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ORIGINAL CONTRIBUTIONS

Bariatric Surgery in Cirrhotic Patients: a Matched Case-Control Study

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Abstract

Introduction Laparoscopic bariatric surgery (LBS) in liver end-stage organ disease has been proven to improve organ function and patients' symptoms. A series of LBS in patients with cirrhosis have shown good results in weight loss, but increased risk of complications. Current literature is based on clinical series. This paper aims to compare LBS (69% gastric bypass) between patients with cirrhosis and without cirrhosis.

Methods We conducted a retrospective 1:3 matched case-control study including bariatric patients with cirrhosis and without cirrhosis. Demographics, operative variables, postoperative complications, long-term weight loss, and comorbidity resolution were compared between groups.

Results Sixteen Child A patients were included in the patients with cirrhosis (PC) group and 48 in patients without cirrhosis (control) group. Mean age was 50 years; preoperative BMI was 39 ± 6.8 kg/m^2. Laparoscopic gastric bypass and laparoscopic sleeve gastrectomy were performed in 69% and 31%, respectively. Follow-up was 81% at 2 years for both groups. PC group had a higher rate of overall (31% vs. 6%; $p < 0.05$) and severe (Clavien-Dindo ≥ III; 13% vs. 0%; $p = 0.013$) complications than that of the control group. Mean %EWL of PC at 2 years of follow-up was 84.9%, without differences compared with that of the control group (83.1%). Comorbidity remission in PC was 14%, 50%, and 85% for hypertension, type 2 diabetes, and dyslipidemia, respectively. Patients without cirrhosis had a higher resolution rate of hypertension (65% vs. 14%, $p = 0.03$).

Conclusion LBS is effective for weight loss and comorbidity resolution in patients with obesity and Child A liver cirrhosis. However, these results are accompanied by significantly increased risk of complications.

Keywords Liver cirrhosis · Bariatric surgery · Bariatric morbidity · Non-alcoholic steatohepatitis (NASH)

Introduction

Laparoscopic bariatric surgery (LBS) is the most effective intervention to treat patients with obesity and most of their associated comorbidities. In addition to the substantial weight loss effect of LBS, several obesity-associated diseases achieve optimal control or disease remission which decreases long-term morbidity and improves overall survival [1, 2]. It has been demonstrated that LBS may prevent or delay the onset of severe comorbid diseases such as type 2 diabetes mellitus (T2DM) and arterial hypertension (AHT) [3, 4]. Even more, LBS may reduce the occurrence of severe complications of comorbid diseases such as micro and macrovascular complications in diabetic patients [5–7]. On the other hand, once organ damage has been already established, such as heart failure, end-stage renal disease, or liver cirrhosis, weight loss may improve organ function and patient's symptoms [8–12]. Particularly in heart failure and end-stage renal disease, LBS improves cardiac and renal function, increasing the eligibility for receiving organ transplantation [9–12].

The liver is frequently affected by obesity as non-alcoholic fatty liver disease (NAFLD), which may progress to a more severe and liver-damaging stage known as non-alcoholic steatohepatitis (NASH). NAFLD and NASH prevalence increases in parallel with the increase in body mass index [13]

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(BMI), and the main concern of NASH is the risk of progressing to liver cirrhosis. Although there are pharmacological treatments targeted to control NASH, lifestyle changes and weight loss are probably the most effective treatments. Thus, LBS emerges as an appealing treatment against obesity, NASH, and other comorbid diseases. Unfortunately, some patients seek LBS when liver damage is already established. In this scenario, performing intra-abdominal surgeries in patients with established liver cirrhosis carry an eight-fold increase in morbidity for Child A patients, and even higher for child B and C [14, 15]. Studies have shown that postoperative morbidity is in direct relation with the degree of liver dysfunction. Thus, the Child-Turcotte-Pugh (CPT) and the model for end-stage liver disease (MELD) scores behave as fair predictors for surgical morbidity [14–16]. Current reports of laparoscopic LBS on patients with cirrhosis (PC) are based mainly on clinical series performed in Child A patients showing that LBS in this population is feasible and produces significant weight loss. However, it is associated with an increase in medical and surgical complications [17]. Only one study has performed a direct comparison between patients with and without cirrhosis submitted to laparoscopic sleeve gastrectomy (LSG), but laparoscopic gastric bypass (LRYGB) has not been compared between this populations. Thus, our study aims to report the results of surgical and medical morbidity, comorbidity resolution, and mid-term weight loss after LBS in a 3:1 matched comparison between patients with and without cirrhosis.

