Risk Factors for Anastomotic Leak and Mortality in Diabetic Patients Undergoing Colectomy

Analysis From a Statewide Surgical Quality Collaborative

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Objectives: To determine the risk factors in diabetic patients that are associated with increased postcolectomy mortality and anastomotic leak.

Design: A prospectively acquired statewide database of patients who underwent colectomy was reviewed. Primary risk factors were diabetes mellitus, hyperglycemia (glucose level ≥140 mg/dL), steroid use, and emergency surgery. Categorical analysis, univariate logistic regression, and multivariate regression were used to evaluate the effects of these risk factors on outcomes.

Setting: Participating hospitals within the Michigan Surgical Quality Collaborative.

Patients: Database review of patients from hospitals within the Michigan Surgical Quality Collaborative.

Main Outcome Measures: Anastomotic leak and 30-day mortality rate.

Results: Of 5123 patients, 153 (3.0%) had leaks and 153 (3.0%) died. Preoperative hyperglycemia occurred in 15.6% of patients, only 54% of whom were known to have diabetes. Multivariate analysis showed that the risk of leak for patients with and without diabetes increased only by preoperative steroid use (P < .05). Mortality among diabetic patients was associated with emergency surgery (P < .01) and anastomotic leak (P < .05); it was not associated with hyperglycemia. Mortality among nondiabetic patients was associated with hyperglycemia (P < .005). The presence of an anastomotic leak was associated with increased mortality among diabetic patients (26.3% vs 4.5%; P < .001) compared with nondiabetic patients (6.0% vs 2.5%; P < .05).

Conclusions: The presence of diabetes did not have an effect on the presence of an anastomotic leak, but diabetic patients who had a leak had more than a 4-fold higher mortality compared with nondiabetic patients. Preoperative steroid use led to increased rates of anastomotic leak in diabetic patients. Mortality was associated with hyperglycemia for nondiabetic patients only. Improved screening may identify high-risk patients who would benefit from perioperative intervention.


DIABETES MELLITUS AND perioperative hyperglycemia have been associated with poor clinical outcomes in surgical patients.1,2 In addition, they have been shown to be markers for morbidity in both cardiac and noncardiac general surgery patients.3,4 Currently, more than 18 million people in the United States have diabetes mellitus, with another estimated 7 million thought to have undiagnosed diabetes. Furthermore, 79 million Americans are considered to be “prediabetic,” with elevated fasting glucose and/or hemoglobin A1c levels.5 In a recent analysis of more than 39 000 noncardiac surgery patients, 21% of nondiabetic patients were found to have either undiagnosed diabetes or impaired fasting glucose.6 Efforts are being made to identify patients at risk and provide appropriate glycemic control in order to minimize complications occurring in and around the time of surgery. Improvement in these areas may be especially important in the setting of colon surgery, given that colectomy is commonly
performed and is associated with a morbidity that approaches 30%.7

To date, a number of investigators have studied the relationship among hyperglycemia, diabetes, and postoperative complications in patients who underwent a colectomy.1 Many of these studies are from single institutions, but much larger populations are now available for review with the National Surgical Quality Improvement Program database. Although this database has been utilized to study various outcomes in colon and rectal surgery, it does not encompass several important areas such as anastomotic leak.8

The Michigan Surgical Quality Collaborative (MSQC) was established as part of an effort to improve surgical quality and outcomes. It represents a partnership among participating Michigan hospitals, the American College of Surgeons, and the Blue Cross Blue Shield Michigan/Blue Care Network, the dominant third-party payer in the state.9 This collaborative is based on the American College of Surgeons—National Surgical Quality Improvement Program system, but it encompasses a unique infrastructure for quality improvement. Within the MSQC, a “Colectomy Project” was developed that contains a new data field with 25 different elements of interest to colorectal surgeons. This project includes patient information from 22 hospitals across the state of Michigan. Specific initiatives, leading to best practices, have already been implemented for colectomy and other disease entities such as myocardial ischemia and surgical site infection.9

The goal of our study was to define the prevalence of preoperative hyperglycemia and diabetes mellitus in patients who underwent a colectomy and to determine whether hyperglycemia and/or diabetes mellitus are associated with postoperative complications (in particular, anastomotic leak). Furthermore, we sought to identify certain subsets of diabetic patients who are at particular risk of postoperative morbidity and mortality.

