Relation of Bariatric Surgery to Inpatient Cardiovascular Outcomes (from the National Inpatient Sample)

Tran Nguyen, MD, Talal Alzahrani, MD MPH MS, Ari Mandler, BS, Mohammad Alarfaj, MD, Gurusher Panjrath, MD, and Joseph Krepp, MD*

Approximately one in 3 patients in the United States are obese. There is a strong association between obesity and an increased rate of cardiovascular disease (CVD)-related mortality. Bariatric surgery (BS) has emerged as an effective strategy to achieve reduction of excess weight. Our study aims to explore the relationship between BS and major adverse cardiovascular events (MACE) among obese hospitalized patients in the United States. This is a retrospective study of all obese adult patients with BMI ≥35 kg/m^2 (n= 1,700,943) in the National Inpatient Sample between 2012 and 2016. Differences in the clinical characteristics of obese patients with a history of BS versus obese patients without a history of BS were analyzed as well as the association between BS and MACE after adjusting for CVD risk factors. Among 50,296 obese patients with a history of BS (2.96%), the mean age was 53 ± 12 years with the majority being female (75.32%) and Caucasian (71.85%). Multivariate analysis revealed that obese patients with a history of BS had a1.6-fold decrease odds of MACE compared with patients without BS (OR 0.62; 95% CI, 0.60 to 0.65; p <0.001). In conclusion, this study illustrates that among obese patients with BMI ≥35 kg/m^2, history of BS was associated with a significantly lower odds of inpatient MACE, after adjusting for CVD risk factors.
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Cardiovascular disease (CVD) is the leading cause of mortality worldwide, with obesity being a major, modifiable risk factor for CVD .[1] Obesity, defined as a Body Mass Index (BMI) of 30 kg/m^2 or more, currently encompasses more than one third of the adult population in the United States.[2] Obesity is associated with CVD-related morbidity and mortality, including coronary heart disease, stroke, venous thrombosis events, congestive heart failure, and atrial fibrillation.[3-6] Although interventions targeting weight loss have resulted in reduction of CVD risk factors[7,8] and all cause-mortality, randomized controlled trials and meta-analyses have not demonstrated the benefit of lifestyle and dietary weight loss on lowering CVD events.[9,10] Bariatric surgery (BS) is an effective and durable treatment for class II (BMI 35.0 to 39.9 kg/m^2) or class III (BMI ≥ 40 kg/m^2) obesity, providing significant and sustained weight loss in comparison to lifestyle and medical management alone[11,12] as well as improved glycemic control.[13,14] However, the effect of BS on cardiovascular outcomes has remained inconclusive as available randomized controlled trials and observational studies have been limited by small sample sizes, localized databases, and inclusion of outdated procedures.[15-18] This study aims to investigate the relation between BS and inpatient MACE among obese patients using a large and contemporary national database in the United States.

Methods

The 2012-2016 National Inpatient Sample (NIS) data from the Healthcare Cost and Utilization Project (HCUP) was used for this study. The NIS is the largest all-payer inpatient care database in the United States. Only adult patients with class II (BMI 35.0 to 39.9 kg/m^2, ICD 9/10 codes V85.35/ Z68.35) or class III obesity (BMI > 40 kg/m^2, ICD 9/10 codes V85.4x/ Z68.4x) were included (n= 1,700, 943) in the study. Patients' BMIs were stratified into different classes, instead of reflected as patient BMIs.

First, a univariate analysis was performed to study differences in clinical characteristics between obese patients with any identifiable history of BS (gastric bypass, sleeve gastrectomy, or presence of laparoscopic banding device) (identified by ICD9/10 codes V45.86 / Z98.84, respectively) (n= 50,296) versus obese patients without a history of BS (n= 1,650,647). Baseline characteristics and their corresponding ICD9/10 codes are listed in Table S1.

A logistic regression model was then constructed to study the association between undergoing BS and MACE, including all-cause mortality, cardiac arrest, acute heart failure, acute myocardial infarction (MI), and cerebrovascular accident after adjusting for CVD risk factors including gender, hospital region, All Patients Refined Diagnosis Related Groups severity and risk of mortality, diabetes, hypertension, hyperlipidemia, chronic kidney disease (CKD), prior MI, peripheral arterial disease, chronic obstructive pulmonary

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*Corresponding author: Tel: 202-741-2323; fax: 202-741-2324.
E-mail address: jkrepp@mfa.gwu.edu (J. Krepp).

