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Original article

Predictive factors of biliary complications after bariatric surgery

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Abstract

Background: Obesity and rapid weight loss are risk factors for gallstone development. Bariatric surgery and significant postoperative weight loss are associated with postoperative biliary complications.

Objective: We aim to identify predictive factors of biliary complications after bariatric surgery.

Setting: University hospital.

Methods: After Institutional Review Board approval, charts at a single institution were reviewed to identify patients with biliary complications after bariatric surgery from 2005 to 2012. Data collected included baseline patients demographic characteristics, perioperative parameters, and postoperative biliary complications. Parameters were analyzed using paired and unpaired Student *t* test for continuous variables and χ^2 test for categorical variables. Univariate and multivariate analyses were used to assess risk factors for complications after bariatric surgery. All tests were 2 tailed; results with $P < .05$ were considered statistically significant.

Results: One hundred thirty-eight (3.6%) of 3765 patients who underwent bariatric surgery developed postoperative biliary complications. Mean time from surgery to biliary complication was 1.8 ± 1.4 years. Complications included acute cholecystitis (18.1%), chronic cholecystitis (70.2%), acute pancreatitis (9.4%), choledocholithiasis (5.7%), and jaundice (2.8%). Interventions were laparoscopic (n = 134, 97.0%) and open (n = 1, .7%) cholecystectomy. Forty patients (28.9%) had known cholelithiasis before surgery. There were no mortalities. Univariate analysis identified female gender, age > 50, cholelithiasis at time of bariatric procedure, and Roux-en-Y gastric bypass independent of excess weight loss as predictive factors of biliary complications. Multivariate analysis confirmed advanced age as an independent predictive factor.

Conclusion: The results of our study suggest that patients of advanced age are at higher risk of biliary complications. However, the indications for prophylactic cholecystectomy at time of bariatric surgery remain unclear. (Surg Obes Relat Dis 2016;▮:00–00.)

Keywords: Postoperative complications; Bariatric surgery; Cholelithiasis

Obesity, defined as body mass index ≥ 30 kg/m^2, has more than doubled in the past 25 years, with close to half the U.S. population now defined as obese [1]. The treatment of obesity includes medical therapies such as behavioral therapy, pharmacotherapies, and dietary modification. However, numerous studies have found that bariatric surgery results in greater weight loss with higher remission rates of co-morbid conditions compared with nonsurgical management [2], and bariatric surgery has proved to be the most

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effective and durable treatment of obesity and related co-morbidities [3,4]. The most common surgical interventions are Roux-en-Y gastric bypass, sleeve gastrectomy, and adjustable gastric banding. Laparoscopic Roux-en-Y gastric bypass (LRYGB) remains the gold standard in bariatric surgery, and the number of LRYGB has almost tripled from 2003 to 2008 [5].

Obesity is a well-established risk factor for the development of gallstones [6]. However, the rapid weight loss associated with bariatric surgery also predisposes patients to cholelithiasis. This likely is due to mobilization of endogenous cholesterol during weight loss; decreased biliary motility secondary to reduced caloric intakes; and decreased secretion of cholecystokinin, especially in the setting of duodenal exclusion in gastric bypass or duodenal switch. The development of cholelithiasis after bariatric surgery has been reported to be as high as 71% [7] but is more commonly reported to be around 32%–42% [8]. Because of this, prophylactic cholecystectomy during gastric bypass was historically recommended in the era of open surgery [9]. The current management of gallbladder pathology remains a point of contention, ranging from prophylactic cholecystectomy, to cholecystectomy in the setting of biliary symptoms or presence of stones and sludge on preoperative or intraoperative ultrasound, to expectant management with or without ursodeoxycholic acid (Ursodiol). Because of the wide range of clinical practices and unclear implications of leaving a gallbladder in situ during bariatric surgery, we aimed to identify those patients who are most at risk of developing postoperative biliary complications in an effort to potentially guide preventative therapy.

Methods

After Institutional Review Board approval and following Health Insurance Portability and Accountability Act regulations, a historical cohort study was conducted using our prospectively maintained bariatric surgery registry. Those who underwent LRYGB, laparoscopic sleeve gastrectomy (LSG), laparoscopic adjustable gastric banding (LAGB), laparoscopic gastric plication (LGP), and revisional bariatric surgery without concomitant cholecystectomy from March 2005 to April 2012 at a single academic institution were included in this study. The electronic medical records of these patients were reviewed to identify those with postoperative biliary complications including acute pancreatitis (AP), choledocholithiasis, jaundice, acute cholecystitis, and chronic cholecystitis. Those patients who had previously undergone cholecystectomy (n = 169, 4.5%) were excluded from the study. Demographic data regarding presentation, symptomology, length of stay, complications, diagnostic workup, and therapeutic interventions were collected. This cohort of patients was matched and compared with a 1:1 cohort who underwent bariatric surgery without postoperative biliary complications. Matching was based on age, gender, body mass index (BMI) at time of surgery, type of procedure, and duration of follow-up. Parameters were analyzed using paired and unpaired Student t tests for continuous variables and χ^2 test for categorical variables. Univariate and multivariate analyses were used to assess the risk factors for complications after bariatric surgery. All tests were 2 tailed and results with a $P < .05$ were considered statistically significant.

