



Clostridium difficile and Laparoscopic Bariatric Surgery: an Analysis of the Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program Database

ThucNhi T. Dang¹  · Jerry T. Dang² · Muhammad Moolla³ · Noah Switzer² · Karen Madsen¹ · Daniel W. Birch² · Shahzeer Karmali²

Published online: 26 February 2019
© Springer Science+Business Media, LLC, part of Springer Nature 2019

Abstract

Background Obesity is associated with disturbances in the gut microbiota which is a risk factor for *Clostridium difficile* infection (CDI). Bariatric surgery can induce substantive changes to the gut microbiota which may affect the risk of developing CDI.

Methods The Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program captures variables specific to bariatric surgery from 832 centers. Patients undergoing laparoscopic Roux-en-Y gastric bypass (LRYGB) or laparoscopic sleeve gastrectomy (LSG) in 2016 and 2017 were identified. Primary outcomes included the prevalence and predictors of CDI after bariatric surgery. A multivariable logistic regression model determined preoperative factors predictive of 30-day CDI.

Results A total of 78,222 LRYGB and 222,968 LSG were included. The overall incidence of CDI was low with 0.13% developing CDI. Rates of CDI were two times higher after LRYGB compared to LSG (0.2 vs 0.1%, $p < 0.001$). Although CDI rates were low, CDI was associated with increased post-operative complications. Multivariable analysis identified chronic kidney disease (OR 2.37, 95%CI 1.09–5.15, $p = 0.03$) and history of venous thromboembolism (OR 2.06, 95%CI 1.29–3.29, $p = 0.002$) as being most predictive of developing CDI with more than a twofold increase in risk. Patients undergoing LRYGB had an increased risk of CDI compared to LSG (OR 1.65, 95%CI 1.31–2.09, $p < 0.001$). White race, female sex, and obstructive sleep apnea also increased risk of CDI.

Conclusions The incidence of CDI following bariatric surgery is relatively low with LRYGB having a higher risk than LSG. Furthermore, CDI is associated with significant adverse outcomes post-operatively but had no increased risk of mortality.

Keywords Bariatric surgery · Clostridium difficile infection · Roux-en-Y gastric bypass · Sleeve gastrectomy

✉ ThucNhi T. Dang
thucnhi@ualberta.ca

Jerry T. Dang
dang2@ualberta.ca

Muhammad Moolla
Muhammad.Moolla@ualberta.ca

Noah Switzer
nswitzer@ualberta.ca

Karen Madsen
kmadsen@ualberta.ca

Daniel W. Birch
dbirch@ualberta.ca

Shahzeer Karmali
shahzeer@ualberta.ca

¹ Division of Gastroenterology, Department of Medicine, University of Alberta Hospital, University of Alberta, 8440 112 Street NW, Edmonton, AB T6G 2B7, Canada

² Department of Surgery, University of Alberta, Edmonton, Alberta, Canada

³ Faculty of Medicine and Dentistry, University of Alberta, Edmonton, Alberta, Canada

Introduction

Clostridium difficile infections (CDIs) are becoming the most common nosocomial infection in the USA and was the leading cause of gastroenteritis-associated death with an estimated 29,000 deaths in 2011 [1, 2]. Sex, age, underlying inflammatory bowel disease (IBD), exposure to antibiotics, chronic proton pump inhibitor (PPI) use, and healthcare facility contact have all been linked with increased risk of CDI [2–6]. In the case of IBD, antibiotic exposure, and PPI use, the increased risk of CDI is thought to be related to disruption in the colonic microbiota [3–6]. In addition to traditional risk factors, obesity has been found to be an independent risk factor for both CDI [7] and more severe CDI [8]. Although the mechanism by which obesity increases CDI is unclear, the increased risk is also thought to be related to changes in the microbiota seen in obesity [9, 10].

Bariatric surgery is the most effective treatment for severe obesity which results in sustained weight loss [11] and reduction in obesity-related comorbidities and mortality [12, 13]. Of the bariatric procedures, laparoscopic Roux-en-Y gastric bypass (LRYGB) and laparoscopic sleeve gastrectomy (LSG) are the two most commonly performed [14], both of which have been shown to alter the gut microbiota [15–17]. Data on the relationship between obesity, bariatric surgery, and CDI is scarce, and as such, our study aimed to retrospectively investigate the association between bariatric surgery and CDI.

Methods

Design and Population

Data was collected from the Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program (MBSAQIP) database between 2016 and 2017. Data from 2015 was not included as CDI was not coded prior to 2016. The data registry collects prospective, risk-adjusted data, based on standardized definitions for preoperative, intra-operative, and post-operative variables that are specific for metabolic and bariatric surgery [18]. Data are abstracted by trained metabolic and bariatric surgical clinical reviewers at each site who are regularly audited for accuracy. This data comes from 832 centers in the USA and Canada.

