



Longitudinal Comparison of the Effect of Gastric Bypass to Sleeve Gastrectomy on Liver Function in a Bariatric Cohort: Tehran Obesity Treatment Study (TOTS)

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Abstract

Background Patients with morbid obesity commonly have fatty liver disease and elevated liver enzymes. While surgery effectively induces weight loss, bariatric techniques may differ regarding liver function improvement.

Objectives To evaluate and compare the trends of liver function recovery after gastric bypass surgery (GB) with sleeve gastrectomy (SG).

Setting University hospitals, Iran.

Methods Adult bariatric candidates without a history of alcohol consumption or other etiologies of liver disease who underwent SG ($n = 682$) or GB ($n = 355$) were included. Trends of weight loss parameters and alanine transaminase (ALT), aspartate transaminase (AST), and alkaline phosphatase (ALP) at 0, 6 (in 90.4%), 12 (in 83.5%), and 24 months (in 67.1%) were compared using generalized estimating equations method.

Results Overall, 1037 patients with mean age of 38.4 ± 11.2 and mean body mass index of 44.9 ± 6.2 kg/m² were analyzed. Seventy-eight percent of patients had fatty liver by ultrasound. Both GB and SG patients lost significant weight, with GB patients having a higher percentage of excess weight loss at 24 months (80.1% vs. 75.9%, $P_{\text{between-group}} = .008$). SG patients showed more favorable trends in liver chemistries with significantly lower ALT at 12 months and AST and ALP levels at 6 and 12 months. However, the two groups were comparable at 24 months. Significantly more GB patients developed high ALT at 6 and high AST at 6 and 12 months. Undergoing GB was associated with smaller 0–12-month changes in ALT, AST, and ALP.

Conclusions Bariatric surgery resulted in improvement in liver function parameters, with SG showing advantages over GB in the first postoperative year.

Keywords Bariatric surgery · Gastric bypass · Nonalcoholic fatty liver disease · Liver function tests · Morbid obesity

Introduction

With the growing obesity pandemic, its associated complications are also on the rise, making nonalcoholic fatty liver disease (NAFLD) the leading cause of chronic liver disease in

many countries including the USA [1]. While the prevalence of the condition ranges from 6.3 to 33% in the general population, it can reach up to 69% in patients with type 2 diabetes mellitus (T2D) [2–4]. Bariatric surgeons yet may encounter this condition in up to 94% of their patients with morbid obesity [5]. Storage of extra fat in the liver and consequent steatosis can take the form of nonalcoholic fatty liver (NAFL), a relatively benign condition that imposes very little risk of progression, or nonalcoholic steatohepatitis (NASH), the inflammatory form of the disease involving hepatocyte injury. The latter presentation can progress to liver fibrosis, cirrhosis, and on rare occasions, hepatocellular carcinoma [6, 7].

The degree of liver damage due to NAFLD is reflected in macroscopic and microscopic histologic changes in liver parenchyma as well as liver function alterations evident by the

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rise in liver chemistries. Serum aspartate transaminase (AST) and the more liver-specific alanine transaminase (ALT) are often elevated in patients with obesity and morbid obesity [6]. Alkaline phosphatase (ALP) is another biomarker of liver function that reflects the mixed-pattern liver damage induced by NAFLD [8].

Bariatric surgery has become the mainstay of treatment in morbid obesity and is expected to halt and reverse the liver damage mainly by inducing weight loss [9, 10]. Histologic derangements and hepatocyte injury are expected to resolve postoperatively, which in turn should result in normalization of liver chemistries in the blood [11]. While all bariatric techniques induce significant weight loss, their individual effects on the liver are still under investigation. Gastric bypass (GB) and sleeve gastrectomy (SG) are the two most commonly performed bariatric surgery procedures worldwide [12]. We have previously shown the comparable effectiveness of these two procedures on weight loss and resolution of metabolic syndrome in our bariatric cohort [13]. However, there has recently been a concern that some patients may experience an initial deterioration of liver function, which could hinder the postoperative course [14, 15]. We thus aimed to investigate the longitudinal effect of these two bariatric surgical methods on liver chemistries in a 2-year follow-up.

Material and Methods

Study Design and Participants

The Tehran Obesity Treatment Study (TOTS) is a prospective cohort of patients with morbid obesity who undergo bariatric surgery, mainly SG (gastric tube created over a 36-F bougie with exclusion of 80% of the stomach) or one of two types of GB procedures, Roux-en-Y (using an alimentary limb of 100–150 cm and a biliopancreatic limb of 50 cm) or mini-gastric bypass (a loop gastroenterostomy of 150–200 cm) [16]. For the present study, all patients aged 15–65 years with morbid obesity class II (body mass index (BMI) between 35 and 39.9 kg/m²) who had comorbidities or class III (BMI \geq 40 kg/m²) presenting to our bariatric center from March 2013 to March 2017 were evaluated to enter the study. From the potential 1191 patients in our cohort, after exclusion of patients with a history of heavy alcohol consumption (average daily pure alcohol consumption of \geq 20 g for women and \geq 30 g for men, or history of past excessive drinking) ($n = 64$), seropositivity for viral hepatitis ($n = 6$), and other causes of liver pathology ($n = 84$), 1037 cases were included.