Patients undergoing bariatric surgery at our institution undergo evaluation by a multidisciplinary team including evaluations by medical internists, psychiatrists, and nutritionists. Patients are counseled on preoperative cessation of tobacco and alcohol use. We routinely perform preoperative right upper quadrant (RUQ) ultrasound to evaluate for cholelithiasis and fatty liver disease. Patients with gallstones and biliary symptoms undergo simultaneous cholecystectomy at the time of bariatric surgery. Asymptomatic patients with stones do not typically undergo simultaneous cholecystectomy.

Postoperatively patients are evaluated at 1 week, 1 month, 3 months, 6 months, 9 months, 12 month, and 18 months after surgery, after which they are followed annually. Postoperative laboratory examinations are performed every 6 months and include complete blood cell count, complete metabolic profile, serum folate, serum iron and total iron binding capacity, vitamin D, vitamin B_{12}, vitamin B_1, and glycosylated hemoglobin (HbA1C). All patients are required to take postoperative multivitamins and antisecretory agents (most commonly famotidine); depending on surgeon preference, the majority is also prescribed Ursodiol for the first 6 months after surgery. Only patients with signs or symptoms concerning for biliary disease undergo postoperative RUQ ultrasonography.

Results

A total of 3765 patients underwent bariatric surgery at the Cleveland Clinic during the study period. These patients were followed for a mean of 20.28 ± 20.13 months. One hundred thirty-eight patients (3.8%) developed biliary complications after bariatric surgery. The mean age at time of bariatric surgery was 53.0 ± 12.0 years and the population had a male/female ratio of 1:3.6. The average number of co-morbidities, including diabetes, hypertension, hyperlipidemia, and obstructive sleep apnea, among patients before bariatric surgery was 3.4. The mean weight before bariatric surgery was 133.5 kg with mean initial excess weight of 64.7 ± 25.1 kg and mean BMI of 47.9 ± 8.4 kg/m^2. Mean initial excess weight loss was 64.7 ± 25.1 kg with percent excess weight loss (%EWL) of 72.2 ± 28.76%. The majority of patients underwent a Roux-en-Y gastric bypass (82.6%); the remainder had sleeve gastrectomy (8.5%), gastric banding (6.5%), revisional bariatric procedures (1.4%), and one gastric plication (0.7%). Of the patients

Table 1
Baseline characteristics of patients with biliary complications

Factor	(N = 138)
Age (mean)	53 ± 12
Gender	
Male	30, 21.7%
Female	108, 78.2%
Time from bariatric surgery to biliary procedure (mean)	1.8 ± 1.4 yr
Co-morbidities (mean)	3.4 ± 1.8
Type of bariatric surgery	
RYGB	114, 82.6%
SG	12, 8.6%
LAGB	9, 6.5%
Revisional	2, 1.4%
GP	1, .7%
Ursodiol prophylaxis	
Yes	103, 74.6%
No	35, 25.3%
Gallstones before surgery	
Yes	40, 28.9%
No	96, 69.5%

GP = gastric plication; LAGB = laparoscopic adjustable gastric banding; RYGB = Roux-en-Y gastric bypass; revisional = revisional bariatric surgery; SG = sleeve gastrectomy.

who developed biliary complications, the majority (74.6%) was prescribed Ursodiol prophylaxis at 300 mg 3 times daily; the remainder (25.3%) was not. A description of patients who developed biliary complications is summarized in Table 1.