METHODS

A retrospective review of the MSQC database was performed for our study, which involved more than 5000 patients. The data accrual occurred from February 2008 through December 2010. Our study was approved by the Human Investigation Committee at the William Beaumont Hospital Research Institute.

To create uniformity in data acquisition, the MSQC database is confined to a subset of Current Procedural Terminology codes for colectomy, which subset is referred to as the “colon bucket.” Four such codes are included, and they involve operations with a primary intra-abdominal anastomosis, without permanent ileostomy or rectal resection. The Current Procedural Terminology codes included in the database are 44140, 44204, 44160, and 44205. The first 2 include open and laparoscopic segmental colectomies with primary anastomosis. The latter 2 include open and laparoscopic partial colectomies involving removal of the terminal ileum with ileocolostomy. This list encompasses, therefore, open and laparoscopic right and left hemicolectomies. Ileocecal and sigmoid resections are included in the data for right and left hemicolectomies, respectively (Figure 1).

The primary study end points were anastomotic leak and 30-day mortality. Primary risk factors were known diabetes mellitus and hyperglycemia. All blood glucose levels were obtained preoperatively within 90 days of surgery. In the database, patients were not included in the “diabetes” category if their hyperglycemia was controlled by diet alone. Independent of the “diabetes” category, hyperglycemia was defined as blood glucose level of higher than 140 mg/dL. (to convert to millimoles per liter, multiply by 0.0555); that is, some patients with hyperglycemia were already known to have diabetes, whereas others had not been diagnosed with diabetes. A blood glucose level of 140 mg/dL was used as a cutoff in accordance with data from the American Diabetes Association and from previous studies that have used this level to define hyperglycemia in nonfasting blood samples.10

Additional categorical variables included preoperative steroid use, emergent surgery, laparoscopic surgery, and American Society of Anesthesiologists score. “Emergent” surgery was defined as an operation that is performed as soon as possible and no later than 12 hours after admission to the hospital or the onset of symptomatology.11 Preoperative steroid use is defined by the MSQC database as the regular administration of oral or parenteral corticosteroids for a chronic medical condition in the 30 days prior to surgery. This does not include the use of topical, inhaled, or rectal steroids. It also does not include short-course steroids (≤10 days).11 Albumin level, body mass index, duration of surgery, and estimated blood loss were analyzed as continuous variables. Statistical significance was determined by use of χ2 analysis, the Mann-Whitney U rank sum test, analysis of variance, and the t test. Appropriate tests were used, based on variable type (continuous vs categorical) and the variable’s distribution. Logistic regression (univariate and stepwise multivariate) was used to determine which variables significantly influenced the primary and secondary end points. All statistical analyses used MedCalc version 11.3.1.0. Statistical inference was based on a threshold P<.05. OpenEpi version 2, an open-source calculator from the Centers for Disease Control and Prevention, was used for power calculations.

