dL was associated with nearly a 5-fold increased odds for developing hyperglycemia in the postoperative setting. Given that mild hyperglycemia is a relatively common occurrence preoperatively and is oftentimes considered unproblematic, these findings suggest that even mild preoperative hyperglycemia may have consequences and that additional glycemic optimization in the preoperative phase may be beneficial to encompass and optimize these newly at-risk individuals.

In addition to preoperative blood glucose control, other significant predictors for postoperative hyperglycemia included age ≥45 years, BMI ≥35 kg/m^2, diagnosis of diabetes, and ASA classification III/IV. The link between a patient's preoperative characteristics and the development of postoperative hyperglycemia suggests that the hyperglycemia that develops after surgery is likely more than just a result of the postsurgery stress response. Rather, a patient's preoperative characteristics, such as underlying blood glucose control, may directly contribute to the pathogenesis of hyperglycemia after surgery. This relationship

offers surgeons the opportunity to treat or adjust these baseline characteristics with the goal of reducing postoperative hyperglycemia and its associated complications.

Taking these results into consideration, we have initiated a quality-improvement project focused on perioperative glucose management in patients undergoing elective colorectal surgery at our institution. Part of these new protocols are standardized screening guidelines, including preoperative blood glucose checks on all patients aged ≥45 years or with a BMI ≥35 kg/m^2 to assess for undiagnosed diabetes and to potentially improve glycemic control before surgery. On the postoperative side, the central tenet of this project is directed at creating a basal-bolus insulin therapy order set that will be initiated by the surgery team. This initiative is based on prior studies that have shown that insulin therapy can reduce the complication rates associated with hyperglycemia.[2,16] Furthermore, in a randomized control trial in general surgery patients with type 2 diabetes, basal-bolus insulin therapy was more effective than sliding-scale insulin administration in regards to postoperative glycemic control, without an increase in significant hypoglycemia.[17] The American Diabetes Association now recommends that basal-bolus insulin therapy be the preferred method of glycemic control for patients with diabetes, including those with poor or no oral intake. For those with better nutritional intake, the American Diabetes Association recommends the addition of a prandial dose of insulin.[18] Predetermined basal-bolus insulin protocols, such as those being developed at our institution, help to reduce the reliance on sliding-scale insulin regimes and serve to educate prescribers, including surgeons and surgery residents, on the appropriate and effective dosing of basal-bolus insulin therapy postoperatviely.[19] Our study, among others, emphasizes the association between postoperative hyperglycemia with worse outcomes after surgery and calls for improved glycemic management in surgical patients.

This study has notable limitations. As a retrospective study, it was not designed to determine if hyperglycemia can directly result in the complications seen but can only infer associations. Further investigation into the inflammatory and vascular changes directly induced by hyperglycemia and the effects these changes have on the development of adverse outcomes after surgery is warranted. We also acknowledge that there is sample bias inherent to a single-institution study of this scope. However, by limiting our analysis to patients undergoing elective colorectal resection at a single institution, we reduce potential confounding effects owing to differences in surgical technique and perioperative management. By defining the diagnosis of diabetes based on its appearance in the patient's chart, we also miss any patients with undiagnosed diabetes and likely underrepresent the true incidence of diabetes in our population. In addition, we may potentially underestimate both the true incidence of preoperative hyperglycemia and postoperative complications if patients, respectively, did not have blood glucose values drawn preoperatively or were lost to follow-up after their surgeries. Finally, although we used multivariate regression models to assess for the effect of confounding variables, we acknowledge that there are likely additional significant variables that, upon incorporation into our model, may adjust the results seen. Future studies utilizing comprehensive databases that include preoperative, intraoperative, and postoperative blood glucose values are warranted to further assess the relationship of preoperative blood glucose to postoperative hyperglycemia and complications after surgery.

In conclusion, in a cohort of patients undergoing elective colorectal surgery, postoperative hyperglycemia >180 mg/dL was more significantly associated with adverse outcomes after surgery than was preoperative hyperglycemia. Notably, preoperative hyperglycemia was a predictor for the development of postoperative hyperglycemia after elective colorectal surgery, with the degree of association increasing with the severity of preoperative hyperglycemia. Other significant predictors included age ≥45 years, BMI ≥35 kg/m^2, diagnosis of diabetes, and ASA classification III/IV. Overall, these findings suggest that improved preoperative glycemic control may reduce the incidence of postoperative hyperglycemic events and may lead to improved clinical outcomes after elective colorectal surgery.

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Conflict of interest/Disclosure

The authors have indicated that they have no conflicts of interest regarding the content of this article.

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Discussion

Dr Jon Gould (Milwaukee, WI): Thank you. I'd like to congratulate Dr. Chen and colleagues from Northwestern for contributing this study to the body of literature that examines the impact of diabetes and hyperglycemia on surgical outcomes. This work is important, as the relationship between outcomes, including morbidity and most notably surgical-site infections in many series as well as mortality to postoperative hyperglycemia in procedures such as cardiac, vascular, and bariatric surgery, as you elucidated, has been demonstrated previously. The relationship in colon surgery is not as well defined.

Demonstrating that post-op hyperglycemia is a risk factor for morbidity and mortality is useful only to the extent that it can be used to improve outcomes. Understanding which patients are at risk for post-op hyperglycemia is really the key. Much of the work at this point has focused on hemoglobin A1c and most often in patients previously identified as diabetic. This is really a nice contribution that kind of puts a different spin on things.

I have several questions, and I'll ask them one at a time, that might help us better understand this study and some of the limitations.

