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ORIGINAL ARTICLE

Metabolic Syndrome Is a Significant Predictor of Postoperative Morbidity and Mortality Following Bariatric Surgery

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Abstract

Introduction/Purpose Metabolic syndrome is commonly demonstrated in patients with morbid obesity undergoing bariatric surgery. The purpose of this study was to determine the effect of metabolic syndrome on morbidity and mortality following bariatric surgery.

Materials and Methods The National Surgical Quality Improvement Program (NSQIP) dataset was queried for patients who underwent bariatric surgical procedures between 2012 and 2014. Patient demographics, comorbid conditions, bariatric procedure type, and postoperative complications were analyzed. Metabolic syndrome was defined as having a body mass index > 30 kg/m^2 in the presence of the comorbid conditions of hypertension and diabetes. Regression analysis was used to determine the relationship between metabolic syndrome and postoperative morbidity and mortality.

Results During the study interval, 59,404 patients underwent bariatric surgery (Roux-en-Y gastric bypass = 28,263, sleeve gastrectomy = 30,239, revision = 422, and biliopancreatic diversion = 480). The mean body mass index was 45.9 kg/m^2, and the mean age was 45 years. Of the cohort, 30,104 (50.6%) patients had a diagnosis of hypertension, 16,558 (27.8%) had diabetes mellitus, and 12,803 (21.5%) met the criteria for metabolic syndrome. Patients with metabolic syndrome were more likely to have Roux-en-Y gastric bypass procedure, a history of congestive heart failure, severe COPD, renal failure, and diminished functional status ($p < 0.0001$). Morbidity was greater for patients with metabolic syndrome (7.5% vs. 5%; $p < 0.0001$), and patients in this subset also had a 3.2-fold increased risk of mortality ($p < 0.0001$).

Discussion Metabolic syndrome is prevalent in patients who undergo bariatric surgery. We have demonstrated that patients with the constellation of comorbid conditions defining metabolic syndrome are at an increased risk of morbidity and mortality following bariatric surgery. Patients and surgeons should be informed of the potential increased risk in this patient population.

Keywords Obesity · Bariatrics · Outcomes

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Introduction/Purpose

Metabolic syndrome is a disorder hallmarked by a decrease in insulin sensitivity leading to a state of hyperinsulinemia.[1] It is actually a cluster of conditions that together increase a patient's risk of heart disease, stroke, and diabetes. Metabolic syndrome includes hypertension, hyperglycemia, central obesity, and abnormal cholesterol levels.[2] A diagnosis of metabolic syndrome is associated with a 1.5–2.5-fold increase in overall and cardiovascular mortality.[1,2] Weight loss has been shown to elicit an improvement and often resolution of metabolic syndrome comorbidities, although the impact of weight loss attained through non-surgical means is often transient.

Bariatric surgery, in general, has been demonstrated to lead to long-term weight loss and a decreased overall mortality.[3] Patients with metabolic syndrome have much to gain with bariatric

surgery; however, the risk associated with surgery in this specific patient population has not been well described. The aim of this study was to determine 30-day perioperative outcomes in patients with metabolic syndrome following bariatric surgery.

Materials and Methods

The American College of Surgeons National Surgical Quality Improvement Program (NSQIP) datasets from 2012 to 2014 were queried for patients with a BMI greater than or equal to 30 kg/m^2 who underwent one of the following bariatric procedures: Roux-en-Y gastric bypass (Current Procedural Terminology (CPT) 43644, 43645, or 43846), sleeve gastrectomy (CPT 43775 or 43843), biliopancreatic diversion (BPD) (CPT 43845), or bariatric revision (CPT 43848, 43860, or 43865).

A total of 61,495 patients met initial inclusion criteria. Patients were excluded from analysis if any of the following exclusion criteria were present: age greater than or equal to 90 years ($n = 1$), unknown age ($n = 1$), BMI < 30 kg/m^2 ($n = 1049$), disseminated cancer ($n = 13$), primary surgery classified as an emergency ($n = 178$) or non-elective ($n = 667$), unrelated concurrent surgery such as abdominal wall hernia repair or colorectal procedure ($n = 27$), American Society of Anesthesiologists (ASA) class V ($n = 1$), or preoperative diagnosis of sepsis or systemic inflammatory response syndrome (SIRS) ($n = 154$). The final study cohort included 59,404 patients.