The majority of biliary complications after bariatric surgery were chronic and acute cholecystitis (70.2% and 18.1%, respectively). Other complications were biliary pancreatitis or jaundice (12.2%) and choledocholithiasis (5.7%). All of the 138 patients who developed biliary complications required operative intervention, namely cholecystectomy. The majority of cholecystectomies were completed laparoscopically (97%; n = 134) with a conversion rate of 4.3% (n = 6); 1 patient underwent open cholecystectomy without laparoscopic exploration (0.7%). Six patients (4.3%) underwent common bile-duct exploration with sludge or stone extraction, and 1 patient (0.7%) underwent intraoperative endoscopic retrograde cholangiopancreatography (ERCP). Final pathologic examinations of gallbladder specimens revealed chronic cholecystitis (74.6%), acute cholecystitis (7.2%), gangrenous cholecystitis (2.8%), cholelithiasis (10.8%), and cholesterolosis (0.7%). Three patients had normal gallbladder specimens (2.1%), and 2 specimens were not available for review at our institution (1.4%). Mean length of hospital stay after cholecystectomy was 1.5 days. There were no mortalities in our series. Outcomes of patients who developed biliary complications are summarized in Table 2. As outlined in Table 3, univariate analysis revealed the presence of preoperative gallstones, advanced age, female gender, undergoing RYGB, and preoperative diabetes as predictive factors of postoperative biliary complications. Mutivariate analysis was then performed for the 2 most prevalent postoperative biliary complications (chronic cholecystitis and pancreatitis), which revealed advanced age, defined as age >50 years, as an independent predictive factor of acute pancreatitis and chronic cholecystitis, as shown in Table 4.

Table 2
Outcomes of patients with biliary complications

Factor	(N = 138)
Type of biliary complication	
Pancreatitis	13 (9.4%)
Choledocholithiasis	8 (5.7%)
Jaundice	4 (2.8%)
Acute cholecystitis	25 (18.2%)
Chronic cholecystitis	97 (70.2%)
Imaging findings at time of complication	
No findings	12 (8.6%)
Gallstones	85 (61.5%)
Sludge	32 (23.1%)
Choledocholithiasis	6 (4.3%)
Sludge and stones	3 (2.1%)
Gallbladder pathologic conditions	
Normal	3 (2.1%)
Cholesterolosis	1 (0.7%)
Acute cholecystitis	10 (7.2%)
Chronic cholecystitis	103 (74.6%)
Gangrenous cholecystitis	4 (2.8%)
Cholelithiasis	10.8%)
Missing specimen	2 (1.4%)
Type of biliary intervention	
LC	89 (64.4%)
LC with IOC	45 (32.6%)
OC	1 (0.7%)
Conversion rate from laparoscopic to open	6 (4.3%)
Intraoperative ERCP	1 (0.7%)
Operative time (min)	86.0 ± 47.1
Length of hospital stay (d)	1.5 ± 1.8

ERCP = endoscopic retrograde cholangiopancreatography; IOC = intraoperative cholangiogram; LC = laparoscopic cholecystectomy; OC = open cholecystectomy.

Table 3
Univariate analysis of postoperative biliary complications

Factor	Biliary Complication	Control	*P*
Age (yr)	53.0	45.8	.000002
Diabetes (%)	21.0	47.8	<.05
Gallstones (%)	28.9	9.4	<.05
RYGB (%)	82.6	74.6	<.05
Female (%)	78.2	68.1	.055436
Ursodiol (%)	74.6	68.8	.28
SG (%)	8.6	10.8	.54
BMI (kg/m^2)	47.9	47.3	.62

BMI = body mass index; RYGB = Roux-en-Y gastric bypass; SG = sleeve gastrectomy.

Discussion

Obesity and rapid weight loss are both associated with an increased incidence of gallbladder pathology [10]. The risk

Table 4
Multivariate analysis of predictive factors of chronic cholecystitis and acute pancreatitis

	Standard error	*t* Stat	*P*
Age	.002	2.28	.02
RYGB	.29	–1.32	.19
BMI preop	.004	–.77	.44
Preop stones	.07	.59	.57
Urdodiol	.08	–.23	.82
Gender	.08	–.21	.83
Diabetes	.08	–.04	.97

BMI = body mass index; preop = preoperative; RYGB = Roux-en-Y gastric bypass.

of gallstone formation is increased 8-fold in patients with BMI >40 kg/m^2 [11,12]. The development of cholelithiasis after rapid weight loss is due to mobilization of the body's store of cholesterol. Supersaturation of bile due to relative increase in proportion of cholesterol compared with solubilizing bile salts and phosphatidylcholine molecules prevents complete micellar solubilization of cholesterol, resulting in precipitation of cholesterol crystals and subsequent stone formation. The gastrointestinal hormone cholecystokinin causes significant gallbladder emptying of up to 70%–80% of fasting volumes [13]; duodenal exclusion after gastric bypass may thus contribute to gallstone formation. Division of the hepatic branch of the left vagus nerve during dissection of the lesser curvature may also result in decreased gallbladder contractility [10].

