Morbidly Obese Patients Awaiting Liver Transplantation—Sleeve Gastrectomy: Safety and Efficacy From a Liver Transplant Unit Experience

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ABSTRACT

Background. The prevalence of obesity has increased dramatically, even in the population awaiting a liver transplantation. Despite their associated complications, we cannot consider morbid obesity any longer as an absolute contraindication to liver transplantation. Dietary approaches alone are usually completely ineffective. Bariatric surgery is the gold-standard treatment for morbid obesity and can be performed before, during, or after transplantation.

Materials and methods. At our Liver Transplantation Unit, a single surgeon performed a sleeve gastrectomy in 8 patients with liver cirrhosis due to nonalcoholic steatohepatitis, alcohol, or HCV. The Child score was A in 6 patients and B in the remaining 2 patients. Two of our patients had portal hypertension with mild esophageal varices. The procedure was performed laparoscopically in 7 cases (87.5%); in the other case, it was performed by open approach due to portal hypertension and according to patient preferences.

Results. Patients showed no postoperative morbidity or mortality. The mean postoperative body mass index of our patients was 37.4, 33.3, and 30.3 kg/m^2 at 3, 6, and 12 months after surgery, respectively. The mean percentage excess weight loss of our patients was 42.9%, 62.2%, and 76.3% at 3, 6, and 12 months. Two of the patients have already undergone a successful liver transplant.

Conclusion. Bariatric surgery in selected patients with compensated cirrhosis and without significative portal hypertension is reasonable. There are not clear guidelines on the use of bariatric surgery in patients with cirrhosis. In our experience, the sleeve gastrectomy is safe and effective in the treatment of patients with compensated cirrhosis; in a short time, the sleeve gastrectomy can improve candidacy in morbidly obese patients awaiting transplantation.

IN recent years, obesity has constantly increased until reaching an epidemic level worldwide. Patients awaiting a liver transplant are not an exception. With increasing frequency when evaluating a possible candidate to enter the transplant waiting list, we find that they present morbid obesity and comorbidities associated with this condition such as diabetes mellitus, arterial hypertension, sleep apnea, and hyperuricemia (within the so-called metabolic syndrome).

Nonalcoholic fat liver disease (NAFLD), which can vary from a simple hepatic steatosis to a nonalcoholic steatohepatitis (NASH), an established hepatic cirrhosis or the development of hepatocellular carcinoma, is becoming one of the leading causes of liver disease in the developed world.

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NASH is already the second leading cause of liver disease among adult waiting-list registrants in the United States. Although rates of alcoholic cirrhosis and viral liver disease are in decline, rates of NAFLD are increasing and may become the leading cause of liver transplantation in the next decade [1,2]. Furthermore, NASH prevalence may be underestimated; many times, cryptogenic cirrhosis is really NASH [3].

A body mass index (BMI) greater than 40 kg/m^2 has been considered a relative contraindication for liver transplantation in many centers [4]. Morbidly obese patients have shown an increased rate of perioperative complications and mortality after liver transplant surgery in many studies [5–9]. Moreover, obese patients routinely present other morbidities, so they often see their access to transplant waiting lists greatly diminished.

In recent years, more and more studies are finding that the risk of complications in these patients is so high that it justifies limiting their access to transplantation [10–12].

Some authors even suggest that as obesity is a risk factor for adverse outcomes in cirrhotic patients, including portal vein thrombosis, hepatocellular carcinoma (HCC), infection and liver decompensation. Obese patients would have a higher survival benefit than lean patients awaiting liver transplantation [13].

We can no longer consider obesity as a contraindication for transplantation.

We know that obesity is also frequent after liver transplantation (both in patients with previous obesity and nonobese patients) and has a significant impact on long-term survival after transplantation, increasing the risk of mortality from Novo neoplasms, especially because of cardiovascular causes. The problem of morbid obesity not only effects the doctors in charge of evaluating the transplant candidates but also those responsible for the subsequent follow-up.

With more obese patients in pretransplant consultation and because their inclusion on the waiting list can't be avoided, we will need to know which treatments can be applied to facilitate their access to the realization of the transplant and minimize risk.