Methods

A retrospective analysis of the prospectively collected LBS database of our center was performed. All patients with preoperative diagnosis of liver cirrhosis and those diagnosed intraoperatively, who consecutively underwent a LBS from July 2006 to January 2017 were identified (patients with cirrhosis, PC). A control group of patients without cirrhosis (control group) who underwent LBS in the same period was utilized for a 3:1 matching process. Each case was matched with three controls by gender, age, BMI, comorbidities, and type of surgery.

For both groups, demographics and clinical data, laboratory exams, preoperative abdominal ultrasonography, and upper gastrointestinal (GI) endoscopy were collected. Weight and percent of total weight loss (%TWL) were registered every 3 months during the first year following surgery, and then annually. Obesity-related comorbidities were monitored and classified as resolved when clinical and laboratory parameters remain normal without treatment [18].

Early (< 30 days following surgery) and late complications were registered and graded using the Clavien-Dindo (CD) classification, for which CD ≥ III is considered a severe complication [19]. Postoperative hepatic decompensation was defined as the development of encephalopathy, ascites, renal failure, or upper GI bleeding. Additionally, we searched for the development of liver decompensations, hepatocarcinoma, or the need for liver transplantation as late complications.

The statistical analysis was performed using the SPSS v0.25 software. We used *t* test to analyze continuous variables. Dichotomous outcomes were analyzed with chi-squared test. Continuous variables were reported as mean ± standard deviation and categorical variables as percentages. Differences were considered significant when p value < 0.05.

Results

Sixteen patients with obesity and liver cirrhosis out of 6302 bariatric patients (0.25%) underwent LBS in our center between July 2006 and January 2017. The 1:3 matched control group included 48 patients. The 2-year median follow-up of the whole series was 81%. Demographic and preoperative data are summarized in Table 1. For both groups, the mean age was 50 years, 69% of patients were female, and preoperative BMI was 39 ± 6.8 in the PC group and 39 ± 6.3 in the control group; T2DM was present in 25% of patients, AHT and dyslipidemia in 44% of patients, and LRYGB and LSG were performed in 69% and 31% of patients, respectively.

Four patients had a preoperative diagnosis of cirrhosis and it was confirmed by intraoperative liver biopsy. Twelve patients were diagnosed intraoperatively and 8 of them had a liver biopsy according to surgeons' criteria. However, the 4 patients who did not have liver biopsy had an operative report describing morphological liver features of cirrhosis. Analyzing preoperative workup, all cirrhotic patients were Child A with a mean MELD of 7.38 ± 1 and three patients (19%) had small esophageal varices as a marker of portal hypertension.

Mean operative time was 111 ± 57 min in the PC group and 98 ± 37 min in the control group ($p = 0.17$). Subgroup analysis did not show differences in operative time for LRYGB or LSG between PC and control group. Of note, two patients in PC group had a concomitant cholecystectomy, and three patients in the control group had concomitant surgery: a cholecystectomy, a hiatal hernia repair, and a ventral hernia repair. There were no conversions to open surgery or reoperations in both groups. The mean length of hospital stay was 3 days for both groups (Table 1).

Regarding morbidity, PC had higher morbidity rates as compared with the control group (31% vs. 6%; $p < 0.05$). There were no differences in mild complication rates between groups (CD < III). However, PC presented a higher rate of severe complications (CD ≥ III; 13% vs. 0%; $p = 0.013$, Table 2). After 2 years of follow-up, the MELD score had a

Table 1 Demographic and perioperative variables in patients with and without cirrhosis

	Patients with cirrhosis	Patients without cirrhosis	*p* value
n	16	48	-
Age (years), mean (SD)	50 (± 8)	50 (± 8)	NS
Gender (female: male)	11:5	33:15	NS
Type of surgery, *n* (%)			
LRYGB	11 (69%)	33 (69%)	NS
LSG	5 (31%)	15 (31%)	NS
Cirrhosis etiology, *n* (%)			
NASH	11 (69%)	-	-
Primary biliary cirrhosis	2 (12%)	-	-
Unknown	3 (19%)	-	-
Upper GI endoscopy, *n* (%)			
Esophageal varices	3 (19%)	-	-
Preoperative comorbidities; *n* (%)			
Type 2 diabetes mellitus	4 (25%)	11 (23%)	NS
Hypertension	7 (44%)	23 (48%)	NS
Insulin-resistance	10 (63%)	23 (48%)	NS
Dyslipidemia	7 (44%)	25 (52%)	NS
Preoperative BMI; mean (SD)	39.3 (± 6.8)	39.1 (± 6.3)	NS
Operative time; mean (SD)	115 (± 44)	98 (± 37)	NS
LRYGB	124 (± 48)[a]	111 (± 35)[b]	NS
LSG	98(± 32)[a]	71 (± 24)	NS
Length of stay; days, mean (SD)	3 (± 1)	3 (± 1)	NS
Conversion	0	0	NS
Reoperation	0	0	NS

