ORIGINAL CONTRIBUTIONS



Sleeve Gastrectomy After Liver Transplantation: Feasibility and Outcomes

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Abstract

Background Knowledge regarding the feasibility and safety of sleeve gastrectomy (SG) in obese liver transplant recipients is scarce. We report our experience of sleeve gastrectomy following liver transplantation (LT).

Methods All patients who had undergone LT and subsequently underwent SG at our institution were retrospectively reviewed. Surgical outcomes, liver and kidney function tests, outcomes of obesity-related comorbidities, and excess weight loss were analyzed.

Results Between May 2008 and February 2015, six consecutive patients underwent SG after LT. Three procedures (50%) were performed totally by laparoscopy, and three by upfront laparotomy for concomitant incisional hernia complex repair. Within the first 30 days, one complication occurred: early gastric fistula that required multiple endoscopic procedures and re-intervention, followed by death 19 months after SG due to multi-organ failure. Another patient had one late complication: chronic infection on a parietal mesh successfully controlled by mesh removal. Excess weight loss averaged 76% at 2 years with a median BMI of 28 (21–39) kg/m².

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Median follow-up was 37.2 months (range 13–101 months). Median length of stay was 9 days (range: 6–81 days). *Conclusions* SG is technically feasible after LT and resulted in weight loss without adversely affecting graft function and immunosuppression. However, morbidity and mortality are high.

Keywords Sleeve gastrectomy \cdot Liver transplantation \cdot Bariatric surgery \cdot Non-alcoholic fatty liver disease \cdot Excess weight loss

Introduction

According to the World Health Organization, a body mass index (BMI) ≥ 25 , ≥ 30 , and ≥ 35 kg/m² define overweight, obesity, and severe obesity, respectively. Worldwide, more than 1.9 billion adults were overweight in 2014 of whom, over 600 million met the criteria for obesity [1]. In the setting of liver transplantation, the US Organ Procurement and Transplantation Network and the Scientific Registry of Transplant Recipients reported that 54% of patients undergoing orthotopic liver transplant (OLT) were either overweight or obese, and 7% of patients who received liver transplant were considered severely or morbidly obese [2]. In 2025, nonalcoholic steatohepatitis (NASH) is predicted to become the main cause of liver failure requiring liver transplantation (LT) in the USA [3]. Morbid obesity has been associated with both increased mortality on the LT waitlist [4], and adverse impact on outcomes with reduced patient and graft survivals [5].

Subsequently, bariatric surgery (BS) has been proposed before, during, and after LT [6–8].

BS in obese LT recipient includes the followings potential specific risks: (i) technical difficulties due to adhesions in the left upper quadrant, (ii) infection and poor healing as a result

of immunosuppression, and (iii) potential graft rejection due to impaired immunosuppression pharmacokinetics [8]. The purpose of the present study was to assess the feasibility and outcomes of sleeve gastrectomy (SG) in severely obese patients following previous LT.

Materials and Methods

The institutional review board approved this observational descriptive study of consecutive severely obese patients submitted from 2008 to 2015 to SG after LT.

Patients were considered candidates for SG after LT if they had a body mass index (BMI) of 35 kg/m² or greater with weight-related comorbidities. Preoperative management of patients was standard for obese patients including a comprehensive medical evaluation and counseling by a multidisciplinary board (bariatric surgeon, endocrinologist, psychologist, and dietician) for at least 6 months, as requested by the French guidelines for bariatric surgery [9]. Decision to proceed to BS was discussed at the BS board with the participation of hepatologists and liver surgeons.

A bariatric surgeon assisted by a liver surgeon performed all cases of SG. BS was performed upfront by laparotomy in patients needing combined complex repair of LT incision hernia.

Oral calcineurin inhibitor-based immunosuppression was continued throughout the perioperative period. Thromboprophylaxis with enoxaparin for 3 weeks was started 6 h after BS. Postoperatively patients were transferred to the liver ICU for 24 h and then to the liver unit ward. Liver and kidney function tests were measured daily and liver Doppler ultrasonography was performed at day 1 and 5 days after BS.

Outcomes

Postoperative mortality and morbidity were assessed within 90 days of BS or at any time during hospitalization for surgery. Metabolic and bariatric surgery results are reported according to the American Society for Metabolic and Bariatric Surgery standards [10]. Weight loss was measured as percent of excess weight loss (%EWL) and body mass index (BMI) reduction. The %EWL was defined as the ratio between the weight lost after surgery and the overweight according to the formula: [(initial weight) – (postop weight)]/[(initial weight) – (ideal weight)], in which ideal weight is defined by the weight corresponding to a BMI of 25 kg/m².

The outcome of the following comorbidities was assessed whenever present: diabetes mellitus (DM), hypertension (HT), dyslipidemia, obstructive sleep apnea syndrome (OSAS), and non-alcoholic fatty liver disease (NAFLD). Each comorbidity outcome was assessed as worsened, stable, or improved.