RESULTS

A total of 5123 patients who underwent a colectomy were analyzed; of these patients, 889 were known to have diabetes (Table 1 and Table 2). Data on preoperative glucose levels were available for 4450 patients (86.9%), of whom 694 (15.6%) had levels of 140 mg/dL or higher. The distribution of preoperative glucose levels is shown.
**Table 1. Clinical and Demographic Characteristics of 4234 Nondiabetic Patients From Hospitals in the Michigan Surgical Quality Collaborative**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Emergency Surgery</th>
<th>Nonemergency Surgery</th>
<th>Statistical Test</th>
<th>P Value</th>
<th>Patients With Missing Data, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>438/438 (100.0)</td>
<td>3796/3796 (100.0)</td>
<td>5.58</td>
<td>&gt;0.05</td>
<td>0.0</td>
</tr>
<tr>
<td>Albumin level, median (IQR), g/dL</td>
<td>335/438 (76.5)</td>
<td>2502/3796 (65.9)</td>
<td>7.34</td>
<td>&lt;0.001</td>
<td>33.0</td>
</tr>
<tr>
<td>Anastomotic leak</td>
<td>18/435 (4.1)</td>
<td>116/3778 (3.1)</td>
<td>1.12</td>
<td>&gt;0.05</td>
<td>0.5</td>
</tr>
<tr>
<td>ASA score, median (IQR)</td>
<td>437/438 (99.8)</td>
<td>3793/3796 (99.9)</td>
<td>10.8</td>
<td>&lt;0.001</td>
<td>0.6</td>
</tr>
<tr>
<td>Blood glucose level ≥140 mg/dL</td>
<td>92/400 (23.0)</td>
<td>226/3188 (7.1)</td>
<td>109.4</td>
<td>&lt;0.001</td>
<td>15.3</td>
</tr>
<tr>
<td>BMI, median (IQR)</td>
<td>417/438 (95.2)</td>
<td>3777/3796 (99.5)</td>
<td>4.18</td>
<td>&lt;0.001</td>
<td>1.0</td>
</tr>
<tr>
<td>Death</td>
<td>39/438 (8.9)</td>
<td>69/3796 (1.8)</td>
<td>76.5</td>
<td>&lt;0.001</td>
<td>0.0</td>
</tr>
<tr>
<td>Duration of surgery, median (IQR), min</td>
<td>438/438 (100.0)</td>
<td>3796/3796 (100.0)</td>
<td>9.39</td>
<td>&lt;0.001</td>
<td>0.0</td>
</tr>
<tr>
<td>Estimated blood loss, median (IQR), mL</td>
<td>414/438 (94.5)</td>
<td>3686/3796 (97.1)</td>
<td>5.09</td>
<td>&lt;0.001</td>
<td>3.2</td>
</tr>
<tr>
<td>Laparoscopic surgery performed</td>
<td>28/438 (6.4)</td>
<td>1730/3796 (45.6)</td>
<td>247</td>
<td>&lt;0.001</td>
<td>0.0</td>
</tr>
<tr>
<td>Male</td>
<td>188/438 (42.9)</td>
<td>1769/3796 (46.6)</td>
<td>1.99</td>
<td>&gt;0.05</td>
<td>0.0</td>
</tr>
<tr>
<td>Steroid use</td>
<td>26/438 (5.9)</td>
<td>153/3796 (4.0)</td>
<td>3.07</td>
<td>&lt;0.001</td>
<td>0.0</td>
</tr>
</tbody>
</table>

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); IQR, interquartile range.

SI conversion factors: To convert albumin to grams per liter, multiply by 10 (to convert to millimoles per liter, multiply by 0.0555).

*a* The *t* test.

*b* The Mann-Whitney U rank sum test (*z* score).

*c* Analysis.

