OBES SURG
DOI 10.1007/s11695-017-2847-7

ORIGINAL CONTRIBUTIONS

Laparoscopic Sleeve Gastrectomy for Morbid Obesity in Patients After Orthotopic Liver Transplant: a Matched Case-Control Study

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Abstract

Introduction Obesity is frequently encountered in patients with orthotopic liver transplant (OLT). The role of bariatric surgery is still unclear for this specific population. The aim of this study was to review our experience with laparoscopic sleeve gastrectomy (LSG) after OLT.

Material and Methods We performed a retrospective case-control study of patients undergoing LSG after OLT from 2010 to 2016. OLT-LSG patients were matched by age, sex, body mass index (BMI), and year to non-OLT patients undergoing LSG. Demographics, operative variables, postoperative events, and long-term weight loss with comorbidity resolution were collected and compared between cases and controls.

Results Of 303 patients undergoing LSG, 12 (4%) had previous OLT. They were matched to 36 non-OLT patients. No difference was found between groups in the American Society of Anesthesiologists class, mean operative time, or postoperative morbidity. The non-OLT group, however, had a significantly shorter mean hospital stay than the OLT group (1.7 vs 3.1 days; $P < .001$). There were no conversions to open procedures. For patients with long-term follow-up, change in BMI after LSG was similar between the groups, but the non-OLT patients had significantly more excess body weight loss at 2 years (53.7 vs 45.2%; $P < .001$). Similar resolution of comorbid conditions was noted in both groups. LSG caused no changes in dosage of immunosuppressive medications, and no liver complications occurred.

Conclusion LSG after OLT in appropriately selected patients appears to have similar outcomes to LSG in non-OLT patients.

Keywords Bariatric surgery · Laparoscopic sleeve gastrectomy · Orthotopic liver transplant

Abbreviations

BMI	body mass index
EBWL	excess body weight loss
LSG	laparoscopic sleeve gastrectomy
NASH	non-alcoholic steatohepatitis
OLT	orthotopic liver transplant
RYGB	Roux-en-Y gastric bypass

Introduction

Obesity had reached epidemic conditions [1]. Nearly half of the US population matches criteria for obesity [2, 3]. The rates of obesity and obesity-related comorbid conditions are increasing in patients with complex and complicated medical conditions [4, 5]. Bariatric surgery has resulted in effective weight loss and resolution or improvement of comorbid conditions in patients with morbid obesity [6]. Because of the increasing safety and efficacy of obesity surgery, more patients with complex conditions are being referred to bariatric teams for operative treatment [4].

Patients with end-stage liver disease are greatly affected by the obesity epidemic, with the liver disease as either the primary cause or a contributing factor [7]. Obesity-related liver disease, non-alcoholic steatohepatitis (NASH), is becoming a more frequently encountered indication for liver transplant.

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Published online: 01 August 2017

NASH is present in 9.7 to 47.5% of patients undergoing orthotopic liver transplant (OLT) and will become the most common indication for liver transplant in the next decade [8, 9]. In addition, immunosuppressive therapy, fewer post-OLT dietary limitations, and decreased physical activity contribute to excessive weight gain after OLT. Consequently, metabolic syndrome—obesity, hypertension, hyperglycemia, and dyslipidemia—have negative effects on early graft and patient survival [10–12].

Non-operative treatment of severe obesity rarely achieves permanent weight reduction [13]. If non-operative weight loss management fails, metabolic surgery should be considered [14]. The literature is limited regarding the outcomes of weight-loss surgery after OLT. Open sleeve gastrectomy for obesity after OLT was described in 2007 because of potential intraoperative technical difficulties associated with minimally invasive surgery [15]. Lazzati et al. [1] considered bariatric operations after liver transplant to be technically challenging with higher morbidity than in the non-transplant population; consequently, half of all reported cases of bariatric surgery after solid organ transplant underwent open sleeve gastrectomy. Few studies have investigated the use of laparoscopic sleeve gastrectomy (LSG) as treatment option for patients after OLT [15–18]. However, no comparison study of outcomes after sleeve gastrectomy exists in the literature in OLT and non-OLT patients. The goal of our study was to report the experience at a single institution with post-OLT patients undergoing LSG for morbid obesity and to compare outcomes after LSG between OLT and non-OLT patients.