Liver ultrasound categorized patients as normal or having grade I–III fatty liver based on the degree of steatosis, with the latter broadly grouped as NAFLD. Anthropometrics and laboratory indices including liver enzymes and lipid profile were recorded preoperatively and at 6, 12, and 24 months

postoperatively. High transaminase levels were defined as AST or ALT level \geq 40 U/L, and ideal body weight as that equivalent to a BMI of 25 kg/m². Homeostatic model assessment for insulin resistance index (HOMA-IR) was used to determine insulin resistance (IR) in patients, which was defined as HOMA-IR \geq 2.5.

Statistical Analysis

Continuous variables are expressed as mean \pm standard deviation (SD), categorical data as frequency and percentages, and non-normally distributed data as median [25–75 inter-quartile range (IQR)]. Normally-distributed variables were analyzed using two-tailed, independent samples *t* test; non-normally distributed variables using Mann–Whitney test; and categorical variables using chi-squared test. Generalized estimating equations (GEE) method was used to evaluate and compare the trends of BMI, percentage of excess weight loss (%EWL), ALT, AST, ALP, and NAFLD prevalence. Bonferroni post hoc test was used to determine during which intervals the difference in trends occurred. Overall change over time in each group (P_{trend}), general group difference in outcome variable ($P_{\text{between-group}}$), and group by time interaction effect ($P_{\text{interaction}}$, the difference in change over time between groups) were checked in separate models and reported. Association of change (Δ) in liver chemistries between preoperative and 12 or 24 months postoperative values with study variables was analyzed using univariate and multivariate linear regression analyses. A *P* value $< .05$ was considered statistically significant.

Results

Of the total 1037 patients, 682 underwent SG and 355 underwent GB. The mean age of participants was 38.4 ± 11.2 years with a mean BMI of 44.9 ± 6.2 kg/m² and 81.9% were female. Overall, 78% of the participants had fatty liver. Hypertension was present in 22.2%, T2D in 19.4%, and insulin resistance in 79.1% of patients (Table 1). The GB group had a higher prevalence of females, BMI, fasting plasma glucose, hemoglobin A1C, and prevalence of T2D but lower cholesterol, low-density lipoprotein, and prevalence of high AST.

Follow-up rates were 90.4% (887/990) at 6 months, 83.5% (711/851) at 12 months, and 67.1% (256/378) at 24 months, comparable between the two surgery groups. Patients in both groups lost significant weight throughout the follow-up period (P_{trend} (SG and GB) $< .001$ for both BMI and %EWL, Table 2). GB patients demonstrated a greater change over time regarding both BMI and %EWL ($P_{\text{interaction}} < .001$ for BMI and $= .004$ for %EWL) and achieved a significantly higher %EWL at 24 months: 80.1% vs. 75.9% ($P_{\text{between-group}} = .008$ for %EWL, Fig. 1a, b). Percentage of total body weight loss

Table 1 Baseline characteristics of study participants by surgery group

Variables	Total N = 1037	SG N = 682 (65.8%)	GB N = 355 (34.2%)	P value
Age (year)	38.4 ± 11.2	38.2 ± 11.7	38.8 ± 10.4	.402
Sex, female	849 (81.9)	534 (78.3)	315 (88.7)	<.001*
Weight (kg) [range 74–206]	121.0 ± 20.7	120.5 ± 20.9	121.9 ± 20.3	.318
WC (cm)	124.4 ± 14.0	124.1 ± 14.1	125.1 ± 13.9	.286
BMI (kg/m ²) [range 30.9–70.2]	44.9 ± 6.2	44.4 ± 6.0	45.7 ± 6.4	.001*
BMI group				.035*
< 40 kg/m ²	207 (20)	149 (21.8)	58 (16.3)	
≥ 40 kg/m ²	830 (80)	533 (78.2)	297 (83.7)	
Smoking status				.146
Never smokers	791 (80.9)	514 (79.6)	277 (83.4)	
Current smokers	129 (13.2)	95 (14.7)	34 (10.2)	
Former smokers	58 (5.9)	37 (5.7)	21 (6.3)	
Hypertension	230 (22.2)	150 (22.0)	80 (22.5)	.842
Diabetes mellitus	201 (19.4)	104 (15.2)	97 (27.3)	<.001*
Fatty liver	809 (78.0)	527 (77.3)	282 (79.4)	.425
Fatty liver grade				.878
Grade I	265 (25.6)	173 (25.4)	92 (25.9)	
Grade II	352 (33.9)	228 (33.4)	124 (34.9)	
Grade III	192 (18.5)	126 (18.5)	66 (18.6)	
FPG (mg/dl)	108.1 ± 36.1	105.5 ± 30.7	113.1 ± 44.2	.004*
HbA1C (%)	5.7 ± 1.1	5.6 ± 1.0	5.9 ± 1.3	<.001*
TG (mg/dl)	142 [103–190]	140 [103–189.5]	144 [101–195.5]	.959
Cholesterol (mg/dl)	194.2 ± 43.1	197.2 ± 44.2	188.5 ± 40.5	.002*
HDL (mg/dl)	48.0 ± 11.7	47.8 ± 11.6	48.5 ± 11.9	.382
LDL (mg/dl)	112.0 ± 33.4	114.9 ± 33.7	106.4 ± 32.1	<.001*
AST (U/L)	23.7 ± 14.4	24.0 ± 14.3	23.1 ± 14.6	.340
High AST (≥ 40 U/L)	94 (9.1)	71 (10.4)	23 (6.5)	.036*
ALT (U/L)	29.7 ± 23.0	30.5 ± 22.9	28.2 ± 23.0	.137
High ALT (≥ 40 U/L)	181 (17.5)	130 (19.1)	51 (14.4)	.060
AST/ALT ratio	0.90 ± 0.33	0.89 ± 0.31	0.92 ± 0.36	.116
High AST/ALT (≥ 1)	311 (30.0)	205 (30.1)	106 (29.9)	.958
ALP (U/L)	193.0 ± 81.5	191.6 ± 91.2	195.7 ± 59.2	.446
High ALP (≥ 100 U/L)	944 (93.7)	612 (93.0)	332 (95.1)	.186
Serum albumin (g/L)	4.3 ± 0.4	4.3 ± 0.4	4.3 ± 0.3	.155
Platelet count (10 ⁶ /μL)	284.0 ± 67.7	284.6 ± 67.0	283.0 ± 69.0	.724
Fasting insulin (mIU/L)	17.8 [11.6–25.1]	18.0 [12.1–25.4]	17.4 [10.3–24.4]	.051
HOMA-IR ^a	4.4 [2.8–6.7]	4.4 [2.9–6.8]	4.3 [2.6–6.6]	.514
IR ^b	659 (79.1)	436 (80.1)	223 (77.2)	.313