Demographic and 30-day perioperative information was collected for the cohort (Table 1). Metabolic syndrome was defined, based on the data available in NSQIP, as patients with a preoperative body mass index ≥ 30 kg/m^2 in the setting of hypertension requiring at least one medication and diabetes mellitus. This definition is used to remain consistent with previous research examining the impact of metabolic syndrome on procedures other than bariatric surgery as well as literature following outcomes after bariatric surgery.[4,5] The primary outcome was 30-day postoperative complications including reoperation, septic shock, shock, myocardial infarction, urinary tract infection, acute renal insufficiency, failure to wean from the ventilator, pulmonary embolism, pneumonia, dehiscence, surgical site infection, and mortality.

The Medical College of Wisconsin (Milwaukee, WI) Institutional Review Board approved this study. SPSS version 21 (IBM corp.) was used for all statistical analyses. Categorical data were analyzed with chi-square tests, while Student's t test (parametric data) or Mann-Whitney U test (non-parametric data) was used for analyses of continuous data. Univariate regression analyses were used to determine the effect of metabolic syndrome on the risk of postoperative complications. Multivariate logistic regression analyses were performed controlling for the type of procedure, ASA classification, and gender. Regression results are expressed as odds ratios (OR) and 95% confidence intervals (95% CI). A p value of < 0.05 was considered significant.

Results

Of the 59,404 included patients, the mean BMI was 45.9 kg/m^2. Of the entire cohort, 21.5% of patients had concomitant hypertension and diabetes and therefore met the criteria for metabolic syndrome. Demographic and clinical characteristics are indicated in Table 1. The mean BMI in the metabolic syndrome group was 46.1 kg/m^2 compared to 45.9 kg/m^2 in those without metabolic syndrome ($p = 0.009$). Patients with metabolic syndrome were older (51.9 vs. 42.8 years, $p < 0.001$) and were less likely to be female (67.7% females with metabolic syndrome vs. 82.2% females without metabolic syndrome, $p < 0.001$). Patients in the metabolic syndrome group were more likely to have comorbid conditions and were 3.63 times more likely than the non-metabolic syndrome group to have an American Society of Anesthesiologist category of class III or IV (95% CI 3.43–3.84; $p < 0.0001$).

The majority of patients in this study underwent a sleeve gastrectomy (50.9%, $n = 30,239$) which was also the most common procedure performed in patients without metabolic syndrome (53.8%, $n = 25,053$). Patients with metabolic syndrome, however, were more likely to have a gastric bypass (57.9%, $n = 7410$). Patients who underwent a biliopancreatic diversion were more likely to have metabolic syndrome whereas those who underwent a revision were more likely to not have metabolic syndrome. Patients with metabolic syndrome were found to have a longer hospital length of stay compared to those patients without metabolic syndrome (2.34 vs. 2.11 days, $p < 0.001$).

The overall incidence of postoperative complications was 5.7% ($n = 3393$). Patients with metabolic syndrome were 1.56 times more likely to have a complication than those patients without metabolic syndrome (95% CI 1.44–1.68; $p < 0.0001$). The presence of metabolic syndrome was also predictive of patients having two or more complications (2.1% vs. 1.2%; OR 1.74; $p < 0.0001$). Of the complications experienced, the most common was return to the operating room (2.2% with metabolic syndrome vs. 1.9% without metabolic syndrome, $p = 0.02$). The overall number of complications experienced by patients with metabolic syndrome was more than those experienced by patients with hypertension or diabetes mellitus alone (7.8% vs. 6.8% and 7.3% respectively, $p < 0.0001$). Complications including septic shock, shock, myocardial infarction, urinary tract infection, acute renal insufficiency, failure to wean from the ventilator, pneumonia, and organ space surgical site infection were more common in patients with metabolic syndrome versus those without (Table 2). The mortality rate across the cohort was 0.1% ($n = 66$). Patients with metabolic syndrome experienced a 3.3-fold increased risk of mortality compared to those without metabolic syndrome (95% CI 2.0–5.2; $p < 0.0001$).