Methods

Patient Selection

We retrospectively searched for the records of patients undergoing LSG at our institution between July 1, 2010, and December 31, 2016, and 12 were found to have previous OLT. We also identified a matched non-OLT group undergoing LSG during the same time period for comparison. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study, formal consent is not required. Approval from our institutional review board was obtained. Data collected from the medical record included patient demographics, comorbid conditions, American Society of Anesthesiologists classification scores, operative details, and postoperative morbidity and mortality and outcomes, including postoperative length of stay. Operative time was calculated from first incision to the skin closure. Our primary end point was overall major morbidity and all other operative outcomes were secondary outcomes. All postoperative major and minor complications were tracked for 90 days following the procedure and were graded by the Clavien-Dindo classification system [19] and reported as minor (grade I and II) or major (grade III–V). All patients were followed up for at least 2 months after surgery.

Each identified patient with OLT and LSG was matched in a random fashion to 3 patients undergoing LSG only, according to patient age, sex, preoperative body mass index (BMI), and year of surgery. Weight-loss outcomes were assessed using BMI and percentage of excess body weight loss (EBWL).

Surgical Technique

For LSG, the laparoscopic intervention was started by mobilizing the great curvature of the stomach starting 4 cm proximal to the pylorus and proceeding to the left crus of the diaphragm. An ultrasonic scalpel was used for dividing the gastroepiploic branches and short gastric vessels. A 36F to 42F bougie was introduced into the stomach by the anesthesiologist, and vertical gastrectomy was accomplished using 4.8-mm staple cartridges along the bougie. In most cases, mobilization of the stomach was challenging because of adhesions from previous abdominal surgeries. The disconnected part of the stomach was extracted from the abdominal cavity, and the remnant stomach was checked by intraoperative esophagogastroscopy for bleeding and leaks.

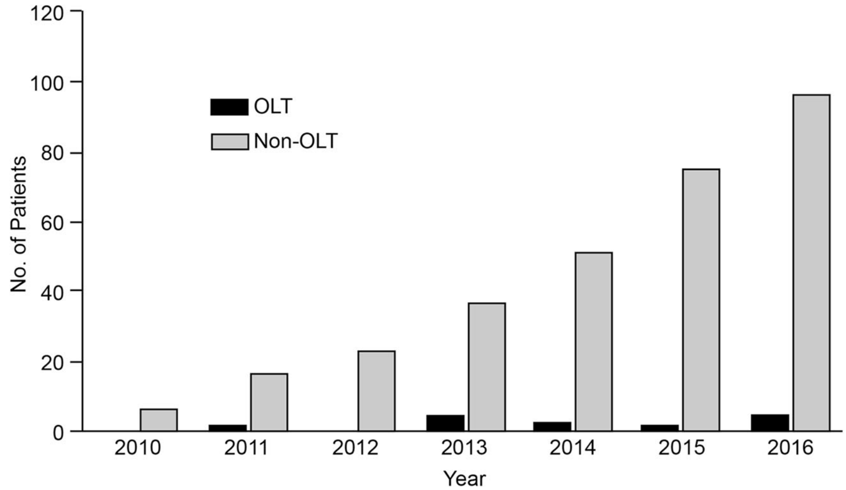
Statistical Analysis

Continuous variables are expressed as mean (SD) and categorical variables are reported as number (percentage). Standard statistical analysis was performed. Significance was noted at $P < .05$.

Results

During the study period, 303 patients underwent LSG; of these, 12 (4%) had a previous OLT (Fig. 1, Table 1). Mean (SD) age was 56.6 (8.9) years, and pre-LSG BMI was 45.31 (6.19). Liver disease diagnoses included viral hepatitis C ($n = 5$), NASH ($n = 4$), autoimmune hepatitis ($n = 1$), alcoholic cirrhosis ($n = 1$), and cryptogenic cirrhosis ($n = 1$). The mean (SD) time between OLT and LSG was 63.1 (33.2) months. Four patients had complications within 90 days after surgery (33% morbidity rate), and the mean length of stay was 3.1 (1.2) days.