Dietary approaches alone to correct obesity before the transplant are usually completely ineffective. Exercise, again, is often not possible in advanced liver disease.

Placement of intraluminal devices such as gastric balloons are a possibility for our patients [14]. However, its results are only acceptable in the short term and may also have complications in patients with esophageal varicose veins or hypertensive gastropathy.

On the other hand, outcomes following bariatric surgery in the general population are excellent with very low mortality rates. Compared with nonsurgical treatment of obesity, operative intervention leads to greater body weight loss and higher remission rates of type 2 diabetes and metabolic syndrome and can improve long-term survival in those patients [15–17].

Although liver cirrhosis has long been a contraindication, even absolute, for the realization of bariatric surgery, there are more and more cases with good results, so we know there are possibilities for our candidates for liver transplantation.

Among the different surgical techniques that we can use in patients awaiting a liver transplant, those considered only restrictive (the sleeve gastrectomy or adjustable gastric band) are considered preferable to mixed techniques or malabsorption creating techniques (such as Roux-en-Y gastric bypass) because these show different advantages. On the one hand, they do not interfere with the absorption of immunosuppressive medication (narrow therapeutic margin). On the other hand, they do not leave the stomach or duodenum excluded, with which it is possible to endoscopically access these viscera in case of digestive bleeding or, if necessary, to accede to the papilla and the biliary tree postoperatively, after the liver transplantation. In addition, they are sometimes considered, perhaps incorrectly, as technically easier. Between the 2 restrictive techniques mentioned above, the sleeve gastrectomy is preferable, usually performed with a laparoscopic approach, because the efficacy in terms of weight loss is greater than with the adjustable band. This also implies the existence of a foreign body in an immunosuppressed patient, and it is not uncommon to need to perform reinterventions for withdrawal of the device due to different complications.

Given the possibility of having bariatric surgery in the patient awaiting liver transplantation, we would be presented with 3 different scenarios: the procedure before the transplant, at same time as the transplant, or after the transplant.

Performing bariatric surgery prior to transplantation has the advantage that, a few months after the intervention, the patient will no longer present with morbid obesity and we can perform the transplant in optimal conditions. The problem is that although we may not consider hepatic cirrhosis as an absolute contraindication to the procedure, decompensated hepatic cirrhosis, with esophageal varicose veins or ascites, can be a contraindication. Bariatric surgery will be possible only in a part of our patients, especially in patients with an acceptable liver function and HCC. Bariatric surgery is a "bridge" treatment for transplantation, similar to the radiofrequency ablation or transarterial chemoembolization, and is often associated with them.

Different publications report the results of bariatric surgery in cirrhotic patients, especially with sleeve gastrectomy but also with adjustable gastric band or gastric bypass. Some describe an increase in morbidity and mortality compared to noncirrhotic patients, and others show better outcomes. However, most of the series are small, in most cases incidental diagnosis of liver cirrhosis in the intraoperative period of bariatric surgery, and most patients have a Child score A [18–22].

Performing a sleeve gastrectomy following liver transplantation in the same surgical intervention, which has been published in recent years [23], would have the advantage of a single intervention, and the gastric surgery could be performed in a moment without portal hypertension. The

drawback of this strategy is that it will increase surgical time, and we will add the morbidity and mortality of bariatric surgery in a complex high-risk patient to the mortality of liver transplantation. The existence of a digestive hemorrhage or a gastric fistula can also complicate the postoperative course of a liver transplant. We would not find any advantage at the time of the transplant or in the initial postoperative time because the patient would still have initially the same weight situation, with the added problem of a more precarious nutritional situation in the immediate post-transplant time. In addition, we would have the logistical problem of having an expert bariatric surgeon available just after the liver transplant, always with urgent character and very often at night or in the early morning.

Finally, there is the possibility of delaying the bariatric intervention and performing it later in the transplanted patient. This allows surgery in a patient with good liver function and with a more reduced maintenance immunosuppression. However, we would only be acting on the long-term evolution of the patient, without any incidence on the initial post-transplant evolution. In addition, surgery may be more complex due to postoperative abdominal adhesions secondary to transplantation, and it may not be possible to perform the procedure laparoscopically, which is always preferable [24,25].