SD, standard deviation; *LRYGB*, laparoscopic Roux-Y gastric bypass; *LSG*, laparoscopic sleeve gastrectomy; *NASH*, non-alcoholic steatohepatitis; *GI*, gastrointestinal; *BMI*, body mass index

[a] Both groups include one patient with concomitant laparoscopic cholecystectomy performed

[b] Three patients underwent concomitant procedures: one a laparoscopic cholecystectomy, one a laparoscopic hiatal hernia repair, and one patient a ventral hernia repair

non-significant rise to 8.63 ± 3 ($p = 0.52$), and there were no liver decompensations. Long-term morbidity was detected in one patient with cirrhosis who developed a hepatocarcinoma 6 years after surgery requiring orthotopic liver transplantation. We report one late death in the PC group due to a traffic accident.

Table 2 Morbidity and comorbidities remission rate in obese patients with and without cirrhosis submitted to laparoscopic bariatric surgery

	Patients with cirrhosis, *n* (%)	Control, *n* (%)	*p* value
Overall morbidity	5 (31%)	3 (6%)	0.009
Clavien-Dindo < III	3 (19%)	3 (6%)	NS
Clavien-Dindo ≥ III	2 (12%)	0 (0%)	0.013
Comorbidity remission			
Arterial hypertension	1/7 (14%)	15/23 (65%)	0.03
Type 2 diabetes mellitus	2/4 (50%)	7/11 (64%)	NS
Dyslipidemia	6/7 (86%)	20/25 (80%)	NS

Overall morbidity rate was higher in patients with cirrhosis (31% vs. 6%; chi-square $p = 0.009$). There were no differences in mild morbidity rate, defined as Clavien-Dindo < III. Severe morbidity rates, defined as Clavien-Dindo ≥ III, were higher in patients with cirrhosis (12% vs. 0%: chi-square $p = 0.013$). There were no differences in the remission rate of type 2 diabetes mellitus and dyslipidemia. However, patients with cirrhosis presented a lower remission rate of arteria hypertension as compared with patients without cirrhosis (14% vs. 65%; chi-square $p = 0.03$)

The mean %TWL for PC at 3, 6, 12, and 24 months was 17.8% (± 3.7), 22.7% (± 3.9), 27.4% (± 7.5), and 28% (± 8.3), respectively. The mean %TWL was compared with that of the control group at 3, 6, 12 and 24 months, showing no differences between groups (Fig. 1a). Subgroup analysis revealed that within the PC group, LRYGB had a non-significant tendency to higher %TWL in the first 18 months, although at 2 years, the %TWL was equivalent (Table 3, Fig. 1).

Finally, postoperative comorbidity resolution in PC was 14%, 50%, and 85% for AHT, T2DM, and dyslipidemia, respectively (Table 2). There were no differences in the resolution rate for T2DM and dyslipidemia between PC and control group. However, patients without cirrhosis had a significantly higher resolution rate of AHT (65% vs. 14%, $p = 0.03$, Table 2).

Discussion

Intra-abdominal surgery in PC represents a challenge for surgeons as they encompass a group of patients with high rates of morbidity and mortality. LBS in end-stage organ disease has been described in cardiac failure, chronic kidney disease, chronic obstructive pulmonary disease, and liver cirrhosis [9–11, 20]. Particularly in PC, clinical series have shown that bariatric surgery is feasible. However, there is an increase in medical and surgical morbidity as compared with the morbidity reported in patients without cirrhosis. In this study, we report the outcomes of LBS (69% gastric bypass) performed in patients with obesity and cirrhosis compared with a matched group of patients with obesity but without cirrhosis, showing that PC have a significant weight loss and comorbidity resolution, but with a significantly higher morbidity rate.