Fig. 1 Laparoscopic sleeve gastrectomies per year for all OLT and non-OLT patients. *OLT* orthotopic liver transplant



For the 12 patients with OLT and LSG, 36 matched patients made up the control group. Table 2 includes the matched case-control analysis. Per the matching, no significant differences in age, sex, and preoperative BMI were identified between the groups. Medical comorbid conditions and the American Society of Anesthesiologists status were well matched except for the incidence of NASH (50 vs 0%; $P < .001$). Operative time and 90-day morbidity were similar. There were no conversions to open surgery, and no 90-day mortality was noted. Length of stay was longer in the OLT group (3.1 vs 1.7 days; $P < .001$). Follow-up duration was similar between the groups (25.3 (5.1) vs 23.6 (2.45) months; $P = .13$), but 2 OLT patients were lost to follow-up (they were international patients who had post-OLT follow-up in their home countries).

Of the 4 complications in the OLT group, 3 were major (25%) and 1 was minor (8.3%). Major complications were poor oral intake, requiring balloon dilatation in 2 cases (grade IIIa) and laparoscopic gastrostomy tube placement in 1 case (grade IIIb). The minor complication was late drain removal from the abdominal cavity in the patient with extensive lysis of adhesions during LSG (grade II).

In the non-OLT group, 1 major (2.7%) and 4 minor (11.1%) complications were noted. Balloon dilatation was necessitated in 1 patient for oral intake difficulties due to the late stricture (grade IIIa). Wound infection developed in 3 patients,

Table 1 Patient characteristics and post-LSG outcomes in OLT patients ($n = 12$)

Pt	Age/sex	OLT indication	Pre-LSG BMI (kg/m^2)	LSG LOS (day)	90-day post-LSG complications	24-month post-LSG BMI (kg/m^2)
1	45/F	Hepatitis C	43	2	None	32
2	57/M	Hepatitis C	48	5	None	[a]
3	44/F	AIH	57	4	Sleeve dilation for poor intake (Cl-IIIa)	41
4	54/M	NASH	53	2	None	37
5	59/M	Hepatitis C	50	4	Sleeve dilation for poor intake (Cl-IIIa)	29
6	63/M	NASH	45	2	None	39
7	66/M	Cryptogenic	42	2	None	[a]
8	48/F	NASH	40	2	None	30
9	67/M	Hepatitis C	34	4	Late drain removal (Cl-II)	N/A
10	58/M	NASH	41	2	None	N/A
11	48/F	EtOH/cirrhosis	42	5	None	N/A
12	70/F	Hepatitis C	47	3	Gastrostomy tube for poor intake (Cl-IIIb)	N/A

Abbreviations: *AIH* autoimmune hepatitis, *BMI* body mass index, *Cl* Clavien-Dindo classification, *EtOH* alcohol, *F* female, *LOS* length of stay, *LSG* laparoscopic sleeve gastrectomy, *M* male, *N/A* not available, *NASH* nonalcoholic steatohepatitis, *OLT* orthotopic liver transplant, *Pt* patient

[a] Patient lost to follow-up (international patient)

Table 2 Patient characteristics and post-LSG outcomes in OLT vs non-OLT patients

Characteristic	Group[a]		*P* value
	OLT (*n* = 12)	Non-OLT (*n* = 36)	
Age (year)	56.6 (8.9)	53.84 (4.7)	.11
BMI (kg/m^2)	45.31 (6.2)	43.16 (5.1)	.24
Men	7 (58.3)	16 (44.4)	.78
Race			
African American	1 (8.3)	4 (11.1)	.64
Middle-Eastern	1 (8.3)	2 (5.5)	.59
White	10 (83.4)	30 (83.3)	.60
Hypertension	11 (91.6)	21 (58.3)	.45
NASH	0	3 (8.3)	.44
Diabetes mellitus	9 (75)	11 (30.6)	.09
High cholesterol/triglycerides	7 (58.3)	17 (47.2)	.46
Cardiac disease	4 (33.3)	11 (30.6)	.57
Obstructive sleep apnea	7 (58.3)	20 (55.6)	.57
GERD	3 (25)	8 (22.2)	.57
Time after OLT (month)	63.08 (33.2)	…	…
ASA class			
II	2 (16.6)	7 (19.4)	.61
III	9 (75.0)	24 (66.7)	.60
IV	1 (8.4)	5 (13.9)	.55
Operative time (min)	122 (54)	125 (6.8)	.74
LOS (day)	3.08 (1.24)	1.7 (0.12)	< .001
	2.5[b]	2.0[b]	
90-day morbidity			
Minor (Cl grade I–II)	1 (8.3)	4 (11.1)	.64
Major (Cl grade III–V)	3 (25.0)	1 (2.7)	.07
Death	0	0	
Follow-up (month)	25.3 (5.1)	23.6 (2.5)	.13