First of all, can you give a little information on the distribution of the different kinds of resections in this series? Were adverse events more likely in specific kinds of resections, such as low anterior or APR, for example, as compared to a right colectomy?

Dr Edmund Chen: Thank you, Dr. Gould. If you break down our surgery cases, they were fairly evenly distributed. Right, left, low anterior, or APR versus subtotal or total resections were each performed in about 25% of cases. Breaking it down by laparoscopic versus open cases, we found that there were more cases performed via the open approach.

When you look at adverse events, the first thing everyone looks at is anastomotic leak, such as whether anastomotic leak would be more significantly associated with patients undergoing low anterior resections. Looking specifically in our patient population, the overall incidence of anastomotic leak was only about 5%. As such, our study was not adequately powered to detect such granular differences in leak rates. It did seem that patients with low anastomoses did have a slightly higher incidence of anastomotic leak, but our study wasn't designed to be able to significantly prove this association.

Looking at laparoscopic versus open cases, in accordance to previous studies, we found no significant difference in anastomotic leak rates between cases performed laparoscopically versus via an open approach.

Looking at our other studied complications, we did find a significant association between patients undergoing a subtotal or total resection with a rise in the baseline creatinine. The unadjusted odds ratio for this relationship was about 3.0. This relationship may allude to the fact that patients undergoing a total abdominal resection or a subtotal colectomy may have a longer duration of surgery or may have potentially additional comorbidities or illnesses. However, given the overall number of complications, our study was not powered to perform any adjustments for clinical covariates on this subgroup analysis.

Looking at the other complications studied, we did not observe any significant differences or trends when broken down by different types of surgeries.

Dr Jon Gould (Milwaukee, WI): The indications for surgery, what were the primary indications? Cancer, IBD? A mix of different things?

Dr Edmund Chen: Indications for surgery were 43% for neoplasm, 21% for inflammatory bowel disease, and about 36% for diverticulitis or other indication.

Dr Jon Gould (Milwaukee, WI): My final question is, in the manuscript, which you provided ahead of time, you did mention basal-bolus insulin therapy, and you mentioned it in discussion as well. You alluded to it here. Did you employ this as a strategy in any of the patients that are included in the previous series?

Dr Edmund Chen: Thank you. This is something that we're trying to roll out right now. The implementation of basal-bolus therapy is haphazard, at least at our institution. If a patient has a history of diabetes, most of the time we put them on a sliding-scale insulin therapy immediately after surgery. That's what we as surgery residents are used to doing. Patients only get switched to basal-bolus therapy after the diabetes management service gets consulted in a day, 2 days, or 3 days and puts them on the basal-bolus insulin therapy.

Using this data series, we were able to examine what insulin medications patients were ordered. In our portion of patients with diabetes, about 30–40% of them were not ordered a basal-bolus therapy. For those that were ordered a basal-bolus therapy, it took about a median of 16 hours for therapy to be initiated. There was also a very large interquartile range, from 6 hours up to 51 hours, to transition patients properly on to basal-bolus therapy, alluding to the variability in initiating this therapy. As such, I think there's a lot of room here for improvement in our patients.

Dr Emre Gorgun (Cleveland, OH): Thank you very much. Very good study. I have 2 questions for you. As you know, one of the CMS monitored metrics is SSI, surgical site infection. I know you included sepsis and anastomotic leak, which is kind of indirectly related to SSI, but probably that's one of the most important aspects when you're looking or studying hyperglycemia or hypoglycemia related to the outcome.

My first question is, did you look specifically, as I mentioned, at important outcome metrics and quality metrics that all the hospitals are monitored for nationwide?

My second question is, it's very good also to look into pre-op and post-op, but we know from SSI reduction bundles and effects, hypothermia, things like this intraoperatively are also very important, and one of the metrics that needs to be monitored is also intraoperative glycemia control. I don't know if you looked at that as well and monitored your patients from that perspective and if you have any outcomes from that perspective.

Dr Edmund Chen: Regarding the first question on SSIs, our initial goal for the study was to look at SSI rates in our patients. Other studies have looked at SSIs, as you have alluded to, and we wanted to contribute to that body of literature. However, as I was pulling the data for this study, I realized that SSIs were not adequately coded for at our institution. The rate of reported SSIs was very low, and it was not an adequate representation of the true SSI incidence rate in our population.

In order to better study SSI rates in the context of hyperglycemia, I think that would require utilizing something like an independently abstracted database like the NSQIP, which I know is more accurate for SSI rates.

In regards to your second question on intraoperative blood glucose, that is also something that we are interested in examining. Intraoperative blood glucose monitoring is part of our quality-improvement project. This project did not specifically look at intraoperative blood glucose values and their relation to postoperative complications, but that is something that we hope to study in the future. Intraoperative blood glucose control is also something that we are working on with our anesthesiologist colleagues in terms of implementing established protocols.

Dr Mary Otterson (Milwaukee, WI): I had 1 additional question. When you note the incidence of your urinary tract infections, do you correct for catheter usage? Do you routinely use catheters for short-duration cases?

Dr Edmund Chen: Thank you for the questions. No, in this study, I did not adjust for catheter usage. I think that would be a very interesting variable to adjust for to see how it would modify our association with UTI.

In terms of routine use of catheterization, we also have ERAS protocols, and so, intraoperatively, we sometimes would use catheters, but we often remove them postoperatively.

Dr Mary Otterson (Milwaukee, WI): You routinely use catheters for every colorectal case and then take them out immediately afterwards?

Dr Edmund Chen: Our catheter usage is not routine and may be attending specific. For example, a quick right hemicolectomy may not have a catheter associated with the case, while a low anterior would have a catheter associated with the case.