Traditionally, surgery in PC has been linked to an increase in morbidity, length of hospital stay, cost charges, and mortality [15, 21–27]. Cardiac and major intra-abdominal operations in PC are considered high-risk procedures, increasing bleeding, infectious complications, renal dysfunction, and surgery-specific complications. These risks are in direct relation with the degree of liver dysfunction, as evaluated with the CTP or MELD score. In general, patients with a CTP class A have a 10% mortality rate and increases to 30% and 76% in classes B and C, respectively [22, 24, 25, 28–30]. Since the MELD score is based on objective laboratory measurements, it has been suggested that the MELD score may predict more accurately the risk of mortality in PC undergoing non-transplant surgery. This assumption is because the MELD score lacks the subjectivity of the CTP criteria on clinical parameters such as the magnitude of ascites and the degree of hepatic encephalopathy. Additionally, it has been demonstrated that the MELD score predicts perioperative mortality rising 1% for each MELD point when it is below 20, and over this threshold, it adds 2% thereafter [14]. However, currently there is no evidence of the superiority of one over the other.

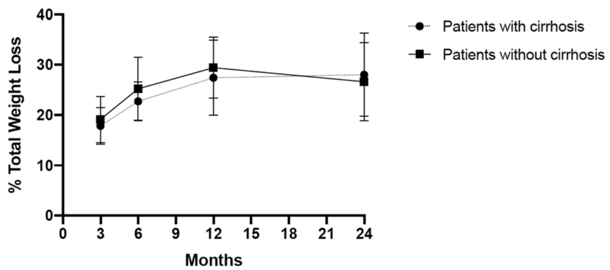
Laparoscopic surgery has been shown to decrease complications in PC, particularly in cholecystectomy and abdominal wall hernia repairs [31]. Regarding bariatric surgery, Brolin et al. [32] published a series of 8 patients undergoing mainly laparotomic Roux-Y gastric bypass showing that 3 out of 8 patients had complications, 1 of 8 had perioperative mortality, and 2 of 8 had late deaths. Further series of LBS have not shown such a high mortality rate, indicating that open surgery may have a detrimental effect in PC [32–47]. In a larger study, Mosko et al. [35] analyzed the database of the Nationwide Inpatient Sample between 1998 and 2007. In this paper, PC submitted to bariatric surgery (not specified whether open or laparoscopic) were compared with patients without cirrhosis. Notably, they demonstrated that PC, even being in the compensated state, presented higher mortality than those without cirrhosis. Expectedly, patients with decompensated cirrhosis had unacceptable higher mortality rates (0.3% for patients without cirrhosis, 0.9% for patients with compensated cirrhosis, and 16.3% for patients with decompensated cirrhosis). Thereafter, most of the published series report LBS mainly in Child A patients with an increase in medical and surgical morbidity, but without an increase in mortality [32–47]. Indeed, the few series that reported mortality after bariatric surgery (open or laparoscopic), the causes of mortality were unrelated to bariatric surgery. Notably, Rebibo et al. [38] published a series of 13 patients with Child A cirrhosis submitted

Table 3 Percentage of total weight loss and excess weight loss for patients with and without cirrhosis

Follow-up	Patients with cirrhosis ($n = 16$)			Patients without cirrhosis ($n = 48$)		
	n (%)	%TWL	%EWL	*n* (%)	%TWL	%EWL
3 months	10 (63%)	17.8	60.9	43 (90%)	19.1	58.9
6 months	8 (50%)	22.7	65.3	42 (88%)	25.2	77.6
12 months	15 (94%)	27.4	80.1	45 (94%)	29.4	90.1
24 months	13 (81%)	28.0	85.6	39 (81%)	26.6	83.2

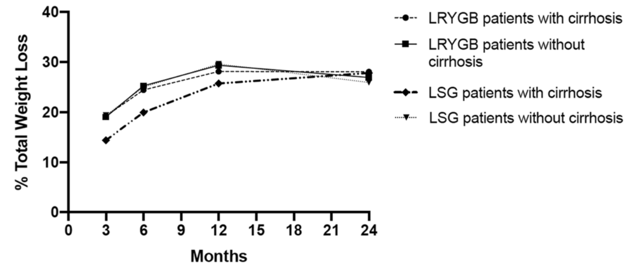
There were no differences in %TWL or %EWL throughout the whole follow-up between groups