Abbreviations: *ASA* American Society of Anesthesiologists, *BMI* body mass index, *Cl* Clavien-Dindo classification, *GERD* gastroesophageal reflux disease, *LOS* length of stay, *LSG* laparoscopic sleeve gastrectomy, *NASH* nonalcoholic steatohepatitis, *OLT* orthotopic liver transplant

[a] Values are mean (SD) or no. of patients (%)

[b] Median

and 1 patient required abdominal drainage for fluid collection approximately 1 week (grade II). The differences between the 2 groups did not reach significance (all complications $P = .25$; major complications $P = .07$).

In patients with more than 3 years of follow-up (6 OLT, 18 non-OLT), no significant difference was found between the groups in change in BMI at 24 months ($P = .46$) (Fig. 2). Mean decrease in BMI of the OLT group was 12.9 vs 9.17 kg/m^2 in the non-OLT group. However, by percentage of EBWL, non-OLT patients had greater weight loss than the OLT group at each post-operative time interval ($P < .001$) (Fig. 3).

In the OLT group, no significant difference was detected in the dosage of immunosuppression (tacrolimus) between the LSG preoperative period (3.6 (3.0) mg/day) and postoperative period (3.6 (2.5), 4.2 (2.2), 3.4 (1.6), and 4.6 (2.3) mg/day at 3, 6, 12, and 24 months, respectively; $P = .47$). Resolution of preoperative comorbid conditions was assessed (Table 3). Preoperatively, 9 OLT patients had metabolic syndrome and diabetes mellitus related to obesity and immunosuppressive therapy, 4 of whom (44.4%) achieved complete resolution of disease 12 months after surgery. In the non-OLT group, resolution of comorbid conditions occurred at similar rates as the OLT group.

Discussion

In the current study, non-OLT patients had greater EBWL than the OLT patients, but the overall BMI decrease was similar.

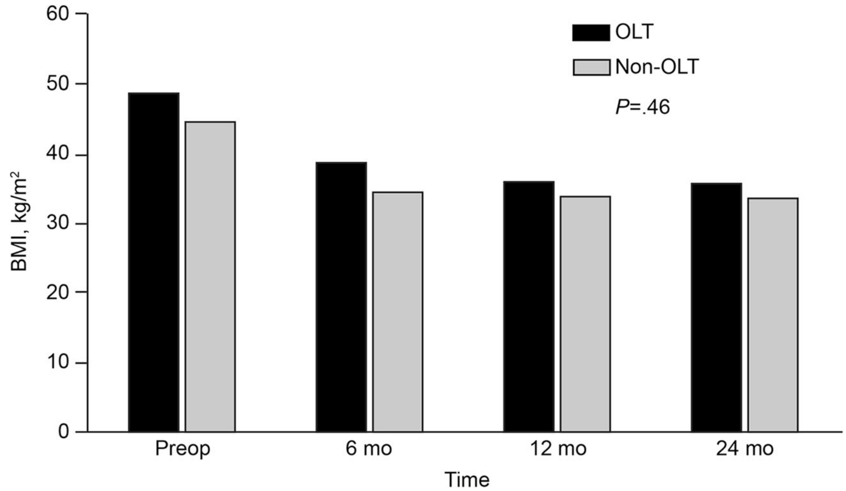


Fig. 2 Comparison of mean body mass index (BMI) for OLT ($n = 6$) and non-OLT ($n = 18$) patients after laparoscopic sleeve gastrectomy. *OLT* orthotopic liver transplant. *Preop* preoperative

The greater weight loss in the non-OLT group may be partly related to the continued need for immunosuppressive therapy after LSG in the OLT group. One study [20] reported several other factors influencing weight loss after bariatric procedures such as age, insulin resistance, behavior modification, information support, expectations, and coping skills. OLT patients may have a more difficult time than non-OLT patients instituting the drastic changes needed after bariatric surgery. Thus, we found that weight loss after LSG was significantly more effective in non-transplant patients but still beneficial in transplant patients.