The average annual rate of all gallstone disease in the general population is reported to be .11%, with a rate of acute cholecystitis of .08%, acute biliary pancreatitis of .019%, and acute cholangitis of .007% [14]. The rate of biliary complications in the bariatric population is higher [11], and in our population, 3.4% developed cholecystitis, .36% developed acute biliary pancreatitis, and .22% developed choledocholithiasis (Table 1).

The current management of gallbladder pathologic conditions remains a point of contention in the field of bariatric surgery and ranges from expectant to prophylactic cholecystectomy at time of bariatric surgery. Our institution performs concurrent cholecystectomy only in the setting of symptomatic gallbladder disease. The use of ursodeoxycholic acid, or Ursodiol, was initially found to reduce the incidence of postoperative gallstone formation from 32% with placebo to as low as 2% [11,15]. However, some subsequent studies have reported that Ursodiol has not been found to reduce incidence of gallstones [8,16]. Given that other studies show statistically significant difference in the rate of postoperative cholecystitis in those who complete their course of Ursodiol compared with those who do not, this discrepancy may be due to compliance [17]. Similarly, our univariate and multivariate analyses did not find a significant difference in the rate of biliary complications in patients based on postoperative Ursodiol use. However, we did not collect data on patient compliance with Ursodiol use.

Other centers perform concomitant cholecystectomy at time of bariatric surgery in the presence of symptomatic cholelithiasis confirmed with preoperative imaging [16,18]. The popularity of prophylactic cholecystectomy, which peaked in 2000 with rates close to 30%, has waned in the age of laparoscopic bariatric surgery to rates $<10\%$ [5,19]. Some studies found increased rates of postoperative complications with concomitant cholecystectomy [10,11], whereas others have failed to find differences in rates of both intraoperative and postoperative complications [19,20]. Studies on length of stay with combined surgery are conflicting, with some finding increased hospital stays [19,20], whereas others fail to find that it does not prolong hospitalization [18,21]. However, in a recent study, the largest group of gastric bypass patients undergoing concomitant cholecystectomy was reported. This found an overall decreased mortality rate as well as decreased long-term complications with concomitant cholecystectomy. Because of the increased incidence of complications with postoperative cholecystectomy after gastric bypass, this group encouraged concomitant cholecystectomy at the time of the bariatric procedure [17].

Given the wide range of practices as well as the conflicting evidence about the risks associated with both concomitant cholecystectomy and postoperative symptomatic cholecystectomy, it would be beneficial to develop a more accurate understanding of which patients will likely require cholecystectomy in the future, thus improving surgical decision making and informed patient consent. In prior studies, age, sex, and preoperative BMI have not been found to significantly affect postoperative development of symptomatic cholelithiasis [7,8,22,23]. Li found that a weight loss of $>25\%$ of preoperative weight was significantly associated with the development of symptomatic gallstones [22]. Similarly, D'Hondt found that a $>50\%$ EWL at 3 months doubles the risk of postoperative cholecystectomy [23]. Other studies have not found significant difference between EWL% and development of cholelithiasis [7,12], and our study confirms that EWL% is not predictive of postoperative complications. On multivariate analysis, age was the only independent predictive factor of postoperative biliary complications. However, given the altered gastrointestinal anatomy after RYGB and associated difficulty in the ability to perform ERCP [24], special consideration may be given to the patient undergoing RYGB in discussing the role of concomitant cholecystectomy. In addition, at our institution we routinely perform preoperative right upper quadrant (RUQ) ultrasounds. However, we offer concomitant cholecystectomy to symptomatic patients only. Given that our analysis did not find an association between the presence of preoperative gallstones and postoperative biliary complications, we suggest that preoperative RUQ ultrasound be reserved for

those patients who report symptoms concerning for biliary pathologic conditions. These findings may help guide preoperative planning as well as the informed consent process in patients with advanced age.

Strengths of this study are that this includes a large cohort of patients maintained in a prospective database of all who undergo bariatric surgery at the Cleveland Clinic. Limitations include that this is a retrospective analysis from a single institution, possibly introducing bias inherent in retrospective analyses and potentially missing patients who sought care or underwent interventions at other institutions. However, the large number of patients enrolled and the high compliance of long-term follow up (a mean of 20.28 mo) are both strengths of the analysis.

Conclusion

The incidence of biliary complications after bariatric surgery is higher than in the general population, likely because of both obesity and rapid weight loss. We identify advanced age as an independent predictive factor in the development of biliary complications. This may help guide preoperative conversations with patients about the risk of future cholecystectomy and guide discussions about concomitant cholecystectomy in those with identified risk factors, particularly in patients undergoing RYGB with resultant altered anatomy precluding endoscopic access to the biliary system.

Disclosures

The authors have no financial disclosures or conflicts of interest.

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