All patients who underwent LRYGB and LSG were identified using current procedural terminology (CPT) codes 43775 and 43644, respectively. Only operations identified as elective and non-emergency were included. Patients with previous bariatric surgery or coded as revisional bariatric surgery were excluded. Demographic data and patient characteristics included age, sex, race, functional status, American Society of Anesthesiologists (ASA) class, and body mass index (BMI). Patient comorbidities that were identified included: hypertension, gastroesophageal

reflux disease, type 2 diabetes, hyperlipidemia, history of venous thromboembolism (VTE), chronic kidney disease (CKD), dialysis dependency, chronic obstructive pulmonary disease, sleep apnea, oxygen dependency, chronic steroid use, smoking status, previous cardiac surgery or percutaneous intervention, and pre-operative therapeutic anticoagulation use.

Outcome Variable

The primary outcome of interest was CDI within 30 days following bariatric surgery from 2016 and 2017. CDI is coded when there is a confirmed positive CDI laboratory test or documentation in the medical record of treatment for CDI.

Major complication was defined as a composite endpoint in the database as any patient who had any of the following within 30 days of surgery:

- Anastomotic leak
- Post-operative bleed
- Pneumonia
- Venous thromboembolism
- Re-intervention (endoscopic or radiologic)
- Reoperation
- Unplanned intubation
- Acute renal failure
- Deep surgical site infection or wound disruption
- Sepsis
- Cardiac arrest and cardiopulmonary resuscitation
- Myocardial infarction
- Coma for greater than 24 hours
- Cerebral vascular accident

Statistical Analysis

Statistical analysis was performed using Stata 15.1 [19]. Descriptive categorical data were expressed as percentages and continuous data were expressed as weighted mean \pm standard deviation (SD). Baseline differences between groups were evaluated by univariate analyses using chi-squared for categorical data and independent sample *t* test for continuous data. Univariate logistic regression was used to compare differences between patients who developed CDI and those who did not.

Multivariable logistic regression analysis was used to determine predictive factors for the development of CDI within 30 days. A purposeful selection algorithm was used, and any variable with $p < 0.10$ was included in multivariable analysis. Patient factors and operative time were included in the model. The threshold for significance was set at $p < 0.05$. The Hosmer-Lemeshow goodness-of-fit test was used to evaluate the goodness of fit of the model.

Results

A total of 301,180 patients who underwent elective LSG and LRYGB in 2016 and 2017 were identified. There were 222,968 (74.0%) patients who underwent LSG and 78,222 (26.0%) who underwent LRYGB. The mean age was 44.5 years (12.0) and 79.6% of patients were female. The total number of CDI cases identified was 383 giving an overall incidence of 0.13% within 30 days post-bariatric surgery. Of the 383 cases of CDI, 269 (70.2%) were diagnosed by *Clostridium difficile* toxin, 45 (11.8%) by DNA polymerase chain reaction, and 29 (7.6%) by other tests for CDI. Only 28 (7.3%) were diagnosed with CDI by unknown methods and 12 (3.1%) with no formal testing. Of cases identified, 97.4% of patients had treatment for CDI. Rates of CDI were two times higher in the LRYGB cohort compared to the LSG cohort (0.2 vs 0.1%, $p < 0.001$). Table 1 illustrates baseline demographics in our cohort and highlights baseline differences in patients who developed compared to those who did not develop CDI within 30 days post-bariatric surgery.

Multivariable analysis identified CKD (OR 2.37 [CI 95% 1.09–5.15, $p = 0.03$]) and history of VTE (OR 2.06 [CI 95% 1.29–3.29, $p = 0.002$]) as being most predictive of developing CDI 30-day post-bariatric surgery with more than a twofold increase in risk. Patients undergoing LRYGB had increased the risk of CDI post-surgically compared to LSG (OR 1.65 [CI 95% 1.31–2.09, $p < 0.001$]). White race, female sex, and obstructive sleep apnea (OSA) also increased risk of post-surgical CDI (Table 2).

Although overall incidence of CDI was low, CDI post-operatively was associated with increased length of stay (LOS) and surgical complications including anastomotic leaks, deep surgical site infection, re-operations, re-intervention, and re-admissions within 30 days. Additionally, it was associated with increased risk of other complications including pneumonia, acute kidney injury (AKI), VTE, sepsis, and unplanned intubation (Table 3). It was not, however, associated with increased risk of death. The rate of complications was higher for LRYGB compared to LSG for almost all complications with an over two times higher composite major complication rate (5.9 vs 2.4%, $p < 0.001$) (Table 3).

Discussion

Bariatric surgery is becoming increasingly popular worldwide as an effective treatment for severe obesity that results in sustained weight loss [11] and reduction of obesity-related comorbidities and mortality [12, 20]. In our study, we found that the short-term incidence of CDI post-bariatric surgery remains low at 0.13%. This is similar to a study by Hussan et al. which found that the incidence of CDI within 30 days post-bariatric surgery ranged from 0.07 to 0.23% depending

on the type of bariatric surgery performed [21]. Although obesity has previously been identified as an independent risk factor for community and hospital onset CDI [7, 22] and more severe infections [8], the relatively low incidence identified in our study as well as by Hussan et al. suggests that obesity may play a much smaller role in CDI. The difference in the incidence of CDI in obese patients found in previous studies compared to our study may be explained by the differing size of the population of the studies: previous studies looking at the relationship between obesity and CDI included only 132 to 196 patients. Compared to national databases comprising 85,453 to 301,180 patients, these smaller studies may have overestimated the impact of obesity on CDI.