Table 1 Preoperative demographic characteristics

Characteristic	Overall ($n = 50,404$)	Metabolic syndrome ($n = 12,803$)	Non-metabolic syndrome ($n = 46,601$)	p value*
Sex, *n* (%)				
Female	46,974 (79.1)	8668 (67.7)	38,306 (82.2)	< 0.0001
Age at operation (y)				
Mean ± SD	44.8 ± 11.7	51.9 ± 10.1	42.8 ± 11.4	< 0.0001
Body mass index (kg/m^2)				
Mean ± SD	45.9 ± 8.2	46.1 ± 8.5	45.9 ± 8.1	0.009
ASA classification, *n* (%)				
Class I	200 (0.3)	10 (0.1)	190 (0.4)	< 0.0001
Class II	16,608 (28.0)	1509 (11.8)	15,099 (32.4)	< 0.0001
Class III	40,968 (69.0)	10,613 (83.0)	30,355 (65.2)	< 0.0001
Class IV	1557 (2.6)	659 (5.2)	898 (1.9)	< 0.0001
Comorbidities, *n* (%)				
Severe COPD	1043 (1.8)	461 (3.6)	582 (1.2)	< 0.0001
Symptomatic CHF	142 (0.2)	82 (0.6)	60 (0.1)	< 0.0001
History of a bleeding disorder	644 (1.1)	274 (2.1)	370 (0.8)	< 0.0001
History of dialysis	169 (0.3)	68 (0.5)	101 (0.2)	< 0.0001
History of acute renal failure	16 (0.0)	12 (0.1)	4 (0.0)	< 0.0001
Diabetes				
IDDM	6183 (10.4)	5212 (40.7)	971 (2.1)	< 0.0001
NIDDM	10,369 (17.5)	7591 (59.3)	2778 (6.0)	< 0.0001
Type of procedure, *n* (%)				
Sleeve gastrectomy	30,239 (50.9)	5186 (40.5)	25,053 (53.8)	< 0.0001
Gastric bypass	28,263 (47.6)	7410 (57.9)	20,853 (44.7)	< 0.0001
BPD/DS	480 (0.8)	155 (1.2)	370 (0.8)	< 0.0001
Revision	422 (0.7)	52 (0.4)	370 (0.8)	< 0.0001
Length of stay, mean, d ± SD	2.18 ± 4.6	2.34 ± 4.5	2.11 ± 4.5	< 0.001

y, years; *COPD*, chronic obstructive pulmonary disease; *IDDM*, insulin-dependent diabetes mellitus; *NIDDM*, non-insulin-dependent diabetes mellitus; *CHF*, congestive heart failure; *MetS*, metabolic syndrome; *BPD/DS*, biliopancreatic diversion/duodenal switch; *d*, days

*p value compares metabolic syndrome to non-metabolic syndrome categories

To further investigate the independent effects of metabolic syndrome on the risk for any complication, we performed a multivariate analysis controlling for procedure type. Patients with metabolic syndrome had a 1.51-fold increase risk of any complication when controlling for procedure type (95% CI 1.40–1.63, $p < 0.001$). When controlling for female gender, the risk for any complication in patients with metabolic syndrome was 1.57-fold (95% CI 1.46–1.70; $p < 0.0001$). When controlling for patients with an ASA class III or IV, patients with metabolic syndrome group experienced a 1.48-fold increased risk of complications compared to those without metabolic syndrome (95% CI 1.37–1.60; $p < 0.0001$).

Discussion

The results of this study demonstrated that patients with metabolic syndrome who undergo bariatric surgery have an increased risk of 30-day morbidity or mortality compared to those patients without metabolic syndrome. Furthermore, patients with metabolic syndrome are more likely to experience two or more complications. Patients with metabolic syndrome have a 3.3-fold higher risk of death within 30 days of bariatric surgery.

Metabolic syndrome has been demonstrated to convey an environment of metabolic stress and systemic inflammation.[6–8] The overall contribution of metabolic syndrome to cardiovascular disease is not completely characterized due to the complex relationships between insulin dysregulation, dyslipidemia, and obesity.[7] Previous studies have suggested that metabolic syndrome may be along a gradient of systemic inflammation and oxidative stress that is further advanced than any one component alone. Stepanova et al. sought to investigate how this environment affects liver disease progression and what components, if any, contribute to a greater degree than the triad itself. In their investigation, overall mortality, cardiovascular mortality, and liver- and diabetes-specific mortality were all

