Pattern of Biliary Disease Following Laparoscopic Sleeve Gastrectomy in Adolescents

Jun Tashiro, Arunachalam A. Thenappan, and Evan P. Nadler

Objective: The use of laparoscopic sleeve gastrectomy (LSG) has risen steadily as a treatment for adolescents with obesity. This study determined whether obstructive biliary complications after rapid, LSG-related weight loss occur similarly in adolescents compared with adults.

Methods: Between 2010 and 2019, 309 patients underwent LSG. Demographics and clinical factors, including pre- and perioperative BMI and weight changes, were included.

Results: Overall, 21 patients (7%) had post-LSG biliary disease (BD), of whom 13 presented with acute pancreatitis (AP) and 8 with biliary colic. No differences existed between those with BD ($n = 21$) and the remaining cohort ($n = 288$). Patients with BD were 16.3 (SD 2.4) years of age at LSG, with a preoperative BMI of 49.3 (SD 6.7) kg/m^2. Preoperative excess BMI loss was 7.1% (SD 11.3%). An ultrasound revealed gallstones (71%) and sludge or crystals (12%). Eighteen patients underwent cholecystectomy between 4 weeks and 29 months after LSG.

Conclusions: Pediatric patients present with BD at a similar rate after LSG compared with adults. The majority of adolescents, however, manifest with AP. Thus, pancreatitis should be high on the differential diagnosis list when evaluating post-LSG abdominal symptoms. Additional studies are warranted to elucidate the pathophysiology of post-LSG AP for prevention in the future because its etiology may or may not be solely related to BD.

Obesity (2019) **27**, 1750-1753. doi:10.1002/oby.22634

Introduction

Obesity is a public health epidemic for children and adolescents in the United States. An estimated one-third of children suffer from obesity; furthermore, up to 29% have obesity-related complications, including high triglyceride levels, hypertension, and early-onset diabetes (1,2). Although behavior modifications, including a regimented diet and exercise program, remain the mainstay of any multidisciplinary weight loss program, laparoscopic sleeve gastrectomy (LSG) has been demonstrated to be a useful adjunct for weight loss when other modalities fail. Early experience with LSG in adolescents has revealed excess weight loss of approximately 40% in the first year postoperatively and has also validated its overall safety for children and adolescents with obesity (3,4).

Biliary complications, such as biliary colic (BC) and cholecystitis, have been reported as a frequent postoperative complication for adult patients undergoing metabolic surgery (5,6). As a result, prophylactic cholecystectomy has been suggested in some patients with demonstrated gallstone disease in an effort to prevent postoperative complications (5). Acute pancreatitis (AP), although rare, has also been reported following metabolic surgical procedures (5). Whereas some have suggested a purely obstructive etiology for AP, others have promoted the possibility of post-LSG metabolic shifts or technical factors contributing to its development (6-8). Most of these analyses have been performed in adults; however, younger age groups may suffer different types of biliary complications, possibly related to a higher sensitivity to changes in physiology (6,9).

In this study, we sought to determine whether obstructive biliary complications after LSG and its incumbent rapid weight loss occur similarly in adolescents as seen in adults. To date, AP has not been studied as a complication of LSG performed in children and adolescents. Thus, our secondary goal was to determine its frequency and whether any variables could predict its occurrence.

Methods

All patients who underwent LSG at Children's National Hospital in Washington, DC, from January 2010 to April 2019 were entered prospectively into our institutional review board–approved adolescent metabolic surgery database. Measures maintained in the database

Division of Pediatric Surgery, Children's National Health System, Washington, DC, USA. Correspondence: Evan P. Nadler (enadler@childrensnational.org)

Disclosure: EPN is paid by W.L. Gore & Associates, Inc., to train those interested in building adolescent weight loss surgery programs. The other authors have no financial affiliations to disclose.

Received: 4 June 2019; **Accepted:** 30 July 2019; **Published online 5 November 2019. doi:10.1002/oby.22634**

included age, weight and BMI (initial, preoperative, day of surgery, and postoperative), laboratory values, and ultrasound findings. Only patients with symptoms suggestive of BC underwent ultrasound assessment of the right upper quadrant prior to their sleeve gastrectomy. Percentage of excess weight loss (%EWL) was calculated as the ratio of the weight lost between time points over the total excess weight. Percentage of excess BMI loss (%EBMIL) was calculated as a ratio of the change in BMI over the initial BMI minus 25, thereby accounting for normal weight BMI.