The overall incidence of CDI post-bariatric surgery was also found to be lower than the incidence of CDI in other surgical populations, which was found to range anywhere from 0.47 to 1.2% [23]. Like other studies [21], multivariable analysis showed that LRYGB increased the risk of post-surgical CDI compared to LSG, even when controlled for baseline patient demographics and comorbidities. One explanation for this difference is that, while there are alterations in the microbiota following both types of bariatric surgery compared to non-operated obese patients [15, 16], patients who have undergone LRYGB sustain more changes in their microbiota compared to LSG [17]. For example, Murphy et al. found that there were increases in microbial diversity in patients with obesity and diabetes following LRYGB but not LSG; specifically, there were increases in *Firmicutes* and *Actinobacteria* but a decrease in *Bacteroides* [17]. Although these sustained changes in the microbiota following bariatric surgery typically occur over weeks to months, a paper by David et al. showed that changes in the microbiota of the distal gut can occur as early as 1 day following dietary intervention. As such, rapid changes in the microbiota can conceivably occur following LRYGB given significant alterations in nutrient delivery and biliary transit induced by anatomic alterations [24]. These early alterations in the gut microbiome seen in LRYGB but not in LSG may be one explanation for the increased incidence of CDI in LRYGB compared to LSG. Other mechanisms that have been proposed to explain the increase in CDI in LRYGB compared to LSG include increased gastric acid suppression [25], rapid oro-fecal transit [26], and frequent use of PPI following LRYGB [21]. In our cohort, CDI was associated with increased LOS in hospital and higher rates of major complications such as anastomotic leaks or deep surgical site infections. While CDI was found to be associated with increased hospital LOS [27], patients who undergo LRYGB typically have longer LOS than LSG, which could increase exposure to nosocomial infections and increase the risk of CDI. Furthermore, LRYGB is associated with increased major complications such as anastomotic leaks or deep surgical infections [28] compared to LSG. This likely leads to higher antibiotic exposure for patients undergoing LRYGB and thus a higher incidence of CDI.