Values are expressed as mean ± SD, number (percentages), or median [IQR]

SG, sleeve gastrectomy; GB, gastric bypass; WC, waist circumference; BMI, body mass index; FPG, fasting plasma glucose; HbA1c, glycosylated hemoglobin; TG, triglyceride; HDL, high-density lipoprotein; LDL, low-density lipoprotein; AST, aspartate transaminase; ALT, alanine transaminase; ALP, alkaline phosphatase; HOMA-IR, homeostatic model assessment-insulin resistance index; IR, insulin resistant

*Denotes statistically significant difference

^aHOMA-IR was calculated in 834 patients

^bIR was defined as HOMA-IR ≥ 2.5

Table 2 Weight loss results, liver chemistries, and fatty liver prevalence over time by surgery group

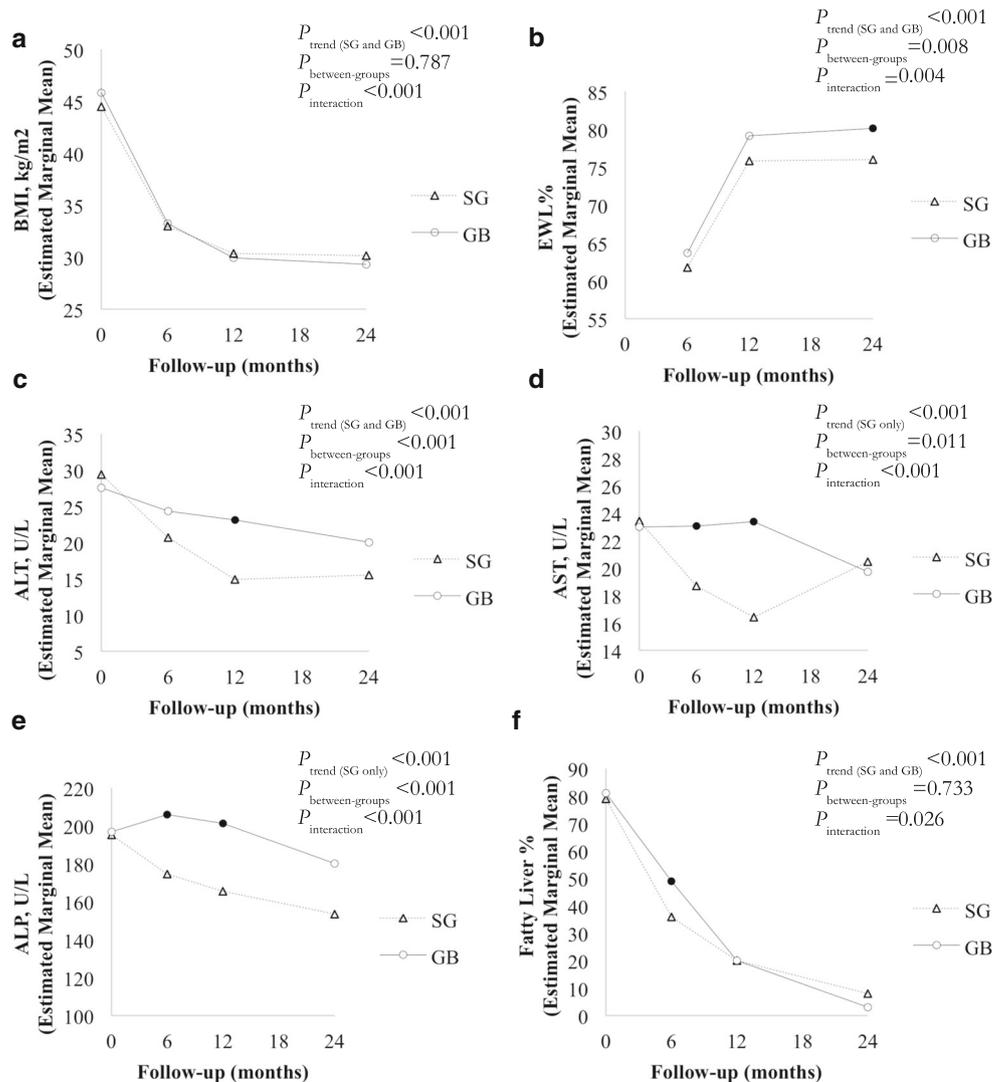
Variables	Surgery	N	Preoperative	Postoperative			<i>P</i> _{trend}	<i>P</i> _{between-groups}	<i>P</i> _{interaction}
				6 months	12 months	24 months			
BMI (kg/m ²)	SG	658	44.5 ± 6.0	33.1 ± 5.0	30.4 ± 4.9	29.9 ± 5.2	< .001*	.787	< .001*
	GB	339	45.8 ± 6.5	33.3 ± 5.3	29.8 ± 4.9	29.3 ± 6.3	< .001*		
EWL%	SG	392	–	61.8 ± 17.2	75.8 ± 20.5	75.9 ± 22.0	< .001*	.008*	.004*
	GB	213	–	63.6 ± 15.9	79.1 ± 19.6	80.1 ± 28.2	< .001*		
AST (U/L)	SG	558	23.4 ± 13.4	18.7 ± 21.5	16.3 ± 6.4	20.4 ± 24.8	< .001*	.011*	< .001*
	GB	312	23.0 ± 14.2	23.1 ± 11.0	23.4 ± 11.8	19.4 ± 7.4	.341		
ALT (U/L)	SG	557	29.3 ± 21.2	20.7 ± 34.6	14.8 ± 8.2	15.4 ± 7.4	< .001*	< .001*	< .001*
	GB	313	27.54 ± 22.2	24.4 ± 19.7	23.2 ± 13.7	19.8 ± 9.4	< .001*		
ALP (U/L)	SG	503	195.2 ± 98.2	171.7 ± 61.9	166.5 ± 58.5	155.3 ± 78.7	< .001*	< .001*	< .001*
	GB	283	196.9 ± 59.9	206.3 ± 72.1	202.7 ± 70.3	179.7 ± 72.9	.708		
Fatty liver, n (%)	SG	571	449 (78.6)	176 (35.5)	62 (20.1)	5 (7.9)	< .001*	.733	.026*
	GB	319	257 (80.6)	140 (49.1)	37 (21.1)	1 (2.4)	< .001*		