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**Table 2. Clinical and Demographic Characteristics of 889 Diabetic Patients From Hospitals in the Michigan Surgical Quality Collaborative**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Emergency Surgery</th>
<th>Nonemergency Surgery</th>
<th>Statistical Test</th>
<th>P Value</th>
<th>Patients With Missing Data, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>99/99 (100.0)</td>
<td>790/790 (100.0)</td>
<td>1.34</td>
<td>&gt;0.05</td>
<td>0.0</td>
</tr>
<tr>
<td>Albumin level, median (IQR), g/dL</td>
<td>75/99 (75.8)</td>
<td>547/790 (69.2)</td>
<td>3.90</td>
<td>&lt;0.005</td>
<td>30.0</td>
</tr>
<tr>
<td>Anastomotic leak</td>
<td>5/98 (5.1)</td>
<td>14/786 (1.8)</td>
<td>3.13</td>
<td>&gt;0.05</td>
<td>0.6</td>
</tr>
<tr>
<td>ASA score, median (IQR)</td>
<td>99/99 (100.0)</td>
<td>790/790 (100.0)</td>
<td>6.31</td>
<td>&lt;0.001</td>
<td>0.0</td>
</tr>
<tr>
<td>Blood glucose level ≥140 mg/dL</td>
<td>63/95 (66.3)</td>
<td>313/767 (40.8)</td>
<td>21.3</td>
<td>&lt;0.001</td>
<td>3.0</td>
</tr>
<tr>
<td>BMI, median (IQR)</td>
<td>95/99 (95.9)</td>
<td>787/790 (99.6)</td>
<td>0.71</td>
<td>&gt;0.05</td>
<td>0.8</td>
</tr>
<tr>
<td>Death</td>
<td>17/99 (17.2)</td>
<td>28/790 (3.5)</td>
<td>31.2</td>
<td>&lt;0.001</td>
<td>0.0</td>
</tr>
<tr>
<td>Duration of surgery, median (IQR), min</td>
<td>99/99 (100.0)</td>
<td>790/790 (100.0)</td>
<td>3.68</td>
<td>&lt;0.005</td>
<td>0.0</td>
</tr>
<tr>
<td>Estimated blood loss, median (IQR), mL</td>
<td>92/99 (92.9)</td>
<td>759/790 (96.1)</td>
<td>3.43</td>
<td>&lt;0.001</td>
<td>4.3</td>
</tr>
<tr>
<td>Laparoscopic surgery performed</td>
<td>8/99 (8.1)</td>
<td>330/790 (41.8)</td>
<td>41.0</td>
<td>&lt;0.001</td>
<td>0.0</td>
</tr>
<tr>
<td>Male</td>
<td>44/99 (44.4)</td>
<td>408/790 (51.8)</td>
<td>1.61</td>
<td>&gt;0.05</td>
<td>0.0</td>
</tr>
<tr>
<td>Steroid use</td>
<td>6/99 (6.1)</td>
<td>29/790 (3.7)</td>
<td>0.77</td>
<td>&gt;0.05</td>
<td>0.0</td>
</tr>
</tbody>
</table>

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); IQR, interquartile range.

SI conversion factors: To convert albumin to grams per liter, multiply by 10 (to convert to millimoles per liter, multiply by 0.0555).

*a* The *t* test.

*b* The Mann-Whitney U rank sum test (*z* score).

*c* Analysis.
for both diabetic and nondiabetic patients in Figure 2. Among the hyperglycemic patients, only 54% were known to have diabetes mellitus. Emergency surgical procedures were performed on 537 of 5123 patients (10.5%). Overall, the rates of anastomotic leak for diabetic patients vs nondiabetic patients were not significantly different (19 of 884 diabetic patients [2.1%] vs 134 of 4213 nondiabetic patients [3.2%]; \( P = .13 \)), and they were not higher for those undergoing emergency surgery. Potential risk factors for anastomotic leak were evaluated using both univariate and multivariate analyses. Among known diabetic patients, only preoperative steroid use (3 of 34 patients who did use steroids [8.8%] vs 16 of 850 patients who did not [1.9%]; \( P = .03 \); odds ratio, 4.60 [95% CI, 1.25-16.9]; 65% power) was significantly associated with anastomotic leak (Figure 3). For nondiabetic patients, preoperative steroid use was not significantly associated with anastomotic leak (10 of 178 patients who did use steroids [5.6%] vs 124 of 4035 patients who did not [3.1%]; \( P = .09 \); 47% power). Hyperglycemia, emergency surgery, American Society of Anesthesiologists score (<3 vs ≥3), sex, and open vs laparoscopic surgery had no significant association with anastomotic leak rates.