Table 1 Patient characteristics

	No. of <i>C. difficile</i> <i>n</i> = 300,797 <i>n</i> (%)	<i>C. difficile</i> <i>n</i> = 383 <i>n</i> (%)	<i>p</i> value	LSG <i>n</i> = 222,958 <i>n</i> (%)	LRYGB <i>n</i> = 78,222 <i>n</i> (%)	<i>p</i> value
Age, years						
Mean (sd)	44.5 (12.0)	45 (13.0)	0.393	44.3 (12.0)	45.3 (11.8)	< 0.001
< 18	531 (0.18)	0 (0.0)	0.269	463 (0.2)	68 (0.1)	< 0.001
18–29	35,717 (11.9)	48 (12.5)		27,541 (12.4)	8224 (10.5)	
30–39	77,594 (25.9)	109 (28.5)		58,505 (26.2)	19,198 (24.5)	
40–49	87,061 (28.9)	83 (21.7)		64,352 (28.9)	22,792 (29.1)	
50–59	66,025 (22.0)	92 (24.0)		47,613 (21.4)	18,504 (23.7)	
≥ 60	33,869 (11.3)	51 (13.3)		24,484 (11.0)	9436 (12.1)	
% female	79.6	84.1	0.031	79.3	80.4	< 0.001
Race/ethnicity						
White	218,194 (72.5)	313 (81.7)	< 0.001	160,068 (71.8)	58,439 (74.7)	< 0.001
Black	53,719 (17.9)	54 (14.1)		42,908 (19.2)	10,865 (13.9)	
Other	28,884 (9.6)	16 (4.2)		19,982 (9.0)	8918 (11.4)	
BMI, kg/m ²						
Mean (sd)	45.3 (7.7)	45.5 (7.3)	0.621	45.0 (7.7)	46.0 (7.9)	< 0.001
< 35	10,038 (3.4)	14 (3.7)	0.516	7877 (3.6)	2175 (2.8)	
35–39	67,423 (22.6)	79 (20.6)		52,111 (23.6)	15,391 (19.8)	
40–44	92,413 (30.9)	114 (29.8)		69,598 (31.5)	22,929 (29.5)	
45–49	61,796 (20.7)	81 (21.2)		44,841 (20.3)	17,036 (21.9)	
49–59	52,311 (17.5)	80 (20.9)		36,546 (16.5)	15,845 (20.4)	
≥ 60	14,725 (4.9)	15 (3.9)		10,348 (4.7)	4392 (5.7)	
Functional status						
Independent	297,625 (99.0)	375 (97.9)	0.010	220,611 (98.9)	77,389 (98.9)	< 0.001
Partially dependent	1872 (0.6)	7 (1.8)		1326 (0.6)	553 (0.7)	
Fully dependent	1300 (0.4)	2 (0.3)		1021 (0.5)	380 (0.4)	
ASA class						
1–2	67,823 (22.3)	60 (15.8)	0.002	54,651 (24.7)	13,232 (16.9)	< 0.001
3	220,937 (73.9)	299 (78.9)		159,791 (72.2)	61,445 (78.7)	
4–5	10,368 (3.5)	20 (5.3)		6946 (3.1)	3442 (4.4)	
Smoking status						
No	275,364 (91.5)	342 (89.3)	0.114	203,792 (91.4)	71,914 (91.9)	< 0.001
Yes	25,433 (8.5)	41 (10.7)		19,166 (8.6)	6308 (8.1)	
Diabetes						
No	222,055 (73.8)	276 (72.1)	< 0.001	171,697 (77.0)	50,634 (64.7)	< 0.001
Non-insulin dependent	53,570 (17.8)	52 (13.6)		36,805 (16.5)	16,817 (21.5)	
Insulin dependent	25,172 (8.4)	55 (14.4)		14,456 (6.5)	10,771 (13.8)	
Hypertension						
No	156,981 (52.2)	182 (47.5)	0.068	119,959 (53.8)	37,204 (47.6)	< 0.001
Yes	143,816 (47.8)	201 (52.5)		102,999 (46.2)	41,018 (52.4)	
GERD						
No	208,720 (69.4)	237 (61.9)	0.001	160,952 (72.2)	48,005 (61.4)	< 0.001
Yes	92,077 (30.6)	146 (38.1)		62,006 (27.8)	30,217 (38.6)	
COPD						
No	295,857 (98.4)	369 (96.3)	0.002	219,440 (98.4)	76,786 (98.2)	< 0.001
Yes	4940 (1.6)	14 (3.7)		3518 (1.6)	1436 (1.8)	
Hyperlipidemia						
No	230,287 (76.6)	271 (70.8)	0.007	174,635 (78.3)	55,923 (71.5)	< 0.001
Yes	70,510 (23.4)	112 (29.2)		48,323 (21.7)	22,299 (28.5)	
Chronic steroids						
No	295,580 (98.3)	374 (97.7)	0.757	218,953 (98.2)	77,001 (98.4)	< 0.001
Yes	5217 (1.7)	9 (2.4)		4005 (1.8)	1221 (1.6)	
Renal insufficiency						
No	298,901 (99.4)	376 (98.2)	0.003	221,543 (99.4)	77,734 (99.4)	0.743
Yes	1896 (0.6)	7 (1.8)		1415 (0.6)	488 (0.6)	
Dialysis dependent						
No	299,867 (99.7)	381 (99.5)	0.453	222,161 (99.6)	78,087 (99.8)	< 0.001
Yes	930 (0.3)	2 (0.5)		797 (0.4)	135 (0.2)	
History of VTE						
No	293,963 (97.7)	358 (93.5)	< 0.001	218,188 (97.9)	76,133 (97.3)	< 0.001
Yes	6834 (2.3)	25 (6.5)		4770 (2.1)	2089 (2.7)	
Therapeutic anticoagulant use						
Yes	292,698 (97.3)	359 (93.7)	< 0.001	220,867 (99.1)	77,337 (98.9)	< 0.001
No	8099 (2.7)	24 (6.3)		2091 (0.9)	885 (1.1)	

Table 1 (continued)

	No. of <i>C. difficile</i> n = 300,797 n (%)	<i>C. difficile</i> n = 383 n (%)	p value	LSG n = 222,958 n (%)	LRYGB n = 78,222 n (%)	p value
Venous stasis						
No	297,828 (99.0)	376 (98.2)	0.096	217,105 (97.4)	75,952 (97.1)	< 0.001
Yes	2969 (1.0)	5 (1.8)		5853 (2.6)	2270 (2.9)	
Oxygen-dependent						
No	298,708 (99.3)	376 (98.2)	0.008	221,543 (99.4)	77,541 (99.1)	< 0.001
Yes	2089 (0.7)	7 (1.8)		1415 (0.6)	681 (0.9)	
Sleep apnea						
No	185,721 (61.8)	204 (53.3)	0.001	142,026 (63.7)	43,899 (56.1)	< 0.001
Yes	115,076 (38.3)	179 (46.7)		80,932 (36.3)	34,323 (43.9)	
History of MI						
No	296,997 (98.7)	373 (97.4)	0.018	220,353 (98.8)	77,017 (98.5)	< 0.001
Yes	3800 (1.3)	10 (2.6)		2605 (1.2)	1205 (1.5)	
Previous major cardiac surgery						
No	297,552 (98.9)	378 (98.7)	0.668	220,553 (98.9)	77,377 (98.9)	0.971
Yes	3245 (1.1)	5 (1.3)		2405 (1.1)	845 (1.1)	
Previous PCI						
No	294,838 (98.0)	369 (96.3)	0.019	218,830 (98.1)	76,377 (97.6)	< 0.001
Yes	5959 (2.0)	14 (3.7)		4128 (1.9)	1845 (2.4)	