Our study found no significant differences in operative time, morbidity, postoperative BMI changes, and follow-up time between OLT and non-OLT patients. Lin et al. [17] reported an operative time of 165 min among 9 OLT patients undergoing sleeve gastrectomy (8 laparoscopic and 1 open), and another study reported 158 min for robotic sleeve gastrectomy after OLT in 1 patient [16]. Another study of 10 consecutive patients undergoing LSG after solid organ transplant (5 liver, 4 kidney, 1 heart) reported a mean operative time similar to ours (122.6 vs 122 min) [18]. Upper abdominal adhesions are always present and will require adhesiolysis, but the majority of patients in our study did not have severe adhesions that precluded a laparoscopic approach or greatly prolonged operative time.

In one study, 3 patients with OLT (33%) had major complications after sleeve gastrectomy, and all of them required reoperation [17]. A study [18] of 10 posttransplant patients reported 2 reoperations due to the bleeding after LSG—1 had had OLT and 1 had kidney transplant. Our patients had no reoperations, and the major complication rate was 25%. Length of stay was significantly longer in the OLT group likely due to the necessity of close monitoring in this specific population. Additionally, there were 3 patients in the OLT group who experienced a major complication that extended their hospital stay. These major complications were all related to poor oral intake and required two upper endoscopies with dilations and one laparoscopic gastrostomy tube placement. We generally are more aggressive in this population than in non-OLT patients to restore PO intake due to required immunosuppressive medications.

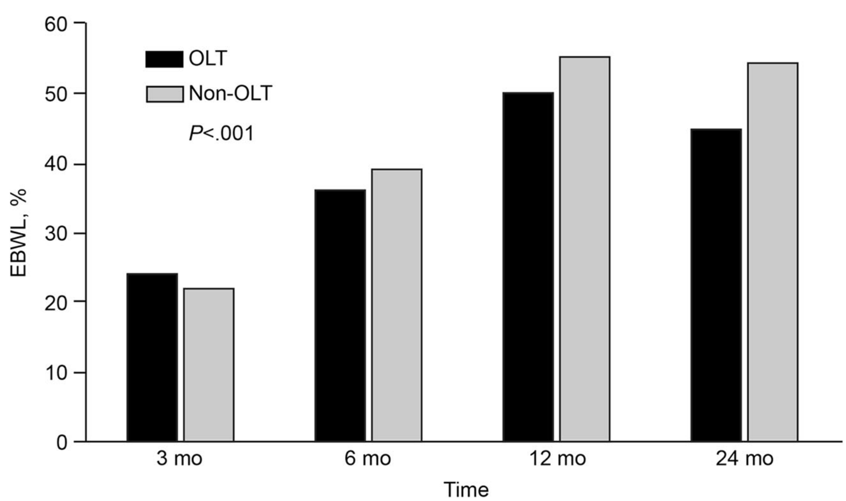


Fig. 3 Comparison of mean excess body weight loss (EBWL) for OLT ($n = 6$) and non-OLT ($n = 18$) patients after laparoscopic sleeve gastrectomy. *OLT* orthotopic liver transplant

Table 3 Resolution of comorbid conditions

CC	OLT patients (*n* = 12)		Non-OLT patients (*n* = 36)		
	CC	CC resolution	CC	CC resolution	*P* value
Diabetes mellitus	9 (75)	4 (44)	11 (31)	4 (36)	> .99
Cardiac disease	4 (33)	1 (25)	11 (31)	3 (27)	> .99
Hypertension	11 (92)	3 (27)	21 (58)	3 (14)	.65
Obstructive sleep apnea	7 (58)	3 (43)	20 (56)	4 (20)	.39
High cholesterol/triglycerides	7 (58)	3 (43)	17 (47)	1 (6)	.12
NASH	0	0	3 (8)	2 (67)	> .99

Values are no. of patients (%)