Statistical Analysis

Quantitative variables are reported as median and range. Paired *t* test was used as appropriate for comparisons. A *p* value < 0.05 was considered statistically significant. All statistical analyses were performed using SPSS Statistics 23.0 (IBM).

Results

Study Population

Between May 2008 and February 2015, six consecutive patients underwent SG after liver transplantation. During the same period 506 LT and 659 bariatric procedures (SG, n = 275; gastric bypass, n = 341; and adjustable gastric banding, n = 43) were performed.

The main patient characteristics are reported in Table 1. All six patients had at least one obesity-related comorbidity. At BS, the median BMI was 41.9 kg/m^2 (range $38-46.1 \text{ kg/m}^2$). The median delay from LT to SG was 44 months (range: 36.0-46.1 months) and the median increase of BMI during this delay was 2 kg/m² (range: $0.0-9.6 \text{ kg/m}^2$).

Three procedures (50%) were performed totally by laparoscopy, and three by upfront laparotomy due to the required combined repair of LT incisional hernia, as already mentioned. No artificial grafts were needed for caval, portal, or arterial reconstruction. Median operative time was 150 min (range: 120–240 min). No intraoperative complications occurred. Median length of stay was 9 days (range: 6–81 days). Median follow-up was 37.2 months (range 13–101 months) and no patient was lost to follow-up.

Postoperative Events

Postoperative mortality occurred in one patient following the sole major complication (1/6 patients, 17%) of the series. The third patient of the cohort developed a leak from the gastric staple line, needing multiple surgical and endoscopic reoperations and a prolonged hospital stay (81 days). When the leak finally healed, the patient developed a gastroparesis, provoking a severe dysphagia to solid. Neither endoscopic exploration nor bolus swallow test ruled out any abnormality. Manometry confirmed total aperistalsis of the stomach remnant. After several weeks of parenteral nutrition, and failure of medical treatment, the SG was converted by laparotomy into a Roux-en-Y gastric bypass (RYGB). The patient developed a leak from the gastric pouch, leading progressively to multiorgan failure and death 19 months after SG and 11 months after conversion to RYGB.

Wound infection of the laparotomy incision (1/6 patients, 17%) occurred in one patient. The latter had been operated on

Case, sex, age at BS (y)) Indication for LT	Delay from LT to BS (months)	BMI (kg/m ²)		Comorbidity at the
			LT	BS	time of BS
1, Male, 46.7	HCV cirrhosis	47.6	46.1	46.1	DM
2, Male, 63.4	HCC + alcoholic cirrhosis	44.6	38.9	39.8	DM, HT, OSAS, DL
3, Female, 62.8	HCC + alcoholic cirrhosis + NASH	70.3	41.8	44.9	DM, HT
4, Female, 65.4	HCC + NASH	37.9	34.1	43.7	DM, HT, DL
5, Male, 52	Acute alcoholic hepatitis	36.0	36.0	38.0	HT, OSAS
6, Male, 57	HCC + alcoholic cirrhosis +HCV	54.0	38.5	40.1	OSAS, Hypothyroidism
Total Male = 4/6 Age = 63 (46.7–65.4)	HCV = 2/6 HCC = 4/6 Alcoholic cirrhosis = 3/6 NASH = 2/6 Acute alcoholic hepatitis = 1/6	44.6 (36.0–70.3)	38.9 (36.0–46.1)	43.7 (38.0–44.9)	DM = 4/6 OSAS = 3/6 HT = 4/6 DL = 2/6
			p = 0.09 (paired t-	test)	

Table 1 Patient characteristics

LT liver transplantation, BS bariatric surgery, BMI body mass index, DM diabetes mellitus, HT hypertension, OSAS obstructive sleep apnea, DL dyslipidemia, HCC hepatocellular carcinoma, NASH non-alcoholic steatohepatitis

for a ventral hernia with an intra-abdominal mesh positioning several months before SG. The infected part of the mesh was removed with a favorable outcome.

The rate of postoperative acute rejection was nil.

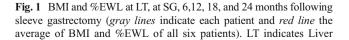
Long-Term Outcomes

Median %EWL and BMI at 1 year were 76% (range: 25%-119%) and 29 kg/m² (range: 21-39 kg/m²), respectively (Fig. 1). Median BMI at BS and last follow-up were 42.7 and 29.8 kg/m² (paired *t* test; *p* = 0.007), respectively.

Liver and kidney function tests values at last follow-up were not significantly different as compared to values before sleeve gastrectomy (paired t test, Table 2). The decrease of HbA1C observed in all four diabetic patients did not reach statistical significance.