Data is presented as mean ± SD unless otherwise stated. Follow-up rates at 6, 12, and 24 months were 91.4% (905/990), 83.5% (833/997), and 64.1% (256/401) respectively

BMI, body mass index; SG, sleeve gastrectomy; GB, gastric bypass; EWL, excess weight loss; AST, aspartate transaminase; ALT, alanine transaminase; ALP, alkaline phosphatase

*Denotes statistically significant difference

Fig. 1 **a** Body mass index (BMI), **b** % excess weight loss (EWL), **c** alanine transaminase (ALT), **d** aspartate transaminase (AST), **e** alkaline phosphatase (ALP), and **f** fatty liver% trends in two groups of bariatric patients undergoing sleeve gastrectomy (SG) or gastric bypass (GB) during 24 months of follow-up. *P* values for comparison of the trends between the two groups are presented on each figure. A solid black marker signifies statistically significant difference between two groups at respective time point. Follow-up rates were 90.4% (887/990) at 6 months, 83.5% (711/851) at 12 months, and 67.1% (256/378) at 24 months



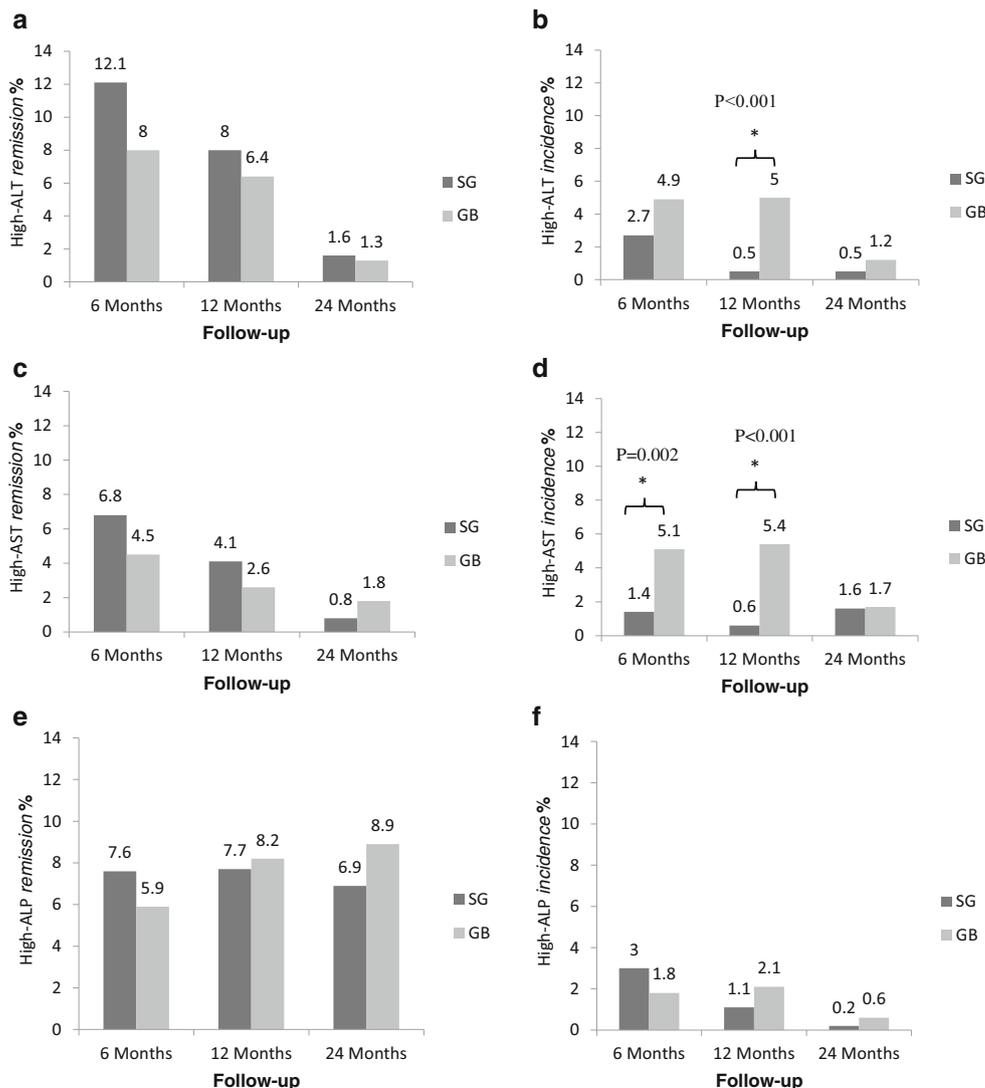
(%TBWL), moreover, was higher in GB patients at 6 and 12 months, $27.7 \pm 5.6\%$ vs. $26.1 \pm 5.5\%$ and $34.5 \pm 8.1\%$ vs. $31.9 \pm 7.6\%$, respectively ($P < .001$); at 24 months, however, %TBWL was comparable between the two groups, $33.0 \pm 11.4\%$ vs. $31.9 \pm 8.5\%$ ($P = .414$).

ALT decreased significantly during the follow-up in both groups ($P_{\text{trend (SG and GB)}} < .001$) but to a greater extent in the SG group ($P_{\text{interaction}} < .001$). SG patients experienced a faster decrease in ALT during the first year, leading to a significantly lower ALT level at 12 months ($P_{\text{between-group}}$ and $P_{\text{interaction}} < .001$, Fig. 1c). On the other hand, AST decreased significantly only in the SG group ($P_{\text{trend (GB)}} = .341$). SG patients demonstrated significantly lower AST values at 6 and 12 months ($P_{\text{interaction}} < .001$, $P_{\text{between-group}} = .011$, Fig. 1d). A similar pattern was also observed for ALP, which only decreased consistently in the SG group throughout the follow-up ($P_{\text{trend (SG)}} < .001$, $P_{\text{trend (GB)}} = .708$), with a significantly different trend than GB patients ($P_{\text{between-group}}$ and $P_{\text{interaction}} < .001$, Fig. 1e).