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Table 1
Baseline demographics and heath characteristics of inpatients with adult obesity of BMI > 35 Kg/m^2

Variable	Bariatric surgery		P value
	No (n= 1,650,647)	Yes (n=50,296)	
Age (years)	54.1±15.6	52.9±12.1	<0.001
Women	1,108,801 (67.19%)	37,869 (75.32%)	<0.001
White	1,048,163 (66.89%)	33,989 (71.85%)	<0.001
Black	313,215 (19.99%)	8,485 (17.94%)	<0.001
Hispanic	145,382 (9.28%)	3,414 (7.22%)	<0.001
Asian or Pacific Islander	13,682 (0.87%)	196 (0.41%)	<0.001
Native American	11,343 (0.72%)	179 (0.38%)	<0.001
Other	35,255 (2.25%)	1,044 (2.21%)	<0.001
Hospital/Hospitalization Characteristics			
Hospital Region			<0.001
Northeast	300,001 (18.17%)	10,568 (21.01%)	
Midwest	434,796 (26.34%)	13,987 (27.81%)	
South	634,302 (38.43%)	16,966 (33.73%)	
West	281,548 (17.06%)	8,775 (17.45%)	
All Patients Refined Diagnosis Related Groups Severity			<0.001
No class specified (0)	333 (0.02%)	6 (0.01%)	
Minor loss of function (1)	115,960 (8.44%)	2,664 (6.36%)	
Moderate loss of function (2)	628,034 (45.68%)	22,982 (54.86%)	
Major loss of function (3)	514,108 (37.40%)	14,004 (33.43%)	
Extreme loss of function (4)	116,271 (8.46%)	2,235 (5.34%)	
All Patients Refined Diagnosis Related Groups Risk of Mortality			<0.001
No class specified (0)	330 (0.02%)	5 (0.01%)	
Minor likelihood of dying (1)	682,566 (49.65%)	25,223 (60.21%)	
Moderate likelihood of dying (2)	350,703 (25.51%)	10,147 (24.22%)	
Major likelihood of dying (3)	244,393 (17.78%)	4,775 (11.40%)	
Extreme likelihood of dying (4)	96,711 (7.04%)	1,740 (4.15%)	
Medical history			
Diabetes Mellitus	748,484 (45.34%)	17,059 (33.92%)	<0.001
Hypertension	804,920 (48.76%)	26,793 (53.27%)	<0.001
Hyperlipidemia	614,021 (37.20%)	14,886 (29.60%)	<0.001
Peripheral Arterial Disease	51,110 (3.10%)	857 (1.70%)	<0.001
Pulmonary Arterial Hypertension	99,732 (6.04%)	1,879 (3.74%)	<0.001
Chronic Obstructive Pulmonary Disease	184,945 (11.20%)	2,987 (5.94%)	<0.001
Chronic Kidney Disease	308,575 (18.69%)	5,606 (11.15%)	<0.001
Tobacco Use Disorder	385,799 (23.37%)	11,462 (22.79%)	0.002
Old Myocardia Infarction	80,539 (4.88%)	1,761 (3.50%)	<0.001
History of Percutaneous Coronary Intervention	76,243 (4.62%)	1,773 (3.53%)	<0.001
History of Coronary Artery Bypass Grafting	51,738 (3.13%)	921 (1.83%)	<0.001
Ischemic Heart Disease	345,014 (20.90%)	6,776 (13.47%)	<0.001
All Heart Failure	389,677 (23.61%)	6,743 (13.41%)	<0.001
Systolic Heart Failure	108,594 (6.58%)	1,561 (3.10%)	<0.001
Diastolic Heart Failure	170,002 (10.30%)	2,828 (5.62%)	<0.001
Cardioversion	15,614 (0.95%)	401 (0.80%)	0.001
Pacemaker	28,615 (1.73%)	863 (1.72%)	0.764
Implantable Cardioverter Defibrillator	24,597 (1.49%)	553 (1.10%)	<0.001
Atrial Fibrillation/ Atrial Flutter	249,228 (15.10%)	6,552 (13.03%)	<0.001

disease, CKD, pulmonary arterial hypertension, atrial fibrillation, and smoking.

The statistical analyses were performed using SAS 9.4 (SAS Institute Cary, North Carfolina). All tests were conducted with p values < 0.05 being defined as significant.

Results

Among 1,700,943 inpatients with class II and III obesity, 50,296 patients (2.96%) were identified with a history of BS. Baseline characteristics are described in Table 1. The mean age of obese patients with a history of BS was 53 years old with the majority being female (75.3%) and Caucasian (71.9%). Differences in baseline characteristics between adult obese patients with and without a history BS are further described in Table 1. Obese patients with a history of BS were notably less likely to have diabetes, hyperlipidemia, CKD, ischemic heart disease, both systolic and diastolic heart failure, atrial fibrillation, and a history of MI. Other findings include a lower percentage of peripheral