ASA American Society of Anesthesiologists, BMI body mass index, COPD chronic obstructive pulmonary disease, VTE venous thromboembolism, GERD gastroesophageal reflux disease, MI myocardial infarction, PCI percutaneous coronary intervention

In our study, the two patient characteristics that were most predictive of CDI post-bariatric surgery were CKD and history of VTE. This is congruent with findings by *Keddis* et al. who found that CKD independently increased the risk of CDI by twofold [29]. Interestingly, a history of VTE also increased the risk of CDI by approximately twofold in our cohort. While there have been studies which have shown that CDI increases the risk of in-hospital VTE [30, 31], there are no studies which show that a history of VTE increases the incidence of in-hospital CDI. One explanation for this could be that a history of VTE, like CKD, is a marker of underlying comorbidity, and higher Charlson comorbidity scores have been associated with increased risk of CDI in the IBD population [32]. Further studies to confirm this association and to understand the mechanism by which CDI is increased in patients with previous VTE are needed. Like other studies [2], female sex and white race were also found to be associated with increased risk

of CDI. Surprisingly, a history of OSA was also found to increase the risk of CDI by 25%, even when controlled for body mass index (BMI) and other comorbidities. Although this is not a traditional risk factor, there is one other study which has shown that OSA can increase the risk of CDI up to tenfold in patients with IBD and pouchitis, although the mechanism remains unknown [33]. Again, further studies are needed to confirm this association and to understand the relationship between OSA and CDI.

Although overall incidence of CDI post-bariatric surgery is low, it was associated with a significant number of adverse outcomes including LOS, re-admissions, post-surgical complications (i.e., anastomotic leaks, deep surgical site infection, re-operations, and re-intervention), and other complications (pneumonia, AKI, VTE, sepsis, and unplanned intubation). Although increased LOS and major complications could result in increased CDI, other studies have found that CDI was

Table 2 Multivariable logistic regression for factors predictive of *Clostridium difficile* infection within 30 days

Factors	Unadjusted odds ratio (95% CI)	p value	Adjusted odds ratio (95% CI)	p value
LRYGB vs LSG	1.96 (1.60–2.40)	< 0.001	1.65 (1.31–2.09)	< 0.001
Female	1.35 (1.03–1.78)	0.03	1.65 (1.24–2.20)	0.001
White race	1.69 (1.31–2.19)	< 0.001	1.65 (1.27–2.14)	< 0.001
History of VTE	3.00 (2.00–4.51)	< 0.001	2.06 (1.29–3.29)	0.002
Renal insufficiency	2.93 (1.39–6.20)	0.005	2.37 (1.09–5.15)	0.03
Obstructive sleep apnea	1.41 (1.15–1.73)	0.001	1.25 (1.01–1.56)	0.04

LRYGB laparoscopic Roux-en-Y gastric bypass, LSG laparoscopic sleeve gastrectomy, VTE venous thromboembolism

Table 3 *Clostridium difficile* infection risk by operation, perioperative factors, and 30-day complications