Our program consists of two independent teams working in conjunction prior to surgery. The multidisciplinary medical weight management team consists of pediatricians, nurse practitioners, child psychologists and psychiatrists, dietitians, and health educators. The surgical team consists of pediatric surgeons, nurse practitioners, and child psychologists as well. To be deemed eligible for sleeve gastrectomy, patients (1) must have a history of obesity for 3 years or more, (2) must have attempted other weight loss programs without success, and (3) must have BMI greater than 35 kg/m^2 with an obesity-related condition or a BMI greater than 40 kg/m^2 without an obesity-related condition. Patients were excluded (1) if they were deemed unable to understand the lifelong dietary commitment after surgery, (2) if they were deemed unable to comply with the requirements of follow-up visits and diagnostic testing, or (3) if there was an untreated mental health disorder.

Prior to surgery, all patients underwent a standard 2-week protein-sparing modified fast. LSG was performed via five incisions, and a 40-French bougie was used for remnant size calibration prior to resection. An absorbable polymer buttress was used for stapling (W.L. Gore & Associates, Inc., Newark, Delaware). Standard postoperative care included the initiation of sugar-free clear liquids on postoperative day 1. Patients were discharged when adequate hydration goals were met. A liquid diet was continued for the first 2 weeks, then patients were guided to a gradual advancement in food texture over the first 3 months. Patients were instructed to return to the clinic for evaluation 2 to 3 weeks after surgery, and then every 3 months for the first year postoperatively, every 6 months in the second year after surgery, and then yearly thereafter. Outcomes measured at each visit included weight loss, food tolerance, and changes in health status.

We screened each patient for biliary symptoms during the history and physical examination for the initial assessment process; if results were positive, a right upper quadrant ultrasound was performed. If a preoperative ultrasound confirmed gallstones, patients were offered a concurrent cholecystectomy. Those with a cholecystectomy prior to LSG were excluded from this study. To define pancreatitis in our cohort, the primary diagnostic criteria were clinical signs and symptoms of pancreatitis, with elevated amylase and/or lipase levels. We defined BC as intermittent epigastric or right upper quadrant pain or tenderness coupled with ultrasound findings of gallstones or sludge, without abnormalities in liver enzyme levels. Pathologic criteria for chronic cholecystitis included chronic inflammation, granulomas, and smooth muscle hypertrophy on pathologic review. Categorical variables were compared using χ^2 or Fisher exact tests when the expected value of any cell was less than five. Continuous variables were compared using Student *t* tests for normally distributed data or Mann-Whitney *U* tests if the data were skewed. All statistical analyses were performed using SPSS Statistics, version 21.0 (IBM Corp., Armonk, New York).

Results

After excluding those with previous or concurrent cholecystectomy, our cohort numbered 309 patients, of whom 227 (74%) were girls. Overall, the mean age at LSG was 17.0 (SD 2.4) years, with an initial weight and BMI of 139 (SD 28) kg and 49.9 (SD 8.9), respectively. Follow-up compliance at 3, 6, and 12 months was 83.7%, 63.7%, and 51.0%, respectively. However, patients from out of the region often received telephone follow-up alone, which might have impacted these percentages. Patients experienced significant weight loss between the initial evaluation and 3 and 6 months postoperatively. At 3 months, %EBMIL was 37.5% (SD 15.3%); at 6 months, it was 50.1% (SD 19.4%). Additional weight loss characteristics are included in Table 1.

Within the study period, 21 patients, 18 (86%) of whom were girls, were found to have biliary disease (BD) after LSG. When comparing patients with BD ($n = 21$) with the remaining overall cohort ($n = 288$), there were no differences in any of the parameters assessed. These included age, sex, and preoperative and operative weight and BMI, along with weight loss measures, including %EBMIL and %EWL in the preoperative (last clinic visit to day of operation) and perioperative (last clinic visit to 3-month follow-up) periods. Additional details on the comparative analysis are shown in Table 2.

Of the patients presenting with BD, 13 presented with AP, whereas 8 presented with BC. Comparing patients who presented with these conditions did not reveal any differences, although preoperative weight trended toward significance and was lower in the AP group. For patients with AP, a right upper quadrant abdominal ultrasound revealed seven (54%) with gallstones and two (15%) with sludge or crystals, and the four remaining had normal imaging. All patients with BC had gallstones on ultrasound. The 18 patients with positive ultrasound findings underwent subsequent cholecystectomy without complication. The mean interval between LSG and cholecystectomy was 8.93 (7.44) months. A total of three patients (0.97%) underwent a

TABLE 1 Cohort characteristics of children and adolescents who underwent LSG, 2010-2019 ($N = 309$)