TWL, total weight loss; *EWL*, excess weight loss; *n*, number; *%EWL*, percentage of excess weight loss; *%TWL*, percentage of total weight loss a



Follow-up	Patients with cirrhosis	Patients without cirrhosis
3 m	10/16	43/48
6 m	8/16	42/48
12 m	15/16	45/48
24 m	13/16	39/48

b



Follow-up	LRYGP patients with cirrhosis	LRYGP patients without cirrhosis	LSG patients with cirrhosis	LSG patients without cirrhosis
3 m	7/11	30/33	3/5	13/15
6 m	4/11	30/33	3/5	12/15
12 m	9/11	32/33	4/5	13/15
24 m	10/11	28/33	3/5	11/15

Fig. 1 Evolution of the % of total weight loss (%TWL). **a** Evolution of the mean %TWL in obese patients with and without cirrhosis submitted to bariatric surgery at 3, 6, 12, and 24 months after surgery with follow-up for each evaluated month. **b** Subgroup analysis of the evolution of %TWL in obese patients with and without cirrhosis who underwent LRYGB or LSG at 3, 6, 12, and 24 months with follow-up for each evaluated month

to LSG with a 1:2 matched control group of patients without cirrhosis. This paper showed no increase either in surgical morbidity or mortality, suggesting that LSG could be a safer alternative in this group of patients. Our study aimed to compare a group of PC submitted to LBS, mainly LRYGB (69%), with a 1:3 matched control group of patients without cirrhosis. The matching process considered age, gender, BMI, comorbidities, and surgical technique. Our results show that PC had a significantly higher overall and severe (CD ≥ III) morbidity rate as compared with patients without cirrhosis. Additionally, morbidity occurred exclusively in LRYGB, supporting the data of Rebibo et al. [38]. Of note, none of our PC had a liver decompensation, and the severe morbidity in this group corresponded to medical morbidity, namely, atrial fibrillation with rapid ventricular response requiring intensive care unit and electrical cardioversion, and an acute kidney injury secondary to dehydration which required intermediate care unit support. On the other hand, the control group presented only mild surgical complications such as port site seroma, upper gastrointestinal bleeding, and a jejuno-jejunal stenosis, all treated conservatively. Thus, our study supports the feasibility of performing LBS in PC considering that medical complications may occur. Therefore, we consider that a hepatology team, as well as an intensive care unit, should be available to follow the postoperative course. It must be noted that in our center, we have an active liver transplant team that supported us in the postoperative care of our patients. However, it should be noted that a drawback of our study is the retrospective design, which pushed a selection bias in performing LBS only in Child A patients. Thus, our results should not be extrapolated to Child B or C patients.

Regarding bariatric procedures, in our institution the decision of undergoing a LSG or LRYGB is based on initial BMI, comorbid conditions, and symptoms of gastroesophageal reflux. Thus, in patients with a BMI higher than 40 kg/m^2, severe comorbidities or a sum of multiple not-severe comorbidities, and gastroesophageal reflux symptoms, makes a LRYGB more probable, although it is not a rigid indication. Thus, regarding the outcomes of LBS itself, we observed that PC presented a significant and sustained weight loss 2 years after surgery, without differences with the control group. Subgroup analysis within the PC group did not show differences between LRYGB and LSG, although there is a tendency to higher %TWL in the LRYGB operated patients in the first 18 months. Anyhow, although PC group submitted to LSG had a slower pace of weight loss, at 2 years, they achieved a %TWL of 27.8, which is an excellent result in weight loss when the aim of the surgery is to control the progression of the liver disease.

Obesity-related comorbidity resolution is another outcome measured in our study. Most of the literature of LBS in PC focuses on safety and perioperative morbidity. In our study, after 2 years of follow-up, PC presented a 50% resolution of T2DM, 86% resolution of dyslipidemia, but only 14% resolution of AHT. When comparing with the control group, there were no differences in the percentage of resolution of T2DM and dyslipidemia, but AHT had a significantly lower resolution rate in PC (Table 2). Traditionally, AHT is resolved in an average of 70% of cases after LBS [48]. However, a series of bariatric surgery in PC have shown variable resolution rates of AHT. Hanipah et al. [44] reported 86% resolution of ATH, and other series have reported 18.7%, 33%, and 42%, which is far below the average of 70% [37, 40, 45]. It is difficult to hypothesize why our patients had such low resolution rate of AHT. One observation concerning this phenomenon is that most PC have normal or low blood pressure, and patients with previous AHT often become normotensive as the liver disease progresses. There are several vascular, neuro-hormonal, and renal adaptations in the hemodynamics of PC [49], and certainly, bariatric surgery may induce changes in those mechanisms as well. Thus, this is a question that remains without a clear answer.