Table 2 Postoperative morbidity and mortality after bariatric surgery

	Overall ($n = 59,404$)	Metabolic syndrome ($n = 12,803$)	Non-metabolic syndrome ($n = 46,601$)	p value*
Any complication, *n* (%)	3393 (5.7)	996 (7.8)	2397 (5.1)	< 0.0001
Mortality, *n* (%)	66 (0.1)	31 (0.2)	35 (0.1)	< 0.0001
Infection, *n* (%)				
Sepsis	231 (0.4)	72 (0.6)	159 (0.3)	< 0.0001
Septic shock	105 (0.2)	38 (0.3)	67 (0.1)	< 0.0001
Superficial SSI	679 (1.1)	214 (1.7)	465 (1.0)	< 0.0001
Deep incisional	89 (0.1)	27 (0.2)	62 (0.1)	< 0.0001
Organ space	355 (0.6)	102 (0.8)	253 (0.5)	0.001
Pneumonia	229 (0.4)	82 (0.6)	147 (0.4)	
Dehiscence	54 (0.1)	9 (0.1)	45 (0.1)	0.04
Cardiac, *n* (%)				
Cardiac arrest	66 (0.1)	31 (0.2)	35 (0.1)	< 0.0001
MI	40 (0.1)	21 (0.2)	19 (0.0)	0.03
Pulmonary, *n* (%)				
Failure to wean	150 (0.3)	62 (0.5)	88 (0.2)	< 0.0001
Reintubation	181 (0.3)	77 (0.6)	104 (0.2)	< 0.0001
Reoperation	1150 (1.9)	279 (2.2)	871 (1.9)	0.02
Other, *n* (%)				
Renal insufficiency	96 (0.2)	57 (0.4)	39 (0.1)	< 0.0001
ARF	48 (0.1)	24 (0.2)	24 (0.1)	< 0.0001
UTI	407 (0.7)	134 (1.0)	273 (0.6)	< 0.0001
CVA	10 (0.0)	5 (0.0)	5 (0.0)	0.03
PE	116 (0.2)	22 (0.2)	94 (0.2)	0.50

SSI, surgical site infection; *MI*, myocardial infarction; *ARF*, acute renal failure; *UTI*, urinary tract infection; *CVA*, cerebrovascular accident; *PE*, pulmonary embolism

*p value compares metabolic syndrome and non-metabolic syndrome categories. SD, standard deviation

independently and significantly increased in patients with metabolic syndrome and non-alcoholic fatty liver disease. When individual components of the diagnosis were evaluated, insulin resistance, hypercholesterolemia, and hypertension were each independent predictors of overall mortality although no component to the same degree as metabolic syndrome itself.[9] This study confirmed findings that a diagnosis of metabolic syndrome and its components, to a lesser degree, independently confer an adverse outcome in patients with liver disease.

Prior to this study, others have sought to describe how the milieu of metabolic syndrome affects patients in the perioperative environment. It has been suggested that patients are at an increased surgical risk above and beyond the known increase in overall cardiovascular mortality.[4,10] Using the NSQIP dataset, Bhayani et al. demonstrated a 2.7-fold increase risk of perioperative death and 1.4-fold increase in perioperative morbidity in patients with metabolic syndrome who undergo liver surgery.[4] Zavlin et al. demonstrated a similar increase in postoperative morbidity in patients with metabolic syndrome undergoing plastic surgical procedures.[11] Patients with metabolic syndrome were found to have a greater than 2.5-fold increase in postoperative complications after panniculectomy compared to patients without metabolic syndrome.

A study by Schumann et al. sought to describe the impact of metabolic syndrome on the incidence of pulmonary adverse events after bariatric surgery.[12] A statistically significant and independent association was demonstrated between patients with metabolic syndrome and postoperative pulmonary complications. The strongest associations were that of the most severe complications, namely acute respiratory distress syndrome (ARDS) and respiratory failure. Furthermore, the presence of pulmonary complications and metabolic syndrome conveyed an increased risk of postoperative mortality at 30-day, 90-day, and 1-year follow-up compared to those without metabolic syndrome.