MATERIALS AND METHODS

Between March 2010 and May 2017 in the Liver Transplant Unit of the University Hospital Doce de Octubre, a sleeve gastrectomy was performed in 8 patients with liver cirrhosis. Two of them presented with radiological data of NAFLD but without histological diagnosis of cirrhosis prior to the bariatric surgery. The other 6 patients were being evaluated in our consultation as possible candidates for liver transplantation with or without indication of entry at that time onto the transplant waiting list.

The intervention was performed in all cases by a single surgeon with experience in both laparoscopic bariatric surgery and liver transplantation.

The main cause of liver disease was nonalcoholic steatohepatitis in 5 cases, alcoholic cirrhosis in 1 case, and hepatitis C in 2 cases.

The hepatic functional situation at the time of bariatric surgery was Child A in 6 cases and Child B in the remaining 2 cases.

Two patients presented portal hypertension with mild esophageal varices with little risk of spontaneous bleeding. No patient had ascites at the time of surgery, although they may have presented it earlier (the patient details are in Table 1).

The intervention was performed by laparoscopy approach in 7 patients (none specified conversion to laparotomy) and by laparotomic approach in 1 patient by the existence of esophageal varicose veins and patient preference.

RESULTS

Patients showed no postoperative morbidity or mortality according to Dindo-Clavien criteria.

The mean postoperative BMI of our patients was 37.44 (standard deviation [SD]: 2.29; range: 35.1–42.3), 33.29 (SD: 2.41; range: 30.1–37.8), and 30.26 kg/m^2 (SD: 4.63; range: 24.2–37) at 3, 6, and 12 months after surgery.

Table 1. Patients' Characteristics

Patient	Age (y)	Sex	Etiology	HCC Status	Child Score	EV
1	41	F	NASH	No	A5	No
2	42	F	HCV	No	A5	Yes
3	59	F	NASH	No	A5	No
4	53	F	NASH	No	A5	No
5	58	M	Alcoholic	Yes	B7	No
6	64	F	NASH	No	A5	No
7	56	F	HCV	No	B7	Yes
8	56	M	NASH	No	A6	No

Abbreviations: EV, esophageal varices; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; NASH, nonalcoholic steatohepatitis.

The mean percentage excess weight loss (%EWL) of our patients was 42.87% (SD: 7.26; range: 34.3–52.4), 62.21% (SD: 8.74; range: 50.6–73.4), and 76.3% (SD: 19.39; range: 50.6–102.2) at 3, 6, and 12 months.

We can see weight loss details in Table 2 and in Fig 1.

Two of the patients have already undergone a successful liver transplant.

The first patient presented with alcoholic cirrhosis and uninodular 4 cm HCC treated previously with transarterial chemoembolization. Its functional score was Child-Pugh B7. His weight was 148 kg, with a BMI of 55 kg/m^2. With an intensive nutritional treatment, his weight was reduced to 119 kg and a BMI of 44.2 kg/m^2, and bariatric surgery was performed at that time. Oral feeding was reintroduced 24 hours after the procedure, and he was discharged on the fourth postoperative day. The transplant was possible 7 months after bariatric surgery, with a weight of 80 kg and a BMI of 29.7 kg/m^2. Months after transplantation, the patient developed a hepatic artery thrombosis that lead to a bile duct stenosis, which motivated several incomes by cholangitis, making several transparietal hepatic dilatations necessary. At the same time, the patient presented moderate protein malnutrition, secondary to scarce intake, reaching a minimum weight of 53 kg (BMI of 19.7 kg/m^2) at 18 months post-transplant. The patient received protein supplements; when his nutritional status improved, he was subjected to a Roux-en-Y hepaticojejunostomy. After 24 months, the patient maintained a weight of 67 kg, with a BMI of 24.9 kg/m^2, percentage total weight loss (%TWL) of 43.7%, and %EWL of 100.4%, a suitable nutritional situation and a preserved liver graft function.