	Results
Age at LSG, y	17.0 ± 2.4
Female sex, *n* (%)	227 (73.5)
Initial weight, kg	138.6 ± 28.4
Initial BMI	49.9 ± 8.9
Operative weight, kg	132.9 ± 27.9
Operative BMI	48.1 ± 9.0
ΔBMI at 3 months	8.5 ± 2.6
ΔBMI at 6 months	11.3 ± 3.3
%EBMIL at 3 months	37.5 ± 15.3
%EBMIL at 6 months	50.1 ± 19.4
%EWL at 3 months	31.7 ± 11.8
%EWL at 6 months	42.0 ± 14.7

Values presented as mean ± SD unless otherwise specified. Initial presentation values at 3- or 6-month postoperative follow-up. All analyses limited to available data.
LSG, laparoscopic sleeve gastrectomy; ΔBMI, change in BMI; %EBMIL, percentage of excess BMI loss; %EWL, percentage of excess weight loss.

TABLE 2 Comparative analysis of children and adolescents who underwent sleeve gastrectomy and presented with and without biliary disease (BD), 2010-2019 (*N* = 309)

	BD, *n* = 21	No BD, *n* = 288	*P value*
Age at LSG, y	16.3 ± 2.4	17.1 ± 2.4	0.172
Female sex, *n* (%)	18 (85.7)	209 (72.5)	0.188
Preoperative weight, kg	137.4 ± 21.1	137.4 ± 28.4	0.989
Preoperative BMI	49.3 ± 6.7	49.6 ± 11.5	0.923
Operative weight, kg	132.8 ± 23.0	133.4 ± 28.2	0.932
Operative BMI	48.1 ± 6.65	48.1 ± 9.1	0.973
Preoperative ΔBMI	2.08 ± 3.81	1.71 ± 7.15	0.836
Perioperative ΔBMI	8.85 ± 4.24	8.11 ± 3.76	0.455
Preoperative %EBMIL	7.1 ± 11.3	5.4 ± 19.8	0.719
Perioperative %EBMIL	37.8 ± 17.3	36.5 ± 17.9	0.787
Preoperative %EWL	8.9 ± 10.5	6.0 ± 13.2	0.371
Perioperative %EWL	31.2 ± 13.5	30.6 ± 16.0	0.889

Values presented as mean ± SD unless otherwise specified. Preoperative refers to period from last clinic visit approximately 1 month before operation to operative date. Perioperative refers to period from last clinic visit approximately 1 month before operation to 3-month postoperative follow-up. All analyses limited to available data.
LSG, laparoscopic sleeve gastrectomy; ΔBMI, change in BMI; %EBMIL, percentage of excess BMI loss; %EWL, percentage of excess weight loss.

TABLE 3 Comparative analysis of children and adolescents who underwent sleeve gastrectomy and presented with biliary colic (BC) and acute pancreatitis (AP), 2010-2019 (*N* = 21)

	AP, *n* = 13	BC, *n* = 8	*P value*
Age at LSG, y	16.1 ± 2.6	16.7 ± 1.9	0.532
Female sex, *n* (%)	11 (84.6)	7 (87.5)	0.854
Preoperative weight, kg	131.1 ± 19.2	152.6 ± 19.1	0.053
Preoperative BMI	47.9 ± 6.0	52.8 ± 7.7	0.176
Operative weight, kg	128.6 ± 22.1	141.3 ± 23.7	0.228
Operative BMI	46.7 ± 5.5	50.3 ± 8.1	0.246
Preoperative ΔBMI	2.26 ± 4.22	1.68 ± 2.96	0.782
Perioperative ΔBMI	9.57 ± 4.51	7.26 ± 3.52	0.330
Preoperative %EBMIL	7.7 ± 11.8	5.7 ± 11.1	0.746
Perioperative %EBMIL	42.2 ± 16.9	28.2 ± 15.7	0.139
Preoperative %EWL	8.8 ± 11.1	9.2 ± 10.3	0.954
Perioperative %EWL	33.3 ± 13.9	26.5 ± 12.6	0.368

Values presented as mean ± SD unless otherwise specified. Preoperative refers to period from last clinic visit approximately 1 month before operation to operative date. Perioperative refers to period from last clinic visit approximately 1 month before operation to 3-month postoperative follow-up. All analyses limited to available data.
LSG, laparoscopic sleeve gastrectomy; ΔBMI, change in BMI; %EBMIL, percentage of excess BMI loss; %EWL, percentage of excess weight loss.

concurrent cholecystectomy for ultrasound-confirmed gallstones and biliary symptoms on the preoperative assessment. On the final pathology report, most cholecystectomy specimens (89%) revealed chronic cholecystitis. Additional details are provided in Table 3.