CC comorbid condition, *NASH* non-alcoholic steatohepatitis, *OLT* orthotopic liver transplant

Similar to findings from other groups [17], we found no difference in postoperative immunosuppression medication needs for our OLT group after LSG: 12 (100%) and 31 (86%) patients had one or more comorbid conditions in the OLT and non-OLT groups, respectively. Resolution of comorbid diseases (≥ 1) was noted in 6 patients (50%) from the OLT and 10 patients (32%) from the non-OLT group, but this difference did not achieve statistical significance ($P = .056$). Three of seven patients with obstructive sleep apnea and with hypercholesterolemia experienced resolution of comorbid conditions in the OLT group. Complete remission of diabetes mellitus in transplant patients after sleeve gastrectomy varies between 25 and 50%, according to different studies [15, 18]. In our study, 4 patients out of 9 with diabetes mellitus in the OLT group had resolution of disease. Two of three non-OLT patients had resolution of NASH on long-term follow-up. In the third patient, complete resolution has not occurred because of insufficient follow-up time.

Unfortunately, a common post-OLT finding is excessive weight gain, as a result of the immunosuppressive therapy (mainly corticosteroids) the patient receives after surgery [16]. In one study [21], more than 20% of lean patients became obese within 2 years after solid organ transplant. Moreover, strong association appears to exist between recent posttransplant antirejection medications and development of new-onset diabetes mellitus [22]. Thus, it is well known that obesity represents a significant risk factor for morbidity and mortality after transplantation and decreases the overall 5-year survival rate [16, 22].

On one hand, pharmacologic treatment alone for morbid obesity after transplantation is limited because of concern for drug interactions [21]. On the other hand, bariatric surgery is an underutilized treatment modality for the obese post-OLT population. This may be partially attributed to the overestimation of technical difficulties or high morbidity concerns by the bariatric surgeon in the OLT patient. Because of this, many post-OLT patients have obesity and obesity-related comorbid conditions.

Alternative endoscopic techniques have been introduced for weight reduction after liver transplant, including a single case study reporting intragastric balloon placement by flexible endoscopy after liver transplant [23]. Gastric banding has also been used for patients after solid organ transplant [24]. Despite the simplicity of these approaches, foreign body implantation in immunosuppressed patients can represent an increased risk of infection, gastric ulcer formation, evolution of reflux disease, and esophagitis, as well as decreased efficacy in achieving substantial weight loss [16, 25]. According to Tichansky et al. [26], performing Roux-en Y gastric bypass (RYGB) may be associated with significant technical difficulties due to previous OLT. Data regarding malabsorption in the setting of immunosuppression and OLT is still unclear. In our opinion, LSG is the preferred bariatric operation over RYGB in OLT due to less complexity and absence of limitations for endoscopic approach to the biliary tree.

Our study has several limitations. First, this was a retrospective matched case-control analysis between two not equal group in terms of previous abdominal surgeries and comorbidities and, therefore, selection bias was unavoidable. Second, we are not able to fully comment on the long-term results such as weight loss, resolution of comorbid conditions, and effects of the restrictive bariatric procedure on immunosuppression therapy dosage because of insufficient follow-up time. Third, we were not able to review our center's large OLT population to assess for those patients who were selected as candidates for LSG. All patients referred to our bariatric team from the transplant center were offered bariatric surgery and there was no significant selection process by either team other than meeting inclusion criteria for bariatric surgery. Fourth, we have small overall number of patients which may contribute to not reaching significant findings, overall morbidity in particular. Consequently, further studies with more patients and longer follow-up are needed to assess the long-term outcomes and evaluate the effectiveness of LSG after OLT.

In conclusion, transplant patients are more complex than typical bariatric patients. Despite this, based on our experience, LSG after OLT in appropriately selected patients appears to have similar outcomes to LSG in non-OLT patients. However, it is recommended that these operations be performed in high-volume centers in collaboration with multidisciplinary services comprising transplant hepatologists, intensive care units, experienced anesthesiologists, and a comprehensive bariatric team capable of appropriate long-term follow-up.

Compliance with Ethical Standards

Ethical Approval Statement For this type of study, formal consent is not required.

Informed Consent Statement Does not apply

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

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