Finally, and regarding the surgical technique of choice in patients with cirrhosis, some considerations must be mentioned. As aforementioned, most data come from clinical series and no prospective trials have been done. The two most common procedures in all series of PC, and currently in the world, are the LSG and LRYGB [50]. Randomized controlled trials have shown that both procedures offer good outcomes in terms of weight loss and comorbid resolution in patients without cirrhosis [51–53]. Thus, in general terms, both procedures may be considered as equivalents. Nevertheless, PC morbidity and potential mortality should be carefully considered when indicating a bariatric procedure. In this context, LRYGB has disadvantages that need to be mentioned. First, the exclusion of the gastric fundus in which potential bleeding may occur from fundus varices could not be treated endoscopically. Second, if the patient requires later liver transplantation (LT), the Roux en-Y configuration makes it hard to access the biliary tree if it is necessary. Third, there is the uncertainty of drug absorption after LRYGB that may compromise the immunosuppression required to avoid graft rejection, although presumably there is no clinical impact [54]. Finally, the frequent use of acetylsalicylic acid and steroids in transplanted patients may increase the risk of a marginal ulcer [55, 56]. Thus, LSG seems to be an appealing option in this group of patients, with advantages such as less vitamin and protein malabsorption than LRYGB, and additionally, LSG maintains the endoscopic access to the biliary tree in the case of later LT. Drug absorption after LSG has been scarcely evaluated; however, it seems reasonable to assume that there is minor impact in drug absorption unless a specific drug requires an acidic luminal environment to be absorbed.

One major disadvantage of LSG is the eventual development of porto-mesenteric vein thrombosis which may induce liver decompensation in patients with cirrhosis. Porto-mesenteric vein thrombosis has been reported after LSG in PC in three cases, one required rivaroxaban treatment without any further complication, the second required intestinal resection due to mesenteric ischemia, and the most severe case required a LT years later due to portal hypertension and refractory ascites [57–59]. Nevertheless, porto-mesenteric vein thrombosis is an infrequent complication and the benefits obtained with LSG in terms of weight loss and comorbidity resolution outweigh the potential risks.

Since NASH-derived cirrhosis is projected to become the leading indication for LT in the next decade, the role of bariatric surgery in potential candidates for LT needs to be addressed. Safwan et al. [60] reported a series of 11 PC with prior bariatric surgery who ultimately underwent a LT due to liver disease progression. In this paper, although they did not perform a direct matched comparison, the patients and graft survival were equivalent to the historical data of their center. On the other hand, Idriss et al. [61] analyzed a cohort of PC submitted to bariatric surgery matched with PC without bariatric surgery. Interestingly, the authors found that bariatric surgery–operated patients had an increased mortality in the waiting list and an increased delisting rate, mostly based on the appearance of malnutrition and sarcopenia. Therefore, although it seems reasonable to think that optimizing body weight, achieving comorbidity control, and even stabilization or regression of liver fibrosis through bariatric surgery [62] may produce a favorable outcome in PC, the long-term outcomes of bariatric surgery in PC are unknown and malnutrition could be a major issue when patients are enlisted. In this context, we believe that a procedure with less impact in nutritional deficiencies should be preferred.

Conclusion

Bariatric surgery in patients with obesity and Child A cirrhosis can be performed in a selected group of patients that will benefit from the weight loss effect of the surgery and its impact on comorbidities improvement, albeit with the risk of increased medical complications. Due to the complexity and increased risk of complication in this group of patients, we believe that this procedure should be carried out in high volume center of bariatric surgery along with integrated multidisciplinary hepatology and liver transplant teams and intensive care units to provide immediate and adequate support in case of surgical or medical complications. Due to its safer surgical profile, lower impact of pharmacokinetics and dynamics of drugs, access to the biliary tree, and lower impact in macro and micronutrients absorption, we believe that whenever possible, sleeve gastrectomy should be the procedure of choice to treat patients with obesity and Child A cirrhosis.

Compliance with Ethical Standards

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

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. For this type of study formal consent is not required.

Informed Consent Informed consent was obtained from all patients before surgery.

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