Discussion

Overall, LSG remains a safe and effective surgical weight loss option in children and adolescents despite the findings of AP and BC in our cohort. Prior reports in the adult metabolic surgery population have shown that symptomatic cholelithiasis occurs at a rate of 8% and that AP occurs at a rate of 0.21% to 1.04% (5,6,10). When comparing the 6-month interval between the pre- and postprocedure periods, Hussan et al. (6) demonstrated that adults who underwent LSG had high odds (5.2 times greater) of developing AP. When directly comparing metabolic surgery procedures, the same analysis revealed that those who underwent LSG had 2.3 times higher odds of developing AP compared with those who underwent Roux-en-Y gastric bypass (RYGB) (6). On analyzing our single-center experience, we found that AP was the prominent postoperative complication of LSG in our child and adolescent population rather than the BC and cholecystitis symptoms reported in adults (10). In the Teen-Longitudinal Assessment of Bariatric Surgery (Teen-LABS) study, investigators reported an incidence of AP of 0.6% occurring in their patients who underwent RYGB and no incidence in their patients who underwent LSG 3 years after initial surgery (11). Our data are more consistent with the adult data, although our rate of AP is higher, which may be explained by our sole use of LSG or by our cohort's younger age at the time of metabolic surgery.

For patients with diagnosed gallstone disease, a direct association with AP has often been suggested. Adults with known gallstone disease have the highest risk (85 times greater odds) of developing AP after LSG compared with those without gallstone disease (6). Additionally, cholecystokinin reaches higher postprandial levels in patients after LSG compared with those after RYGB; increased sensitivity to its release has been proposed as an explanation for gallstone-related AP, particularly in younger patients (6,12). These results provide persuasive evidence for offering prophylactic cholecystectomy in patients with known gallstone disease (i.e., BC). The same analyses, however, also showed that AP can occur in patients without overt BD (6). Therefore, the theory that BD is the only prerequisite for the development of AP is not entirely complete and rather suggests a potential for additional etiologies. Although not included in these data, we trialed the administration of ursodiol at the time of LSG to prevent postoperative biliary complications. Prior studies in the adult population have supported its use for this indication (13,14). However, after initiation of ursodiol therapy two patients returned in the early postoperative period with pancreatitis, and therefore we abandoned this strategy.

Three patients in this cohort presented with AP and no signs of gallbladder pathology (sludge or stones) on ultrasound, as did the two patients who returned with AP after our ursodiol strategy was initiated. These patients were not offered cholecystectomy. Kumaravel et al. (5) reported that among 28 patients with AP after metabolic surgery, only 28% had definite gallstone-related disease; meanwhile, 39% had AP of unknown etiology. This finding is significant because it promotes the possibility of a post-LSG metabolic shift as another contributor to AP. Pancreatic hormone levels, for example, were shown to undergo dramatic shifts in the immediate postoperative period following LSG, different from those affected after RYGB (7). Thus, pancreatic endocrine and exocrine function may undergo significant alteration after LSG, creating an environment that leads to AP when combined with local inflammation from the procedure. However, this theory is merely speculative.

The rapidity of weight loss after metabolic surgery has been proposed as another potential actor in the development of AP. Kumaravel et al. (5) reported %EWL>5% at the first follow-up being associated with a higher rate of AP on a univariate analysis; on a multivariate analysis, however, this variable did not remain significant. This finding could be suggestive of a relationship between the rate of weight loss and metabolic shifts promoting AP. %EBMIL and %EWL in the month leading up to the procedure and in the perioperative period were not found to be independent predictors of BD in general or of AP versus BC in our study. We understand, however, that this analysis is limited by its relatively low numbers of patients affected.

A final, albeit theoretical, promotor of AP is the splenic infarction during the ligation of the short gastric vessels during LSG. Some authors believe that splenic infarction and secondary infection and resultant inflammation could add to the development of AP, primarily because of the poor collateral circulation in the area (8,15). Splenic vein thrombosis due to pancreatitis is much more common (8). Regardless, the surgeon should take care when dividing these attachments to reduce the risk of compromising splenic perfusion.

Although we draw on our considerable single-center experience with weight loss surgery in children and adolescents, there are limitations to this analysis. The single-center data set stipulates a selection bias, as our cohort is more ethnically diverse than other adolescent metabolic surgery cohorts because of our urban location; this very characteristic, however, allows for the thorough collection of data with high resolution. Another possible limitation is that some patients might have had a subclinical course of AP that did not require medical attention. Additionally, laboratory values reflecting changes in fatty acid metabolism were not consistently followed perioperatively or on presentation to the emergency department; therefore, these could not be analyzed to determine whether alterations had occurred after LSG. We focused our study, however, on clinically significant AP; we did not believe it to be prudent to perform surveillance measurement of lipase levels on patients without specific complaints.