	No <i>C. difficile</i> n = 300,797 n (%)	<i>C. difficile</i> n = 383 n (%)	p value	LSG n = 222,958 n (%)	LRYGB N = 78,222 n (%)	p value
Procedure						
Sleeve gastrectomy	222,741 (74.1)	227 (59.3)	< 0.001	222,958 (100.0)	78,222 (100.0)	< 0.001
Roux-en-Y gastric bypass	78,066 (26.0)	156 (40.7)				
Operative time, min						
Mean (sd)	84.0 (46.5)	95.9 (52.4)	< 0.001	71.6 (36.3)	119.3 (53.9)	< 0.001
0–59.9	103,172 (34.3)	96 (25.1)	< 0.001	97,182 (43.6)	6086 (7.8)	< 0.001
61–119.9	143,944 (47.9)	190 (49.6)		14,856 (47.0)	39,278 (50.2)	
120–179.9	41,248 (13.7)	70 (18.3)		17,763 (8.0)	23,555 (30.1)	
> 180	12,433 (4.1)	27 (7.1)		3157 (1.4)	9303 (11.9)	
Length of stay, days						
Median (IQR)	1 (1)	2 (2)	< 0.001	1 (1)	2 (1)	< 0.001
CDI	0 (0.0)	383 (100.0)	< 0.001	227 (0.1)	156 (0.2)	< 0.001
Anastomotic leak	1083 (0.4)	16 (4.2)	< 0.001	686 (0.3)	410 (0.5)	< 0.001
Bleed	2648 (0.9)	7 (3.4)	< 0.001	1357 (0.6)	1,37 (1.7)	< 0.001
Reoperation	3419 (1.1)	37 (9.7)	< 0.001	1791 (0.8)	1665 (2.1)	< 0.001
Re-intervention	3538 (1.2)	46 (12.0)	< 0.001	1784 (0.8)	1800 (2.3)	< 0.001
Readmission	10,738 (3.6)	203 (53.0)	< 0.001	6473 (2.9)	4468 (5.7)	< 0.001
Cardiac complication	177 (0.1)	0 (0.0)	0.635	110 (0.0)	67 (0.1)	< 0.001
Pneumonia	551 (0.2)	13 (3.4)	< 0.001	285 (0.1)	279 (0.4)	< 0.001
Acute kidney injury	331 (0.1)	9 (2.4)	< 0.001	184 (0.1)	156 (0.2)	< 0.001
Venous thromboembolism	774 (0.3)	9 (2.4)	< 0.001	532 (0.2)	251 (0.3)	< 0.001
Deep surgical site infection	699 (0.2)	24 (6.3)	< 0.001	352 (0.2)	371 (0.5)	< 0.001
Wound disruption	158 (0.1)	1 (0.3)	0.076	86 (0.0)	73 (0.1)	< 0.001
Sepsis	241 (0.1)	12 (3.1)	< 0.001	135 (0.1)	124 (0.2)	< 0.001
Unplanned intubation	368 (0.1)	12 (3.1)	< 0.001	212 (0.1)	168 (0.2)	< 0.001
Coma > 24 h	7 (0.0)	0 (0.0)	0.925	5 (0.0)	2 (0.0)	0.875
Cerebral vascular accident	35 (0.0)	0 (0.0)	0.833	29 (0.0)	6 (0.0)	0.234
Major complications	9848 (3.3)	95 (24.8)	< 0.001	5298 (2.4)	4645 (5.9)	< 0.001
Death	250 (0.1)	1 (0.3)	0.228	136 (0.1)	115 (0.2)	< 0.001

LRYGB laparoscopic Roux-en-Y gastric bypass, LSG laparoscopic sleeve gastrectomy, CDI *Clostridium difficile* infection

associated with worse outcomes including increased length of stay in hospital, intensive-care unit admission, longer mechanical ventilation, and mortality [23, 34] in surgical populations. The lack of increased mortality found in our cohort may be explained by the differences in patient population between bariatric surgery patients and other surgical populations; bariatric surgery is performed on an elective basis in highly selected patients who are typically younger with fewer comorbidities compared to other surgical patients. However, the results suggest that increased CDI could be both a result of and a cause of increased LOS and major complications within 30 days following bariatric surgery.

A limitation of this study is the lack of data captured by the MBSAQIP database regarding pre- and post-operative use of PPI and antibiotics, both of which have been found to be independent risk factors for CDI. Additionally, although the database provides robust data,

it only captures data within 30 days of surgery. Thus, CDI or complications that develop beyond this time period are not represented in our study. Despite this, given the large size of our cohort, we are confident that the above-mentioned risk factors still have a role in increasing CDI post-bariatric surgery.

Conclusions

The incidence of CDI following bariatric surgery remains lower than both the inpatient medical and general surgery populations. LRYGB had a higher risk of CDI compared to LSG, although the exact mechanism is unknown. Furthermore, CDI is associated with significant adverse outcomes post-operatively but had no increased risk of mortality.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Ethical Approval This article does not contain any studies with human participants or animals performed by any of the authors.

Informed Consent For this type of study formal consent is not required.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