Antihypertensive medications were stopped in 2/4 patients within 1 year of SG and remained unchanged in the remaining

BMI 50.0 45.0 40.0 35.0 30.0 25.0 20.0 15.0 10.0 5.0 0.0 at LT at Sleeve M6 M12 M18 M24



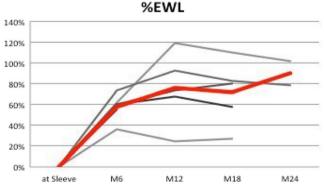
two. Two out of three with OSAS needing upper airway stimulation before SG were weaned of the latter within 6 months of SG.

One patient underwent uneventful partial hepatectomy for recurrent hepatocellular carcinoma (HCC), 49 months after LT for HCC and 13 months after SG.

Discussion

The present series shows that SG after OLT is feasible in patients with severe obesity with significant weight loss at the 1 year follow-up.

The proportion of liver transplant recipients classified as obese has increased from 15% in the early 1990s to 33% in 2011 [11]. Despite conflicting reports [12, 13], BS has emerged as a valuable option to treat obese patients in the setting of LT [6, 14]. As shown in Table 3, BS after LT in adults has been reported so far



Transplantation, BMI for Body Mass Index, %EWL for Percentage of Excess Weight Loss and M for Months

Table 2	Laborato	ry findings	Table 2 Laboratory findings before SG and at last follow-up after	last follow-ul	p after SG											
Case No.	Total bilirubin (umol/L)	lbin	AST/ALT (IU/L)		GGT (IU/L)		ALP (IU/L)		PT (% of normal)	mal)	A1c hemoglobin		Creatinine		Urea	
	Before SG	At last FU	Before SG	At last FU	Before SG	At last FU	Before SG	At last FU	Before SG	At last FU	At last FU Before SG	At last FU	Before SG	At last FU	Before SG	At last FU
_	11	8.6	36/54	18/12	123	23	161	104	100		7.8	5.7	120		9.6	4.9
2	9	4.7	27/93	8/6	200	19	93	78	98	94	6.9	5.8	130	177	9	15.2
3	20	17	1	5/19	191	48	134	246	29		5.8		74		5.5	16.6
4	3	5.7	21/20	45/36	80	244	101	122	100		7.7		72		8.4	6.6
5	15	6.0	16/20	41/14	62	48	122	61	88	90	QN		162		11.1	4.4
9	10	5.0	49/57	37/25	445	72	114	76	100		QN		139		6.4	4.7
P value	0.12		0.40 /0.07		0.20		0.82		0.56		0.16		0.84		0.78	
(paired t test)																
Total	10.5	5.85	31.5/55.5	27.5/16.5	157	48	118	91	66	90	7.05	5.75	125	108.5	7.4	5.75
median [range]	[3-20]	[4.7–8.6]	[3-20] [4.7-8.6] [16/20-116/91] [8/6-41/14] [62-445]	[8/6-41/14]	[62-445]	[19-244]	[19-244] [101-161]	[61–246]	[29–100]	[22–94]	[22-94] [5.8-7.8] [5.5-6.3] [72-162]	[5.5–6.3]	[72–162]	[67–177] [5.5–11.1] [4.4–16.6]	[5.5–11.1]	[4.4–16.6]
A1c Hen	w nidolgor	as measured	A1c Hemoglobin was measured only in diabetic patients (patients 1	patients (patie	ents 1 to 4)											
FU follor	y-up, <i>SG</i> s	leeve gastre	FU follow-up, SG sleeve gastrectomy, ALP alkaline phosphatase, ALT alanine aminotransferase, AST aspartate aminotransferase, PT prothrombin time ratio, ND no diabetes	ine phosphata	ise, ALT ala	nine aminot	ransferase, A	ST aspartate	e aminotrans	ferase, PT1	prothrombin	n time ratio	, ND no dia	betes		

in 37 cases to date, including the current cases, with a mortality and morbidity rate of 11 and 28%, respectively. During the study period, mortality and severe morbidity rates of SG in our center were nil. However, the mortality and morbidity following BS in the general population was 0.12 and 10%, respectively [23, 24].

In our series, patients lost nearly 56% of their excess body weight within 6 months of BS. In addition, liver graft function was preserved or improved in all patients, with no difficulty in maintaining immunosuppression, and no episodes of acute rejection. Four of the six patients were diabetic, and the dosage of HbA1c before and after SG showed improved control of diabetes after SG as shown by decreased levels of HbA1c; however, this was still not significant.

Five of the six patients with a 1 year of follow-up lost 80% of their excess body weight, but one patient did not lose weight after the SG. These results are consistent with the reported failure rates of relevant series (range: 15–25%) [25, 26].

SG might be the favored bariatric surgical technique in the setting of liver transplantation compared to gastric bypass for two main reasons: (i) SG preserves easy endoscopic access to the biliary tract [8, 27] if ever needed; and (ii) SG does not include any intestinal bypass that could impair the absorption of immunosuppressive or other medications [14, 17, 28].