We conclude that pancreatitis is a significant complication after LSG in the pediatric population and that it represents a larger proportion of potential biliary tract–related complications in children and adolescents compared with adults. Although the adult literature has presented several theories for the development of AP, we believe the cause to be from more than one etiology. Overall, our treatment approach to postoperative AP has been generally supportive, with bowel rest and parenteral nutritional support until the resolution of symptoms. Cholecystectomy was offered only when abnormal findings were present on ultrasound and when AP had resolved. Fortunately, none of our patients presenting with AP had severe or life-threatening complications. Thus, clinicians should be aware of AP on the differential diagnosis for younger patients presenting with nonspecific abdominal complaints, including pain, nausea, or dehydration, secondary to intolerance of oral intake. Future research should focus on delineating the alterations in metabolism associated within the immediate postoperative period and their effect on pancreatic dysfunction to help elucidate the cause of AP in patients without overt gallbladder stones, sludge, or crystals. **O**

References

1. Kumar S, Kelly AS. Review of childhood obesity: from epidemiology, etiology, and comorbidities to clinical assessment and treatment. *Mayo Clin Proc* 2017;92:251-265.
2. Skinner AC, Perrin EM, Moss LA, Skelton JA. Cardiometabolic risks and severity of obesity in children and young adults. *N Engl J Med* 2015;373:1307-1317.
3. Nadler EP, Barefoot LC, Qureshi FG. Early results after laparoscopic sleeve gastrectomy in adolescents with morbid obesity. *Surgery* 2012;152:212-217.
4. Speer AL, Parekh J, Qureshi FG, Nadler EP. Thirty-day outcomes for children and adolescents undergoing laparoscopic sleeve gastrectomy at a free-standing children's hospital. *Clin Obes* 2017;7:86-91.
5. Kumaravel A, Zelisko A, Schauer P, Lopez R, Kroh M, Stevens T. Acute pancreatitis in patients after bariatric surgery: incidence, outcomes, and risk factors. *Obes Surg* 2014;24:2025-2030.
6. Hussan H, Ugbarugba E, Porter K, et al. The type of bariatric surgery impacts the risk of acute pancreatitis: a nationwide study. *Clin Transl Gastroenterol* 2018;9:179. doi:10.1038/s41424-018-0045-0
7. Farey JE, Preda TC, Fisher OM, et al. Effect of laparoscopic sleeve gastrectomy on fasting gastrointestinal, pancreatic, and adipose-derived hormones and on non-esterified fatty acids. *Obes Surg* 2017;27:399-407.
8. Kalabin A, Mani VR, Mishra A, Depaz H, Ahmed L. Acute pancreatitis with splenic infarction as early postoperative complication following laparoscopic sleeve gastrectomy. *Case Rep Surg* 2017;2017:8398703. doi:10.1155/2017/8398703
9. Khalil T, Walker JP, Wiener I, et al. Effect of aging on gallbladder contraction and release of cholecystokinin-33 in humans. *Surgery* 1985;98:423-429.
10. Brockmeyer JR, Grover BT, Kallies KJ, Kothari SN. Management of biliary symptoms after bariatric surgery. *Am J Surg* 2015;210:1010-1016; discussion 1016-1017.
11. Inge TH, Zeller MH, Jenkins TM, et al; Teen-LABS Consortium. Perioperative outcomes of adolescents undergoing bariatric surgery: the Teen-Longitudinal Assessment of Bariatric Surgery (Teen-LABS) study. *JAMA Pediatr* 2014;168:47-53.
12. Peterli R, Steinert RE, Woelnerhanssen B, et al. Metabolic and hormonal changes after laparoscopic Roux-en-Y gastric bypass and sleeve gastrectomy: a randomized, prospective trial. *Obes Surg* 2012;22:740-748.
13. Adams LB, Chang C, Pope J, Kim Y, Liu P, Yates A. Randomized, prospective comparison of ursodeoxycholic acid for the prevention of gallstones after sleeve gastrectomy. *Obes Surg* 2016;26:990-994.
14. Miller K, Hell E, Lang B, Lengauer E. Gallstone formation prophylaxis after gastric restrictive procedures for weight loss: a randomized double-blind placebo-controlled trial. *Ann Surg* 2003;238:697-702.
15. Sarwal A, Khullar R, Sharma A, Soni V, Baijal M, Chowbey P. Acute pancreatitis as an unusual early post-operative complication following laparoscopic sleeve gastrectomy. *J Minim Access Surg* 2018;14:164-167.