References

- Hall AJ, Curns AT, McDonald LC, Parashar UD, Lopman BA. The roles of *Clostridium difficile* and norovirus among gastroenteritis-associated deaths in the United States, 1999–2007 *Clin Infect Dis* [Internet]. Oxford University Press; 2012 [cited 2018 Oct 24];55:216–23. Available from: <https://doi.org/10.1093/cid/cis386>
- Lessa FC, Mu Y, Bamberg WM, Beldavs ZG, Dumyati GK, Dunn JR, et al. Burden of *Clostridium difficile* Infection in the United States. *N Engl J Med* [Internet]. Massachusetts Medical Society ; 2015 [cited 2018 Oct 24];372:825–34. Available from: <https://doi.org/10.1056/NEJMoal408913>
- Owens, Jr. RC, Donskey CJ, Gaynes RP, Loo VG, Muto CA. Antimicrobial-associated risk factors for *Clostridium difficile* infection. *Clin Infect Dis* [Internet]. Oxford University Press; 2008 [cited 2018 Oct 24];46:S19–31. Available from: <https://doi.org/10.1086/521859>
- Dial S, Delaney JAC, Barkun AN, Suissa S. Use of gastric acid-suppressive agents and the risk of community-acquired *Clostridium difficile* infection. *JAMA* [Internet]. American Medical Association; 2005 [cited 2018 Oct 24];294:2989. Available from: <https://doi.org/10.1001/jama.294.23.2989>
- Loo VG, Bourgault A-M, Poirier L, Lamothe F, Michaud S, Turgeon N, et al. Host and pathogen factors for *Clostridium difficile* infection and colonization. *N Engl J Med* [Internet]. Massachusetts Medical Society ; 2011 [cited 2018 Oct 24];365:1693–703. Available from: <https://doi.org/10.1056/NEJMoal012413>
- Rodemann JF, Dubberke ER, Reske KA, Seo DH, Stone CD. Incidence of *Clostridium difficile* infection in inflammatory bowel disease. *Clin Gastroenterol Hepatol* [Internet]. W.B. Saunders; 2007 [cited 2018 Oct 24];5:339–44. Available from: <https://www.sciencedirect.com/login.ezproxy.library.ualberta.ca/science/article/pii/S1542356506013255>
- Bishara J, Farah R, Mograbi J, Khalaila W, Abu-Elheja O, Mahamid M, et al. Obesity as a risk factor for *Clostridium difficile* infection. *Clin Infect Dis* [Internet]. Oxford University Press; 2013 [cited 2018 Oct 29];57:489–93. Available from: <https://doi.org/10.1093/cid/cit280>
- Mulki R, Baumann AJ, Alnabelsi T, Sandhu N, Alhamshari Y, Wheeler DS, et al. Body mass index greater than 35 is associated with severe *Clostridium difficile* infection. [cited 2018 Oct 29]; Available from: <https://doi.org/10.1111/apt.13832>
- Ley RE, Tumbaugh PJ, Klein S, Gordon JI. Human gut microbes associated with obesity. *Nature* [Internet]. Nature Publishing Group; 2006 [cited 2018 Oct 29];444:1022–3. Available from: <http://www.nature.com/articles/4441022a>
- Armougom F, Henry M, Vialettes B, Raccach D, Raoult D. Monitoring bacterial community of human gut microbiota reveals an increase in lactobacillus in obese patients and methanogens in anorexic patients. *PLoS One* [Internet]. Public Library of Science; 2009 [cited 2018 Oct 29];4:e7125. Available from: <https://doi.org/10.1371/journal.pone.0007125>
- Courcoulas AP, Christian NJ, Belle SH, Berk PD, Flum DR, Garcia L, et al. Weight change and health outcomes at 3 years after bariatric surgery among individuals with severe obesity. *JAMA* [Internet]. American Medical Association; 2013 [cited 2018 Oct 29];310:2416–25. Available from: <https://doi.org/10.1001/jama.2013.280928>
- Christou N V, Sampalis JS, Liberman M, Look D, Auger S, McLean APH, et al. Surgery decreases long-term mortality, morbidity, and health care use in morbidly obese patients. *Ann Surg* [Internet]. Lippincott, Williams, and Wilkins; 2004 [cited 2018 Oct 29];240:416–23; discussion 423–4. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/15319713>
- Escobar-Morreale HF, Botella-Carretero JJ, Álvarez-Blasco F, Sancho J, San Millán JL. The polycystic ovary Syndrome associated with morbid obesity may resolve after weight loss induced by bariatric surgery. *J Clin Endocrinol Metab* [Internet]. Oxford University Press; 2005 [cited 2018 Oct 29];90:6364–9. Available from: <https://doi.org/10.1210/jc.2005-1490>
- Angrisani L, Santonicola A, Iovino P, Vitiello A, Zundel N, Buchwald H, et al. Bariatric Surgery and Endoluminal procedures: IFSO Worldwide Survey 2014. *Obes Surg* [Internet]. Springer US; 2017 [cited 2018 Oct 29];27:2279–89. Available from: <https://doi.org/10.1007/s11695-017-2666-x>
- Tremaroli V, Karlsson F, Werling M, Ståhlman M, Kovatcheva-Datchary P, Olbers T, et al. Roux-en-Y Gastric bypass and vertical banded gastroplasty induce long-term changes on the human gut microbiome contributing to fat mass regulation. *Cell Metab* [Internet]. Elsevier; 2015 [cited 2018 Oct 29];22:228–38. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/26244932>
- Liu R, Hong J, Xu X, Feng Q, Zhang D, Gu Y, et al. Gut microbiome and serum metabolome alterations in obesity and after weight-loss intervention. *Nat Med* [Internet]. Nature Publishing Group; 2017 [cited 2018 Oct 29];23:859–68. Available from: <https://doi.org/10.1038/nm.4358>
- Murphy R, Tsai P, Jüllig M, Liu A, Plank L, Booth M. Differential changes in gut microbiota after gastric bypass and sleeve gastrectomy bariatric surgery vary according to diabetes remission. *Obes Surg* [Internet]. Springer US; 2017 [cited 2018 Nov 7];27:917–25. Available from: <https://doi.org/10.1007/s11695-016-2399-2>
- 2016 MBSAQIP Standards Manual [Internet]. Available from: <https://www.facs.org/quality-programs/mbsaqip/standards>
- StataCorp. *Stata* (2015) *Stata* statistical software: release 14. LP, College Station, TX;
- Sjöström L. Review of the key results from the Swedish obese subjects (SOS) trial—a prospective controlled intervention study of bariatric surgery. *J Intern Med*. 2013;273:219–34.
- Hussan H, Ugbarugba E, Bailey MT, Porter K, Needleman B, Noria S, et al. The impact of bariatric surgery on short term risk of *Clostridium difficile* admissions. *Obes Surg* [Internet]. Springer US; 2018 [cited 2018 Oct 24];28:2006–13. Available from: <https://doi.org/10.1007/s11695-018-3131-1>
- Leung J, Burke B, Ford D, Garvin G, Korn C, Sulis C, et al. Possible association between obesity and *Clostridium difficile* infection. *Emerg Infect Dis* [Internet]. Centers for Disease Control and Prevention; 2013 [cited 2018 Nov 7];19:1791–8. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/24188730>
- Rodrigues MA, Brady RR, Rodrigues J, Graham C, Gibb AP. *Clostridium difficile* infection in general surgery patients; identification of high-risk populations. *Int J Surg* [Internet]. Elsevier; 2010 [cited 2018 Oct 29];8:368–72. Available from: <https://www.sciencedirect.com/science/article/pii/S1743919110000828>
- David LA, Maurice CF, Carmody RN, Gootenberg DB, Button JE, Wolfe BE, et al. Diet rapidly and reproducibly alters the human gut