Only one de novo non-alcoholic fatty liver disease (NAFLD) was discovered after biopsy examinations during post-LT follow-up (Table 4; patient 6). Vallin et al. showed that de novo and recurrent NAFLD after LT were different entities, with the latter being a more severe disease with an earlier onset [29].

Artificial grafts may be used in LT for caval, portal, or arterial reconstruction, especially when vascular grafts from the donor are not available or adequate in terms of length, size, or quality. Complications like infection and migration of these grafts in the stomach can occur and which can complicate the SG [30]. For optimal outcome, SG should be done with presence of a bariatric surgeon and a liver surgeon. In our series, no artificial or vascular grafts were used.

Major limitations of this work include the retrospective nature of the study and the small number of patients. Larger series are needed to confirm the efficacy of BS in liver transplant recipients. Due to the learning curve effect, we assume that these larger series will also show improved safety of the procedure in this setting of LT.

Multivariate analysis would be of interest to identify the risk factors of morbi-mortality. In order to establish significant results, more patients and more events are needed. Our team previously published a systematic review on bariatric surgery and LT [6]. In that paper, 56 patients were included; however, we still had to use a generalized linear mixed model framework with an underlying Poisson distribution because of the small number of patients and events. Confidence intervals were very large not very informative.

In conclusion, SG is feasible in severely obese patients after LT. It results in an improvement in obesity-related comorbidities

Table 3 Series reporting bariatric surgery performed after liver transplantation	tric surgery	performed after liver tra	insplantation				
1st author (reference), year, country	No. of pts	Follow-up mean (range)	Surgical procedure	Patients undergone laparoscopy ^a (<i>n</i>)	BS complication N (%)	Reoperation N (%)	Mortality n, delay
Duchini et al. [15], 2001, USA	2	27 (18–36)	RYGB	0/2	0	0	0
Tichansky et al. [16], 2005, USA	1	4	RYGB	1/1	0	0	0
Butte et al. [17], 2007 Chili	1	6	SG	0/1	0	0	0
Gentileschi et al. [18], 2009, Italy	1	6	BPD	0/1	0	0	1 at 9 months
							(myocardial infarction)
Elli et al. [19], 2012, USA	2	3	SG	0/2	0	0	0
Lin et al. [8], 2013, USA	6	5 (3-12)	SG	8/9	3(33.3%)	3 (33.3%)	0
Al-Nowayalati et al. [20], 2013,	7	59 (6-103)	RYGB	<i>L</i> /0	4 (57.1%)	NS	2 at 6 months, and 9 months
USA							(multiple-organ dysfunction
							syndrome and metastatic
							esophageal squamous
							carcinoma, respectively)
Pajecki et al. [21], 2014, Brazil	1	10	SG	0/1	0	0	0
Elli et al. [14], 2016, USA	2	2	SG	2/2 robotic	0	0	0
Khoraki et al. [22], 2016, USA	5	33.7 (13–79)	SG	5/5	1(20%)	0	0
Present Study, 2017, France	9	41 (12–94.4)	SG	3/6	2 (33.3%)	1 (16.6%)	1 at 19 months (multi-organ
							failure)
Total	37		SG = 26 RYGB = 10 BPD = 1	Laparoscopic = 17 Robotic = 2 Open = 18	10/36 (27.7%)	4/36 (11.1%)	4/36 (11.1%)
BS bariatric surgery, RYGB Roux-en-Y gastric bypass, SG sleeve gastrectomy, BPD biliopancreatic diversion	x-en-Y gastı	ric bypass, SG sleeve ga	strectomy, BPD bil	iopancreatic diversion			

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^a Conversion rate was 0%

Table 4 Percentage of steatosis(%) of the native liver and thegraft liver after biopsyexaminations during post-LTfollow-up

Case	Indication for LT	Native liver	Liver graft after reperfusion	Liver graft at long term
1	HCV cirrhosis	0%	0%	5% at 2 years
2	HCC on alcoholic cirrhosis	0%	10%	10% at 1 year
3	HCC on alcoholic cirrhosis + NASH	30-40%	0%	0% at 5 years
4	HCC on NASH	30-40%	0%	20% at 4 years
5	Acute alcoholic hepatitis	5%	5%	5% at 1 year
6	HCC on alcoholic cirrhosis +HCV	0%	5%	20% at 1 year 40–50% at 5 years
			p = 0.304 (paired t-test)	

LT liver transplantation, HCC hepatocellular carcinoma, NASH non-alcoholic steatohepatitis

with no impact on graft function. Larger studies are needed to improve the safety of the procedure in this high-risk population towards that seen in the general population. [8, 14–22].

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no competing interests.

Funding None.

Ethical Approval 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.

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

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