Mortality rates following colectomy were significantly higher for diabetic patients than for nondiabetic patients (5.1% vs 2.6%; \( \chi^2 = 15.1; P < .05 \)). Additionally, the mortality rate for patients who had an anastomotic leak was higher than the mortality rate for patients who did not. Among nondiabetic patients, the risk of mortality more than doubled (8 of 134 patients with a leak [6.0%] vs 100 of 4079 patients without a leak [2.5%]; \( P < .05 \); 64% power), whereas among diabetic patients, the risk increased by a factor of nearly 6 (3 of 19 patients with a leak [26.3%] vs 39 of 865 patients without a leak [4.5%]; \( P < .05 \); 88% power) (Figure 4).

Many risk factors (emergency surgery, steroid use, American Society of Anesthesiologists score of ≥3, open procedure, and anastomotic leak) had a greater effect on mortality for diabetic patients than for nondiabetic patients. However, a higher mortality rate after surgery was related to hyperglycemia only for nondiabetic patients: those with hyperglycemia had higher mortality than those without hyperglycemia (27 of 318 nondiabetic patients with hyperglycemia [8.5%] vs 73 of 3270 nondiabetic patients without [2.2%]; \( P < .001 \); 99% power). Among diabetic patients, hyperglycemia did not significantly affect mortality (22 of 376 diabetic patients with hyperglycemia [5.9%] vs 22 of 486 diabetic patients without [4.5%]; \( P = .47 \)). The mortality rate among nondiabetic patients with hyperglycemia (8.5%) was significantly higher than for all diabetic patients (5.1%; \( \chi^2 = 4.13; P < .05 \)) and statistically equivalent to the mortality rate for diabetic patients with hyperglycemia (5.9%; \( \chi^2 = 1.45; P = .23 \)).

**COMMENT**

The effect of diabetes mellitus on colon surgery remains unclear, and reports in the literature have been varied. Several studies have reported an association between diabetes and anastomotic leak for colorectal surgery patients in both univariate and multivariate analy-
Diabetes alone was not found to be a risk factor for anastomotic leak in our study. However, diabetic patients who had an anastomotic leak had a more than 4-fold higher mortality than did nondiabetic patients who had an anastomotic leak, and a 6-fold higher mortality than did diabetic patients who did not have an anastomotic leak. In addition, preoperative steroid use appears to confer a greater risk of anastomotic leak in the colectomy population as a whole, but especially for diabetic patients. In fact, the anastomotic leak rate for diabetic patients who used steroids was more than 4 times higher than it was for diabetic patients who did not use steroids (8.8% vs 1.9%, respectively). The risk of an anastomotic leak for nondiabetic patients who did use steroids (odds ratio, 4.60) was twice as high as that for nondiabetic patients who did not (odds ratio, 2.30). Emergency surgery, age, sex, preoperative hyperglycemia, estimated blood loss, body mass index, albumin level, duration of surgery, and open vs laparoscopic surgery were not factors that were associated with anastomotic leak for diabetic or nondiabetic patients.

Several studies\textsuperscript{17,18} have looked at the effects of preoperative steroid use on anastomotic leak rates in colorectal surgery; however, these studies have not shown statistically significant differences among patients taking these drugs. These outcomes may be due to the relatively small number of patients in these studies\textsuperscript{17,18} and the accompanying lack of power. Our data show significantly increased anastomotic leak rates in diabetic patients taking steroids before surgery. This information could potentially influence intraoperative decision making for these groups of patients. For example, a diabetic patient who used steroids before surgery might merit a colostomy or a diverting loop ileostomy rather than an unprotected primary anastomosis, especially in the setting of multiple comorbidities that could contribute to a rapid deterioration in the event of an anastomotic leak.