The second patient presented with HCV cirrhosis (in a viral sustained response after treatment with direct action antivirals), with a functional stage B7 and small esophageal varicose veins. She weighed 130 kg, with a BMI of 45.5 kg/m^2. After bariatric surgery, she started and oral intake 24 hours after surgery, and she was discharged on the fourth postoperative day. She did not present any morbidity. The transplant was performed 8 months after bariatric surgery when she weighed 96 kg, with a BMI of 33.6 kg/m^2. Eighteen months after bariatric surgery, she maintained weight of 68 kg, with a BMI of 23.8 kg/m^2 (%TWL 47.7%; %EWL 105.6%) with a correct nutritional situation.

Table 2. Patients' Characteristics and Outcomes

Patient	Weight (kg)	BMI (kg/m^2)	%EWL							Follow-up (months)
			3 Months	6 Months	12 Months	24 Months	36 Months	48 Months	60 Months	
1	122.5	49.1	49.2%	69.2%	82.5%	79.2%	70.8%	59.2%	45.8%	65
2	117.0	43.0	-	-	86.9%	98%	89.8%	79.6%	73.5%	74
3	132.0	47.9	52.4%	66.7%	66.7%	61.9%	-	-	-	30
4	125.0	51.4	34.3%	51.4%	54.5%	-	-	-	-	21
5	119.0	44.2	36.7%	73.4%	90.7%	100.4%	-	-	-	28
6	104.0	44.4	37.4%	50.6%	50.6%	48.4%	-	-	-	24
7	130.0	45.5	40.9%	59.6%	10.2%	-	-	-	-	18
8	147.0	44.9	49.2%	64.6%	-	-	-	-	-	6
Mean	124.6	46.3	42.9%	62.2%	76.3%	77.6%	80.3%	69.4%	59.7%	33.3

Abbreviations: BMI, body mass index; %EWL, percentage excess weight loss.

It was not necessary to modify the usual immunosuppression protocol after the transplantation of either of the 2 patients.

DISCUSSION

Due to the significant increase in the incidence of obesity, we must familiarize ourselves with different alternatives in treatment and the implications, during and after the realization, of a solid organ transplant.

Although the increase in general perioperative morbidity and mortality among morbidly obese patients is well documented, data regarding obesity and its impact on liver transplant outcomes are limited. Different studies suggest that obesity can increase postoperative morbidity after liver transplantation [8], but it doesn't affect patient and graft survival [7,10,26,27].

Transplanting patients with morbid obesity can be a great challenge, and it seems reasonable to treat the obesity of our patients before inclusion on the transplant waiting list. In general, it can be ensured that bariatric surgery is the gold-standard treatment for morbid obesity and may be indicated in our patients either before, after, or during liver transplantation if it can be done with similar morbidity and mortality to that of the general population and if the patient doesn't lose enough weight with nonsurgical treatments [28].

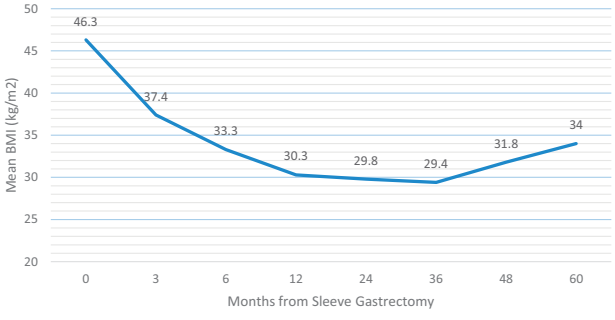

Fig 1. BMI (kg/m^2) from sleeve gastrectomy. Abbreviation: BMI, body mass index.

Morbidity and mortality would only be assumed prior to liver transplantation in patients without decompensation of their liver disease or portal hypertension data [19,21,22].

In the case that bariatric surgery is possible before the transplant, this will facilitate the actual access of the patient to the transplant [20].

In patients with portal hypertension, we would have the option to do a bariatric surgery immediately after transplantation [23,29]. However, we will have to assume, as mentioned, prolonged surgical time and increases in the morbidity and mortality inherent in the transplant. This adds to the morbidity and mortality secondary to the bariatric procedure, which does not have to be necessarily low if we consider that it is a complex patient who has just had a long surgery and presumably is in a more or less compromised hemodynamic functional and immunologic situation.