Table 2
Clinical outcomes of inpatients with adult obesity of BMI > 35 Kg/m^2

	No (n= 1,650,647)	Yes (n=50,296)	
Medical history			
In-hospital Mortality	25,646 (1.55%)	426 (0.85%)	<0.001
Acute Myocardial Infarction	46,560 (2.82%)	660 (1.31%)	<0.001
Cardiac Arrest	10,854 (0.66%)	181 (0.36%)	<0.001
Cerebrovascular accident	22,487 (1.36%)	424 (0.84%)	<0.001
Ischemic Stroke	7,267 (0.44%)	168 (0.33%)	<0.001
Acute on Chronic Heart Failure	130,278 (7.89%)	1,703 (3.39%)	<0.001
Acute Heart Failure	29,371 (1.78%)	423 (0.84%)	<0.001
Major Adverse Cardiovascular Events	228,763 (13.86%)	3,376 (6.71%)	<0.001
Acute Kidney Injury	272,136 (16.49%)	5,819 (11.57%)	<0.001
Systematic Inflammatory Response Syndrome	107,492 (6.51%)	2,510 (4.99%)	<0.001
Sepsis	99,561 (6.03%)	2,302 (4.58%)	<0.001
Shock	33,841 (2.05%)	745 (1.48%)	<0.001
Septic Shock	30,570 (1.85%)	700 (1.39%)	<0.001
Cardiac Shock	6,874 (0.42%)	91 (0.18%)	<0.001
Ventilation	58,478 (3.54%)	1,024 (2.04%)	<0.001
Mechanical Support	1,983 (0.12%)	17 (0.03%)	<0.001
Length of Stay	5.1± 6.4 (days)	4.5 ± 4.7 (days)	<0.001

arterial disease, pulmonary arterial hypertension, chronic obstructive pulmonary disease , history of PCI and history of CABG among obese patients with a history of BS compared with those without history of BS (Table 1).

In terms of clinical outcomes, patients with a history of BS were less likely to have overall MACE (6.71% vs 13.86%, p <0.001) with significantly lower rates of in-hospital death (0.85% vs 1.55%, p <0.001), acute MI, acute heart failure, and stroke stroke (Table 2). Patients with a history of BS were also less likely to have all types of shock − septic and cardiogenic, need for ventilation and mechanical support, acute kidney injury (AKI); they also had shorter hospital stay (4.5 days ± 4.7 compared with 5.1 days ± 6.4, p <0.001) compared with obese patients without history of BS (Table 2).

Among obese patients with class II or class III obesity, a history of BS was associated with a 1.6- fold decreased odds of in-hospital MACE, after adjusting for CVD risk factors (OR = 0.62, 95% CI = 0.60 to 0.65, p<0.001) (Table 3). Interestingly, being in hospital region of Midwest and West was associated with lower likelihood of having MACEs while hospital region of South was correlated with higher likelihood of having MACE. Being female is independently associated with a lower odds of MACE (OR = 0.73, 95% CI = 0.72 to 0.73, p <0.001).

Discussion

This is the first study to examine a large inpatient database to characterize the contemporaneous clinical profile of hospitalized obese patients with a history of BS in the United States in recent years. Our study demonstrated that among obese patients with a BMI ≥35 Kg/m^2, a history of BS was associated with a significantly decreased odds of MACE, including all-cause mortality, cardiac arrest, acute heart failure, acute myocardial infarction, and cerebrovascular accident.

Our data illustrated that most obese inpatients with or without BS status were female, consistent with prior National Health and Nutrition Examination Survey surveys from 1999 through 2016, and furthermore showed the highest prevalence among Caucasians and patients from the South.[19] The prevalence of obesity, as estimated from self-reported height and weight in the 2017 Behavioral Risk Factor Surveillance System, was highest among Southern states.[20]. On the other hand, National Health and Nutrition

Table 3
Multivariable associations between bariatric surgery and MACEs among obese patients in NIS database 2012 to 2016

Characteristics	OR (95% CI)	P-value
History of bariatric surgery	0.623 (0.598-0.649)	<0.001
Women	0.726 (0.718-0.734)	<0.001
Hospital Region (Midwest)	0.889 (0.875-0.904)	<0.001
Hospital region (South)	1.057 (1.041-1.073)	<0.001
Hospital region (West)	0.828 (0.813-0.843)	<0.001
All Patients Refined Diagnosis Related Groups Severity		
Minor loss of function (1)	1.434 (0.951 - 2.614)	0.085
Moderate loss of function (2)	4.944 (3.288 - 7.435)	<0.001
Major loss of function (3)	4.716 (3.137 - 7.090)	<0.001
Extreme loss of function (4)	5.670 (3.772 - 8.521)	<0.001
All Patients Refined Diagnosis Related Group Risk of Mortality		
Minor likelihood of dying (1)	0.108 (0.105 - 0.111)	<0.001
Moderate likelihood of dying (2)	0.252 (0.246 - 0.258)	<0.001
Major likelihood of dying (3)	0.541 (0.530 - 0.553)	<0.001
Hypertension	1.095 (1.079-1.112)	<0.001
Diabetes Mellitus	1.206 (1.192-1.220)	<0.001
Hyperlipidemia	1.514 (1.498-1.532)	<0.001
Chronic Kidney Disease	1.490 (1.467 -1.514)	<0.001
Old Myocardial Infarction	1.623 (1.592-1.655)	<0.001
Peripheral Arterial Disease	1.063 (1.037-1.090)	<0.001
Chronic Obstructive Pulmonary Disease	1.258 (1.241-1.276)	<0.001
Atrial Fibrillation/Flutter	1.870 (1.848-1.893)	<0.001
Chronic Kidney Disease	1.490 (1.467-1.513)	<0.001
Pulmonary Arterial Hypertension	2.437 (2.397-2.477)	<0.001
Tobacco Use Disorder	1.122 (1.106-1.138)	<0.001