Prevalence of fatty liver showed a significant and comparable decrease during the follow-up in both groups ($P_{\text{trend (SG and GB)}} < .001$), from 78.6% and 80.6% at baseline to 7.9% and 2.4% at 24 months in the SG and GB groups, respectively ($P_{\text{between-group}} = .733$). More SG patients experienced resolution of fatty liver during the first 6 months ($P_{\text{interaction}} = .026$, Fig. 1f).

High ALT remission rates were comparable between the two groups, decreasing from 12.1% and 8% at 6 months to 1.6% and 1.3% at 2 years in the SG and GB groups, respectively (Fig. 2a). High ALT incidence rate, on the other hand, was lower in the SG group, with the difference being significant at 12 months (.5% vs. 5%, $P < .05$, Fig. 2b). High AST remission rates were slightly higher in the SG group but none reached statistical significance (Fig. 2c). However, high AST incidence rate was significantly lower in the SG group at 6 and 12 months ($P < .05$ for both comparisons, Fig. 2d). High ALP remission and incidence rates were comparable between the two groups (Fig. 2e, f).

Fig. 2 a–f High alanine transaminase (ALT), aspartate transaminase (AST), and alkaline phosphatase (ALP) remission and incidence rates in the sleeve gastrectomy (SG) and gastric bypass (GB) groups during the 24-month follow-up. Asterisk indicates statistically significant difference between the two groups at the designated follow-up. Follow-up rates were 90.4% (887/990) at 6 months, 83.5% (711/851) at 12 months, and 67.1% (256/378) at 24 months



Multivariate regression analysis (Table 3) revealed that baseline AST level was the strongest determinant of Δ AST 0–12 months (beta 0.91, $P < .001$), followed by surgery type (gastric bypass, beta -7.19 , $P < .001$) and presence of fatty liver (beta -1.91 , $P = .047$). For 0–24 months, only baseline AST correlated with Δ AST (beta 0.87, $P < .001$). In addition, baseline ALT was associated with Δ ALT 0–12 (beta 0.925, $P < .001$) and 0–24 (beta 0.922, $P < .001$). Undergoing GB was the second strongest factor associated negatively with both Δ ALT 0–12 and 0–24 months (beta -8.67 and -5.05 , respectively). For Δ ALP, higher baseline ALP was associated with a greater Δ ALP 0–12 and 0–24 months (beta 0.84 and 0.47, respectively, $P < .001$). Undergoing GB was associated with smaller Δ ALP 0–12 months (beta -36.96 , $P < .001$). Moreover, a significant correlation was found between the baseline ALT and weight change at 6 and 12 months (Pearson coefficients $-.188$ and $-.173$ respectively, $P < .001$) as well as AST and weight change at 12 months (coefficient: $-.143$, $P = .002$), only in the SG group.