In our study, we evaluated postoperative risk in the setting of bariatric surgery. It is estimated that 50% of obese patients have metabolic syndrome.[1] Despite the improving safety profile of bariatric surgery over the past several decades, patient risk stratification is valuable. In this study, we demonstrated an increased 30-day morbidity and mortality after bariatric surgery in patients with metabolic syndrome (Fig. 1). Much like the study by Inabnet et al., patients with metabolic syndrome had a similar BMI to those without metabolic syndrome, suggesting that factors other than weight or BMI alone confer an adverse risk.[13] It was also demonstrated that patients with

metabolic syndrome have increased risk of two or more complications in the 30-day postoperative period.

This study is limited by nature of the data collected in NSQIP. Gastrointestinal leak is a complication that is not specifically identified in NSQIP for bariatric surgery patients. It is likely that these patients are represented in NSQIP by the standard reported complications of sepsis, septic shock, and reoperation. Dyslipidemia is a medical condition that is not captured in NSQIP, nor is waist circumference. This limits the ability to detect metabolic syndrome in patients with procedure codes for bariatric surgical procedures from the data. The criteria for this study, as used in previous studies, did not rely on this data point to make a diagnosis of metabolic syndrome by design, but we acknowledge that this may underestimate the number of patients who have comorbidities constituting metabolic syndrome by the National Heart, Lung, and Blood Institute and the American Heart Association (NHLBI/AHA) as well as the International Diabetes Federation (IDF) definition.[4,14] We are likely underestimating the number of patients with metabolic syndrome who undergo bariatric surgery due to these limitations. The rate of metabolic syndrome reported in the USA varies widely based on the source and the definition of metabolic syndrome that is used. Reported rates vary from approximately 25[6] to 65% in men and 56% in women as reported by the National Health and Nutrition Examination Survey (NHANES) from 2003 to 2006.[15] Further consensus on a standardized definition for metabolic syndrome is needed in order to accurately compare prevalence across studies. The addition of relevant data points within surgical databases will expand the ability to analyze these patient outcomes in a comprehensive way. Despite these limitations, this study contributes to the literature in demonstrating an adverse risk profile in the first 30 days after bariatric surgery for patients with metabolic syndrome.

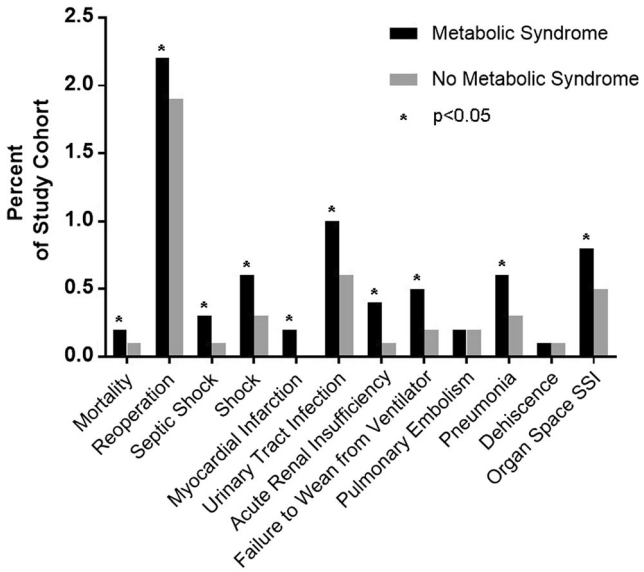

Fig. 1 Postoperative morbidity and mortality after bariatric surgery

Conclusion

We have demonstrated that patients with metabolic syndrome have an increased risk of morbidity and mortality after bariatric surgery. We have also demonstrated that metabolic syndrome patients have a greater risk of two or more complications within 30 days. Demonstrating the elevated perioperative risk of this patient population may allow for greater preoperative optimization and surgical planning prior to these higher risk patients proceeding to the operating room. It may also help with proper risk adjustment and informed consent prior to surgery as well.

Authors' Contributions Kathleen Lak, Melissa Helm, Tammy Kindel, and Jon Gould contributed to this manuscript in conception and study design, drafting and revisions, final approval of the version to be published, and agreement to all aspects of the work.

Compliance with Ethical Standards

The Medical College of Wisconsin (Milwaukee, WI) Institutional Review Board approved this study.

Conflict of Interest Kathleen Lak, Melissa Helm, and Tammy Kindel have no conflicts of interest. Jon Gould is a consultant and speaker for Torax Medical which is not relevant to this manuscript.

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