Examination Survey showed that the prevalence of obesity was highest in Non-Hispanic Blacks in both male (37.0%) and female (55.3%) population; although note should be made that our study reflected an inpatient population.[21]

BS is hypothesized to provide cardiovascular protection though various mechanisms including: reduction in traditional cardiovascular risk factors, decrease in pro-inflammatory and thrombotic biomarkers, microscopic improvements in vascular endothelial function and macroscopic improvements in systolic function, diastolic function, and myocardial structure.[7–8, 22-26] The Look AHEAD (Action for Heath in Diabetes) trial demonstrated an intensive lifestyle intervention among overweight and obese adults with type 2 diabetes resulted in modest weight loss without significant differences in MACE.[9] Weight loss on the order of 10 to 45 kg (9% to 38%) in the Swedish Obesity Study (SOS) bariatric intervention study were required to overcome aging effects and improve cardiovascular risk factors among severely obese patients.[27] Such reduction is difficult to accomplish with intensive lifestyle modification alone.

Our findings are consistent with previous studies supporting the benefits of BS on cardiovascular outcomes. Johnson et al. demonstrated that BS was associated with 60% reduction in major macrovascular events including MI, stroke, and all-cause mortality among moderately and severely obese patients with Type 2 diabetes.[15] The 2012 SOS reported lower rates of cardiovascular mortality, MI and stroke among obese adults after BS; however, more than two thirds of surgeries were vertical banded gastroplasty, which have largely been replaced by more effective metabolic procedures in recent years,[27] as Roux-en-Y gastric bypass for patients with severe obesity is associated with a lower long-term risk of congestive heart failure.[17] Most recently, a Canadian population study demonstrated that BS was associated with substantially lower all-cause mortality and cardiovascular mortality; while recent data from the SOS study illustrated that among patients with obesity, BS was associated with longer life expectancy than usual obesity care.[28,29]

An important strength of this study is the large sample size, allowing us to characterize baseline characteristics and outcomes of obese patients with history of BS across the United States. In addition, by using a multivariate analysis, we were able to adjust for the impact of BS on MACE, through inclusion of baseline characteristics and CVD risk factors.

This study is not without limitations, however. As this is an inpatient, administrative database, there is a reliance on provider-recorded diagnoses using ICD codes. Secondly, NIS does not provide information about the length of time between the date of BS and MACE events, so it is difficult to discern short-term versus long-term effects of BS on cardiovascular outcomes. Furthermore, events that do not result in hospitalizations are not included. Thirdly, ICD9/10 codes V45.86 / Z98.84 is an umbrella code for all BS types so outcomes could not be differentiated among each type of BS. Fourthly, this is a cross-sectional study and despite the use of logistic regression models, there is always the possibility of unknown confounding from variables not included in the final logistic regression model such as socioeconomic class and baseline education level. We also do not have data on the use of medications such as aspirin, statins, antihypertensive agents, or antiplatelet therapies. Although it is possible that patients opting to undergo BS may be more health-conscious than those not choosing to undergo BS potentially introducing bias into the study, logistic regression analysis was used to minimize this potential impact.

In conclusion, among adult inpatients with class II and class III obesity, history of BS was associated with a significantly lower MACE, after adjusting for CVD risk factors. Given the observational nature of the study, our data is hypothesis-generating, and prospective randomized analyses are necessary to study the link between BS and cardiovascular outcomes among obese patients.

Credit Author Statement

Tran Nguyen**:** Conceptualization, Writing- Original draft preparation**,** Reviewing and Editing**;** Talal Alzahrani: Methodology, Data Curation, Software; Ari Mandler: Investigation, Data Curation; Mohammad Alarfaj*:* Investigation, Data Curation; Gurusher Panjrath: Supervision; Joseph Krepp**:** Supervision, Writing- Reviewing and Editing.

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Supplementary materials

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