Discussion

Bariatric surgery effectively results in weight loss and resolution of most obesity-related comorbidities including liver dysfunction [13, 17]. Our comparison of the two most popular bariatric surgeries, SG and GB, demonstrated that both methods, overall, resulted in substantial weight loss and improvements in liver function parameters at 2 years after surgery. SG, moreover, showed noticeable advantages over GB

in normalization of liver transaminases during the first postoperative year.

Improvement in liver parameters after bariatric surgery in our report is in line with other studies [9, 11]. Although a correlation is rationally assumed and frequently reported between the degree of weight loss and liver function recovery [9, 11, 18], the underlying mechanisms by which liver improvement occurs need to be further investigated. Ooi and colleagues showed that ALT normalization could occur in as early as 2 months after surgery, well before ideal weight goals were achieved [10]. More interestingly, however, Alizai et al. showed that an initial marked weight loss might adversely affect liver function, measured by LiMAX test (cytochrome P450 capacity), during the first 6 months after surgery [19]. In our experience, we observed two patients with mild-moderate NAFLD who developed fulminant liver dysfunction at 1 year postoperatively after experiencing superb excess weight losses of 96% at 8 months in one and 104% at 12 months in another [20, 21], similar to other observations [22]. While our patients had undergone mini-gastric bypass and were found to have a too-short common channel postoperatively, we have not seen such dramatic deterioration in any one of our SG patients at our center with similar %EWLs. Accordingly, Mahawar et al. argued that a bypass limb length of more than 150 cm for bypass procedures might put some patients at risk of compromising liver function due to severe malabsorption [14]. Our findings support this hypothesis since our GB patients had comparable weight loss to SG patients at 1 year, yet suboptimal liver recovery. The overall trend, however, followed the desired improvement in liver function for both techniques by 2 years.

Table 3 Multivariate linear regression analysis for delta (Δ) change in aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP) levels at 12- and 24-month follow-ups

Dependent variable	Independent variable	12 months			24 months			Adjusted R^2	
		Standardized beta	<i>B</i> (SE)	<i>P</i> value	Standardized beta	<i>B</i> (SE)	<i>P</i> value	12 months	24 months
Δ AST	Gastric bypass	-0.225	-7.199 (0.831)	< .001	0.016	0.790 (4.193)	.851	.686	.321
	Female	-0.028	-1.295 (1.195)	.279	-0.028	-1.996 (6.030)	.741		
	AST	0.802	0.911 (0.030)	< .001*	0.589	0.873 (0.124)	< .001*		
Δ ALT	Fatty liver	-0.052	-1.913 (0.958)	.047*	.009	0.457 (4.426)	.918	.790	.823
	Gastric bypass	-0.187	-8.679 (0.979)	< .001*	-0.130	-5.053 (1.665)	.003*		
	Female	-0.054	-3.656 (1.463)	.013*	-0.071	-3.840 (2.353)	.106		
	ALT	0.878	0.925 (0.023)	< .001*	0.915	0.922 (.044)	< .001*		
Δ ALP	Fatty liver	-0.009	-0.509 (1.143)	.656	0.043	1.807 (1.794)	.316	.670	.167
	Hypertension	-0.046	-2.467 (1.128)	.029*	-0.042	-1.858 (1.917)	.335		
	Gastric bypass	-0.168	-36.963 (6.063)	< .001*	-0.144	-22.365 (14.612)	.129		
	Female	-0.030	-9.289 (8.510)	.276	0.058	12.834 (21.470)	.551		
	ALP	0.802	0.840 (0.029)	< .001*	0.390	0.476 (0.116)	< .001*		

Follow-up rates were 83.5% (833/997) at 12 months and 64.1% (256/401) at 24 months

SE, standard error

*Denotes statistically significant difference

GB was shown in a large long-term study incorporating liver biopsy to be superior to adjustable gastric banding regarding improvement of all aspects of NAFLD, which correlated with the amount of weight loss [23]; this superiority of GB was also observed in comparison with omega-loop gastric bypass (using a 200-cm omega loop), which despite achieving better weight loss results, caused transient rise in liver transaminases at 1 year [24]. In an interesting study by Billeter et al. comparing GB and SG at 12 months, SG showed significantly better results in terms of ALT and AST improvement and normalization [25]. We demonstrated a similar pattern of transient deterioration and/or later recovery of liver function after GB compared with SG, reflected by significantly higher AST and ALT levels in the short term, lower rates of high ALT/AST remission, and most interestingly, higher incidence rates of high ALT/AST. We speculate that malabsorption may aggravate the suboptimal reparative capacity and antioxidant reserve of the liver [26] in a setting of increased free fatty acid mobilization, oxidation, and free radical species production caused by rapid weight loss [27, 28]. Deficiency of factor VII, protein S, and protein C has been reported after GB surgery but not SG [29]. Kalinowski et al. in a study of GB vs. SG with comparable 1-year %EWL results showed that patients with NAFL or NASH undergoing GB may experience a transient deterioration of liver function evident by increased prothrombin time and ALP and decreased albumin after surgery, returning only to baseline at 1 year in the GB group; patients with NASH who underwent SG, however, did better at 1 month and improved in their AST, ALT, gamma-glutamyl transpeptidase, and lactate dehydrogenase at 1 year [30]. Whether this effect is shared between all malabsorptive procedures remains to be investigated.