After the liver transplant, in patients who already had morbid obesity or develop it later, we still have to consider the possibility of performing bariatric surgery to reduce their long-term complications and increase their survival if conservative treatments fail, with similar indications to those of the general population: BMI $\geq$40 kg/m^2 or BMI $\geq$35 kg/m^2 in association with obesity-related morbidity. This surgery should be done at an indefinite time post-transplant that allows us to meet a patient with adequate liver function and minimal levels of maintenance immunosuppressive therapy. We will still treat a patient undergoing major abdominal surgery, as in the case of other abdominal organ transplants, which can condition adhesions at the time of bariatric surgery. Although the laparoscopic approach remains possible, it seems reasonable to limit these procedures to surgeons with a broad contrasted experience with revisional bariatric surgery and complex patients [25,30].

CONCLUSION

Pursuing bariatric surgery in selected patients with compensated cirrhosis is reasonable. Bariatric surgery should not be performed in cases of decompensated liver cirrhosis with manifestations of significant portal hypertension, such as ascites or esophageal varicose veins.

Therefore, there aren't clear guidelines on the use of bariatric surgery in patients with cirrhosis or a consensus on which kind of procedure is preferable.

In our experience, the sleeve gastrectomy is safe and effective in the treatment of patients with compensated cirrhosis, and in a short period of time (3 to 6 months), it helps patients awaiting a liver transplantation to receive a transplantation in a situation of mild obesity (Fig 1), without a significant worsening of their nutritional situation and without the need to change the usual protocol of immunosuppression in our center.

We believe that the possibility of bariatric surgery should be considered simultaneously to liver transplantation in patients where this was not possible previously due to portal hypertension. These patients should be carefully assessed before advising the performance of these 2 procedures in the same surgical act or the possibility of performing bariatric surgery in a second intervention after stabilizing the hepatic function with lower immunosuppression levels.

Finally, we should be aggressive in the prevention and treatment of obesity in liver transplant patients, including the possibility of bariatric surgery, so as not to see their long-term survival diminished, especially by cardiovascular complications.

In our center we prefer the realization of a sleeve gastrectomy to other techniques in the field of transplant patients or those awaiting solid organs transplantation because it presents good results in terms of weight loss without important interferences in the medication or post-transplant follow-up.

REFERENCES

[1] Charlton MR, Burns JM, Pedersen RA, et al. Frequency and outcomes of liver transplantation for non-alcoholic steatohepatitis in the United States. Gastroenterol 2011;141:1249–53.

[2] Wong RJ, Aguilar M, Cheung R, et al. Nonalcoholic steatohepatitis is the second leading etiology of liver disease among adults awaiting liver transplantation in the United States. Gastroenterol 2015;148:547–55.

[3] Caldwell SH, Oelsner DH, Lezzoni JC, et al. Cryptogenic cirrhosis: clinical characterization and risk factors for underlying disease. Hepatol 1999;29:664–9.

[4] Martin P, DiMartini A, Feng S, et al. Evaluation for liver transplantation in adults: 2013 practice guideline by the American Association for the Study of Liver Diseases and the American Society of Transplantation. Hepatology 2014;59:1144–65.

[5] Nair S, Verma S, Thuluvath PJ. Obesity and its effect on survival in patients undergoing orthotopic liver transplantation in the United States. Hepatology 2002;35:105–9.

[6] Hillingso JG, Wettergren A, Hyoudo M, et al. Obesity increases mortality in liver transplantation—the Danish experience. Transpl Int 2005;18:1231–5.

[7] LaMattina JC, Foley DP, Fernandez LA, et al. Complications associated with liver transplantation in the obese recipient. Clin Transplant 2012;26:910–8.

[8] Hakeem AR, Cockbain AJ, Raza SS, et al. Increased morbidity in overweight and obese liver transplant recipients: a single-center experience of 1325 patients from the United Kingdom. Liver Transpl 2013;19:551–62.

[9] Dick AA, Spitzer AL, Seifert CF, et al. Liver transplantation at the extremes of the body mass index. Liver Transpl 2009;15:968–77.