In addition to the findings regarding anastomotic leaks, diabetic patients were also found to have a higher mortality after colectomy than were nondiabetic patients. However, the subset of patients with the highest postoperative mortality was the hyperglycemic, nondiabetic patient group at 8.5%. Using a multivariate analysis, we found that a preoperative glucose level of higher than 140 mg/dL in the nondiabetic population more than doubled the mortality but was not associated with a higher mortality in diabetic patients. A number of these hyperglycemic “nondiabetic” patients are likely true diabetic patients who have not yet been diagnosed and have therefore gone untreated for their disease. The precise explanations for the results of our study, however, remain uncertain. Both diabetes mellitus and impaired glucose tolerance have been associated with impaired microvascular flow secondary to endothelial dysfunction in a number of studies.\textsuperscript{19-21} The possible reasons for this association at the molecular level include inhibition of nitric oxide–mediated vasodilation, increased release of free fatty acids causing endothelial injury, and direct metabolic injury.\textsuperscript{22} Certainly, adequate blood flow is essential for a durable bowel anastomosis. A recent study,\textsuperscript{23} for example, used laser Doppler measurements to reveal a higher anastomotic leak rate in patients with reduced blood flow at the rectal stump in straight stapled anastomoses to the rectum. It seems likely that the detrimental effects of diabetes mellitus on the microvasculature, combined with the negative effect of steroids on healing, contribute to the higher observed anastomotic leak rates in this population. Furthermore, the associated components of the metabolic syndrome that are often seen in diabetic patients (ie, hypertension, obesity, dyslipidemia, and vascular disease) likely confer a significantly greater risk of postoperative mortality, especially in the event of a leak.\textsuperscript{24}

The concept of “rescue” after surgical complications has become increasingly relevant, and continually emerging data have suggested ways in which this measure can be improved.\textsuperscript{25} Our study further emphasizes the significantly lower rescue rates in diabetic patients undergoing colectomy, especially in the setting of preoperative steroid use. The high mortality following an anastomotic leak in diabetic patients is alarming, and future efforts should be aimed at identifying perioperative management strategies to improve survival.

Our study is limited by the inherent constraints of the MSQC database. Although the database provides useful information about patients’ health status in the form of categorical data points, the full details of their medical histories are not available for review. Although data on the presence of certain medical comorbidities are provided, the degree of severity is difficult to determine. In addition, detailed information regarding factors such as surgical indications, surgeon experience, and type of anastomosis (ie, hand-sewn vs stapled) are not known.

Our study is also limited by its being a retrospective analysis; however, a key strength of our study lies in its utilization of prospective data collection from a large patient population through a statewide surgical quality collaborative. Our study is also considerably larger than previous studies that have examined the effect of diabetes and hyperglycemia on colon and rectal surgical outcomes. From a sample of 153 patients with an anastomotic leak, we have determined that diabetic patients are at a significantly high risk for this complication if they have been using steroids preoperatively and are at an exceptionally increased risk of mortality in the event of a leak. This finding could play an important role in the operative decision making process to limit these risks (ie, by performing fecal diversion). Our study also merits further research to determine whether optimal blood glucose control will improve surgical outcomes, mortality, and rates of rescue following postoperative complications.

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invitational manuscript for important intellectual content: Ziegler, Catto, Riggs, Gates, Grodsky, and Wasvary. Statistical analysis: Riggs and Grodsky. Administrative, technical, and material support: Ziegler, Catto, and Wasvary.

Study supervision: Ziegler, Catto, and Wasvary.

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REFERENCES


ONLINE FIRST

Risky Business?

Collaborative Databases and Quality Improvement

Postoperative complications are expensive. Quality improvement programs require a nuanced understanding of the risks of surgical complications in order to design effective strategies to reduce risks and lower costs. Motivated by pressure to control overall health care spending, third-party payers are increasingly linking reimbursement to quality indicators and process measures supported by outcomes research. For this approach to be fully embraced, all parties (patients, providers, insurers, hospitals, the government, and the public at large) must have confidence that the underlying data are reliable, valid, and robust. Thus, the Michigan Surgical Quality Collaborative, which represents 22 participating hospitals, the American College of Surgeons, and the dominant third-party payer in the state, is a noteworthy alignment of entities that might otherwise have differing perspectives and vested interests.

Through this collaboration, it is now possible to conduct large-scale multi-institutional studies that are sufficiently powered to detect potentially modifiable risk factors for infrequent complications such as anastomotic leakage after colectomy, which occurs in fewer than 5% of cases. However, rigorous analysis of even very large data sets may fail to produce valid quality...