Finally, our results could have been more robust if complemented with liver biopsy results to correlate with histologic features in the liver. In addition, incorporation of variables reflective of liver synthetic capacity, such as albumin and prothrombin time/international normalized ratio could add more insight into this comparison of bariatric surgical procedures. However, these were not feasible in our patients and were beyond the scope of the current report. We are aiming to follow the patients with Fibroscan test in the future to have an additional measure of liver improvement. Last but not least, follow-up rates were not ideal at 2 years after surgery, which considered together with the fewer number of patients in the second postoperative year, could have affected the power of statistical analysis.

Conclusion

We demonstrated transiently better liver function after SG at 1 year compared with GB in our patients with morbid obesity.

While these results are not strong enough to recommend any change in the current practice, it highlights the necessity of more research on the short- and long-term effects of various bariatric techniques on the liver, which may ultimately result in the preference of one technique, especially for patients with established liver problems.

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Compliance with Ethical Standards

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. This study was reviewed and approved by the institutional Human Research Review Committee (No. 2ECRIES 93/03/13) and written informed consent was obtained from all patients prior to enrollment.

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

References

1. Younossi ZM, Stepanova M, Afendy M, et al. Changes in the prevalence of the most common causes of chronic liver diseases in the United States from 1988 to 2008. *Clin Gastroenterol Hepatol.* 2011;9(6):524–30. <https://doi.org/10.1016/j.cgh.2011.03.020>.
2. Chalasani N, Younossi Z, Lavine JE, et al. The diagnosis and management of nonalcoholic fatty liver disease: practice guidance from the American Association for the Study of Liver Diseases. *Hepatology.* 2018;67(1):328–57. <https://doi.org/10.1002/hep.29367>.
3. Leite NC, Salles GF, Araujo ALE, et al. Prevalence and associated factors of non-alcoholic fatty liver disease in patients with type-2 diabetes mellitus. *Liver Int.* 2009;29(1):113–9. <https://doi.org/10.1111/j.1478-3231.2008.01718.x>.
4. Targher G, Bertolini L, Padovani R, et al. Prevalence of nonalcoholic fatty liver disease and its association with cardiovascular disease among type 2 diabetic patients. *Diabetes Care.* 2007;30(5):1212–8. <https://doi.org/10.2337/dc06-2247>.
5. Balupuri S, Cheung AC, Mahawar KK, et al. Non-alcoholic fatty liver disease (NAFLD) and bariatric surgery. In: Agrawal S, editor. *Obesity, bariatric and metabolic surgery: a practical guide.* Cham: Springer International Publishing; 2016. p. 629–36.
6. Vernon G, Baranova A, Younossi ZM. Systematic review: the epidemiology and natural history of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis in adults. *Aliment Pharmacol Ther.* 2011;34(3):274–85. <https://doi.org/10.1111/j.1365-2036.2011.04724.x>.
7. Matteoni CA, Younossi ZM, Gramlich T, et al. Nonalcoholic fatty liver disease: a spectrum of clinical and pathological severity. *Gastroenterology.* 1999;116(6):1413–9.
8. Kwo PY, Cohen SM, Lim JK. ACG clinical guideline: evaluation of abnormal liver chemistries. *Am J Gastroenterol.* 2017;112(1):18–35. <https://doi.org/10.1038/ajg.2016.517>.
9. Burza MA, Romeo S, Kotronen A, et al. Long-term effect of bariatric surgery on liver enzymes in the Swedish Obese Subjects