[10] Perez-Protto SE, Quintini C, Reynolds LF, et al. Comparable graft and patient survival in lean and obese liver transplant recipients. Liver Transpl 2013;19:907–15.

[11] Saab S, Lalezari D, Pruthi P, et al. The impact of obesity on patient survival in liver transplant recipients: a meta-analysis. Liver Transpl 2015;35:164–70.

[12] Peck JR, Latchana N, Michaels A, et al. Diagnosis of morbid obesity may not impact healthcare utilization for orthotopic liver transplantation: a propensity matched study. World J Hepatol 2017;9:595–602.

[13] Schlansky B, Naugler WE, Orloff S, Enestvedt CK. Higher mortality and survival benefit in obese patients awaiting liver transplantation. Transpl 2016;100:2648–55.

[14] Choudhary NS, Puri R, Saraf N, et al. Intragastric balloon as a novel modality for weight loss in patients with cirrhosis and morbid obesity awaiting liver transplantation. Indian J Gastroenterol 2016;35:113–6.

[15] Gloy VL, Briel M, Bhatt D, et al. Bariatric surgery versus non-surgical treatment for obesity: a systematic review and meta-analysis of randomized controlled trials. BMJ 2013;347:f5934.

[16] Arterburn DE, Olsen MK, Smith VA, et al. Association between bariatric surgery and long-term survival. JAMA 2015;313:62–70.

[17] Buchwald H, Avidor Y, Braunwald E, et al. Bariatric surgery: a systematic review and meta-analysis. JAMA 2004;292:1724–37.

[18] Mosko JD, Nguyen GC. Increased perioperative mortality following bariatric surgery among patients with cirrhosis. Clin Gastroenterol Hepatol 2011;9:897–901.

[19] Shimizu H, Phuong V, Maia M, et al. Bariatric surgery in patients with liver cirrhosis. Surg Obes Relat Dis 2013;9:1–6.

[20] Takata MC, Campos GM, Ciovica R, et al. Laparoscopic bariatric surgery improves candidacy in morbidly obese patients awaiting transplantation. Surg Obes Relat Dis 2008;4:15964.

[21] Rebibo L, Gerin O, Verhaeghe P, et al. Laparoscopic sleeve gastrectomy in patients with NASH-related cirrhosis: a case-matched study. Surg Obes Relat Dis 2014;10:405–10.

[22] Lin MY, Tavakol MM, Sarin A, et al. Laparoscopic sleeve gastrectomy is safe and efficacious for pretransplant candidates. Surg Obes Relat Dis 2013;9:653–9.

[23] Heimbach JK, Watt KD, Poterucha JJ, et al. Combined liver transplantation and gastric sleeve resection for patients with medically complicated obesity and end-stage liver disease. Am J Transplant 2013;13:363–8.

[24] Tichansky DS, Madan AK. Laparoscopis Roux-en-Y gastric bypass is safe and feasible after orthotopic liver transplantation. Obes Surg 2005;15:1481–6.

[25] Lin MY, Tavakol MM, Sarin A, et al. Safety and feasibility of sleeve gastrectomy in morbidly obese patients following liver transplantation. Surg Endosc 2013;27:81–5.

[26] Leonard J, Heimbach JK, Malinchoc M, et al. The impact of obesity on long-term outcomes in liver transplant recipients-results of the NIDDK liver transplant database. Am J Transplant 2008;8:667–72.

[27] Singhal A, Wilson GC, Wima K, et al. Impact of recipient morbid obesity on outcomes after liver transplantation. Transplant Int 2015;28:148–55.

[28] Suraweera D, Dutson E, Saab S. Liver transplantation and bariatric surgery. Clin Liver Dis 2017;21:215–30.

[29] Nesher E, Mor E, Shlomai A, et al. Simultaneous liver transplantation and sleeve gastrectomy: Prohibitive combination or a necessity? Obes Surg 2017;27:1387–90.

[30] Elli EF, González-Heredia R, Sánchez-Johnsen L, et al. Sleeve gastrectomy surgery in obese patients post-organ transplantation. Surg Obes Relat Dis 2016;12:528–34.