- microbiome. *Nature* [Internet]. Nature Publishing Group; 2014 [cited 2019 Jan 29];505:559–63. Available from: <http://www.nature.com/articles/nature12820>
25. Smith CD, Herkes SB, Behrns KE, Fairbanks VF, Kelly KA, Sarr MG. Gastric acid secretion and vitamin B12 absorption after vertical Roux-en-Y gastric bypass for morbid obesity. *Ann Surg* [Internet]. Lippincott, Williams, and Wilkins; 1993 [cited 2018 Nov 9];218:91–6. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/8328834>
 26. Anhe Msc FF, Varin T V, Schertzer JD, Marette PHdA The gut microbiota as a mediator of metabolic benefits after bariatric surgery. 2017 [cited 2018 Nov 9]; Available from: <https://doi.org/10.1016/j.jejd.2017.02.002>
 27. Forster AJ, Taljaard M, Oake N, Wilson K, Roth V, van Walraven C. The effect of hospital-acquired infection with *Clostridium difficile* on length of stay in hospital. *CMAJ* [Internet]. CMAJ; 2012 [cited 2018 Nov 12];184:37–42. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/22143235>
 28. Kumar SB, Hamilton BC, Wood SG, Rogers SJ, Carter JT, Lin MY. Is laparoscopic sleeve gastrectomy safer than laparoscopic gastric bypass? a comparison of 30-day complications using the MBSAQIP data registry. *Surg Obes Relat Dis* [Internet]. Elsevier; 2018 [cited 2018 Nov 12];14:264–9. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/29519658>
 29. Keddis MT, Khanna S, Noheria A, Baddour LM, Pardi DS, Qian Q. *Clostridium difficile* infection in patients with chronic kidney disease. 2012 [cited 2018 Nov 7]; Available from: <https://doi.org/10.1016/j.mayocp.2012.05.025>
 30. Barmparas G, Fierro N, Lamb AW, Lee D, Nguyen B, Tran DH, et al. *Clostridium difficile* increases the risk for venous thromboembolism. *Am J Surg* [Internet]. 2014 [cited 2018 Nov 7];208:703–9. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/25175741>
 31. Bhandari S, Mohammed Abdul MK, Dhakal B, Kreuziger LB, Saeian K, Stein D. Increased rate of venous thromboembolism in hospitalized inflammatory bowel disease patients with *clostridium difficile* infection. *Inflamm Bowel Dis* [Internet]. 2017 [cited 2018 Nov 7];23:1847–52. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/28837518>
 32. Maharshak N, Barzilay I, Zinger H, Hod K, Dotan I. *Clostridium difficile* infection in hospitalized patients with inflammatory bowel disease: prevalence, risk factors, and prognosis. *Medicine (Baltimore)* [Internet]. Wolters Kluwer Health; 2018 [cited 2019 Jan 30];97:e9772. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/29384868>
 33. Kistangari G, Lopez R, Shen B. Frequency and risk factors of *Clostridium difficile* infection in hospitalized patients with pouchitis. *Inflamm Bowel Dis* [Internet]. Oxford University Press; 2017 [cited 2018 Nov 8];23:661–71. Available from: <https://academic.oup.com/ibdjournal/article/23/4/661-671/4560767>
 34. Crabtree T, Aitchison D, Meyers BF, Tymkew H, Smith JR, Guthrie TJ, et al. *Clostridium difficile* in cardiac surgery: risk factors and impact on postoperative outcome. 2007 [cited 2018 Nov 8]; Available from: https://ac-els-cdn-com.login.ezproxy.library.ualberta.ca/S0003497506020960/1-s2.0-S0003497506020960-main.pdf?_tid=14925a0e-4001-4e35-a831-3166e8907cba&acdnt=1541662012_c9726724224e319eab8b731b5cc567c7