- (SOS) study. *PLoS One*. 2013;8(3):e60495. <https://doi.org/10.1371/journal.pone.0060495>.
10. Ooi GJ, Burton PR, Doyle L, et al. Effects of bariatric surgery on liver function tests in patients with nonalcoholic fatty liver disease. *Obes Surg*. 2017;27(6):1533–42. <https://doi.org/10.1007/s11695-016-2482-8>.
 11. Bower G, Toma T, Harling L, et al. Bariatric surgery and non-alcoholic fatty liver disease: a systematic review of liver biochemistry and histology. *Obes Surg*. 2015;25(12):2280–9. <https://doi.org/10.1007/s11695-015-1691-x>.
 12. Angrisani L, Santonicola A, Iovino P, et al. Bariatric surgery worldwide 2013. *Obes Surg*. 2015;25(10):1822–32. <https://doi.org/10.1007/s11695-015-1657-z>.
 13. Barzin M, Motamedi MAK, Serahati S, et al. Comparison of the effect of gastric bypass and sleeve gastrectomy on metabolic syndrome and its components in a cohort: Tehran Obesity Treatment Study (TOTS). *Obes Surg*. 2017;27(7):1697–704. <https://doi.org/10.1007/s11695-016-2526-0>.
 14. Mahawar KK, Kumar P, Parmar C, et al. Small bowel limb lengths and Roux-en-Y gastric bypass: a systematic review. *Obes Surg*. 2016;26(3):660–71. <https://doi.org/10.1007/s11695-016-2050-2>.
 15. Mahawar KK. Another fatal outcome with a biliopancreatic limb length of 200 cm with one anastomosis gastric bypass. *Obes Surg*. 2017;27(7):1882–3. <https://doi.org/10.1007/s11695-017-2695-5>.
 16. Barzin M, Hosseini F, Motamedi MA, et al. Bariatric surgery for morbid obesity: Tehran Obesity Treatment Study (TOTS) rationale and study design. *JMIR Res Protoc*. 2016;5(1):e8. <https://doi.org/10.2196/resprot.5214>.
 17. Peterli R, Wolnerhanssen BK, Vetter D, et al. Laparoscopic sleeve gastrectomy versus Roux-Y-gastric bypass for morbid obesity-3-year outcomes of the prospective randomized Swiss Multicenter Bypass Or Sleeve Study (SM-BOSS). *Ann Surg*. 2017;265(3):466–73. <https://doi.org/10.1097/sla.0000000000001929>.
 18. Aller R, Pacheco D, Izaola O, et al. Effect on liver enzymes of biliopancreatic diversion: 4 years of follow-up. *Ann Nutr Metab*. 2015;66(2–3):132–6. <https://doi.org/10.1159/000375506>.
 19. Alizai PH, Wendl J, Roeth AA, et al. Functional liver recovery after bariatric surgery—a prospective cohort study with the LiMAX test. *Obes Surg*. 2015;25(11):2047–53. <https://doi.org/10.1007/s11695-015-1664-0>.
 20. Motamedi MAK, Barzin M, Ebrahimi M, et al. Severe fatal protein malnutrition and liver failure in a morbidly obese patient after mini-gastric bypass surgery: case report. *Int J Surg Case Rep*. 2017;33(71–4). <https://doi.org/10.1016/j.ijscr.2017.02.033>.
 21. Motamedi MAK, Rakhshani N, Khalaj A, et al. Biopsy-proven progressive fatty liver disease nine months post mini-gastric bypass surgery: a case study. *Int J Surg Case Rep*. 2017;39(168–71). <https://doi.org/10.1016/j.ijscr.2017.07.062>.
 22. Tsai JH, Ferrell LD, Tan V, et al. Aggressive non-alcoholic steatohepatitis following rapid weight loss and/or malnutrition. *Mod Pathol*. 2017;30(6):834–42. <https://doi.org/10.1038/modpathol.2017.13>.
 23. Caiazzo R, Lassailly G, Leteurtre E, et al. Roux-en-Y gastric bypass versus adjustable gastric banding to reduce nonalcoholic fatty liver disease: a 5-year controlled longitudinal study. *Ann Surg*. 2014;260(5):893–8; discussion 98–9. <https://doi.org/10.1097/sla.0000000000000945>.
 24. Kruschitz R, Luger M, Kienbacher C, et al. The effect of Roux-en-Y vs. omega-loop gastric bypass on liver, metabolic parameters, and weight loss. *Obes Surg*. 2016;26(9):2204–12. <https://doi.org/10.1007/s11695-016-2083-6>.
 25. Billeter AT, Senft J, Gotthardt D, et al. Combined non-alcoholic fatty liver disease and type 2 diabetes mellitus: sleeve gastrectomy or gastric bypass?—a controlled matched pair study of 34 patients. *Obes Surg*. 2016;26(8):1867–74. <https://doi.org/10.1007/s11695-015-2006-y>.
 26. van Zutphen T, Ciapaite J, Bloks VW, et al. Malnutrition-associated liver steatosis and ATP depletion is caused by peroxisomal and mitochondrial dysfunction. *J Hepatol*. 2016;65(6):1198–208. <https://doi.org/10.1016/j.jhep.2016.05.046>.
 27. Csak T, Ganz M, Pespisa J, et al. Fatty acid and endotoxin activate inflammasomes in mouse hepatocytes that release danger signals to stimulate immune cells. *Hepatology*. 2011;54(1):133–44. <https://doi.org/10.1002/hep.24341>.
 28. Verna EC, Berk PD. Role of fatty acids in the pathogenesis of obesity and fatty liver: impact of bariatric surgery. *Semin Liver Dis*. 2008;28(4):407–26. <https://doi.org/10.1055/s-0028-1091985>.
 29. Lupoli R, Milone M, Di Minno A, et al. Haemostatic and fibrinolytic changes in obese subjects undergoing bariatric surgery: the effect of different surgical procedures. *Blood Transfus*. 2015;13(3):442–7. <https://doi.org/10.2450/2014.0183-14>.
 30. Kalinowski P, Paluszkiewicz R, Ziarkiewicz-Wroblewska B, et al. Liver function in patients with nonalcoholic fatty liver disease randomized to Roux-en-Y gastric bypass versus sleeve gastrectomy: a secondary analysis of a randomized clinical trial. *Ann Surg*. 2017;266(5):738–45. <https://doi.org/10.1097/SLA.0000000000002397>.