Caution for liver injury after bariatric surgery: logistic regression of risk factors for early elevation of liver enzymes after surgery

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Abstract

The reasons for the influence of bariatric surgery (BS) on the early abnormal increase of liver enzymes and liver injury remain unclear. We found abnormal elevation of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) in liver chemistry early after BS. To investigate the risk factors for early elevation of ALT and AST after BS, we performed a regression analysis of 177 patients who underwent BS at our center. Follow-up data before and after BS were collected and divided into two groups according to whether ALT and/or AST increased and exceeded the clinical threshold one month after BS. Logistic regression analysis was used, and independent risk factors were screened. Waist circumference (WC) before BS was an independent risk factor ($P < 0.05$) for increased ALT and AST after BS, but other factors ($P > 0.05$), such as sex, type of BS, or body mass index (BMI), were not. The cutoff of WC to predict abnormal elevation of ALT and AST after BS was 117.35 cm (sensitivity, 0.75; specificity, 0.62) and 113.65 cm (sensitivity, 0.88; specificity, 0.48), respectively. WC is an independent risk factor for early liver injury after BS. Long-term liver-related follow-up is necessary.

Introduction

Bariatric surgery (BS) can improve the adverse metabolic status and hepatocellular pathological status of nonalcoholic fatty liver disease (NAFLD)^{1,2}. However, transient abnormally elevated alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels have been observed in the early stage after BS. ALT and AST are indicators of liver chemistry, and abnormally high levels suggest liver or potential liver cell damage³. This phenomenon has been previously reported in biliopancreatic diversion⁴. However, we found that this phenomenon persisted in other forms of BS, such as sleeve gastrectomy (SG), Roux-en-Y gastric bypass (RYGB), and sleeve gastrectomy with jejunal bypass (SGJB). Liver-related complications or adverse outcomes following BS suggest that we should pay attention to the evaluation of liver status after surgery^{5,6}. To explore the risk factors for early liver injury after BS, we retrospectively reviewed a series of clinical data before and after surgery in patients with obesity who received BS at our center for obesity and metabolic diseases.

Materials And Methods

We conducted a retrospective analysis of 185 patients who underwent BS from July 2019 to September 2020. Basic preoperative clinical data and one-month postoperative follow-up data were collected, including sex, age, surgical method, anthropometric indicators, and laboratory tests. A total of 177 patients were included in this study, excluding 5 patients with missing clinical data and 3 patients with a history of alcohol abuse or seropositivity for hepatitis virus.

The levels of ALT and AST before and one month after surgery were compared and grouped: if the ALT or AST value after surgery was higher than that before surgery and higher than the upper limit of normal value (40 U/L), the patient was included in the study group. If the ALT or AST value after surgery was not

higher than that before surgery or did not exceed the upper limit of normal value, the patient was included in the control group.

Statistical analysis. SPSS 22.0 was used for statistical analysis. A normality test was first performed on the data, and the data with a skewed distribution were represented by the median (interquartile range) and were compared using the Mann-Whitney U test. Continuous variables were classified and converted according to clinical diagnosis or the equivalent (Supplementary Table S1), and univariate logistic regression analysis was performed. Statistically significant indicators were incorporated into multivariate logistic regression equations for further analysis, and odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. The Hosmer-Lemeshow test was used to evaluate the calibration degree of the prediction model. Further, a receiver operating characteristic (ROC) curve was constructed to evaluate the discriminative ability of the prediction model, as well as the sensitivity, specificity, and cutoff. $P < 0.05$ was considered statistically significant.

Table 1
Liver enzymes before and after bariatric surgery

	ALT (U/L)		AST (U/L)	
	Study group, N = 63	Control group, N = 114	Study group, N = 49	Control group, N = 128
Before surgery	45.00(44.30)	46.25(60.15)	31.90(20.55)	28.15(24.65)
1 month after surgery	80.30(55.60) ^b	33.55(25.95) ^{a,b}	57.90(30.85) ^b	29.25(12.88) ^a
ALT alanine aminotransferase, AST aspartate aminotransferase				
^a Difference between the study group and the control group ($P < 0.05$)				
^b Difference within the study group or the control group ($P < 0.05$)				

Table 2

Univariate logistic regression of elevated liver enzyme levels one month after bariatric surgery

Related factors	ALT		AST	
	OR(95%CI)	P value	OR(95%CI)	P value
Sex	0.439(0.232–0.829)	0.011	0.491(0.251–0.961)	0.038
Age				
< 20	Ref.		Ref.	
20–30	0.707(0.285–1.754)	0.454	1.042(0.396–2.740)	0.934
30–40	0.439(0.164–1.179)	0.103	0.570(0.195–1.665)	0.304
> 40	0.361(0.107–1.214)	0.100	0.559(0.153–2.041)	0.379
Bariatric surgery				
SGJB	Ref.		Ref.	
RYGB	0.179(0.036–0.894)	0.036	0.282(0.056–1.415)	0.124
SG	0.373(0.190–0.373)	0.004	0.405(0.200–0.819)	0.012
Body mass index				
25-29.9	0.088(0.011–0.740)	0.025	-	-
30-34.9	0.194(0.082–0.456)	< 0.001	0.245(0.095–0.633)	0.004
35-39.9	0.386(0.181–0.823)	0.014	0.750(0.350–1.607)	0.460
≥ 40	Ref.		Ref.	
Diabetes	0.690(0.323–1.470)	0.336	1.290(0.603–2.758)	0.512
Hypertension	0.998(0.492–2.023)	0.995	1.083(0.512–2.293)	0.834
Preoperative ALT				
≤ 40	Ref.		Ref.	
40–80	1.660(0.813–3.389)	0.164	1.702(0.776–3.733)	0.185
> 80	0.960(0.433–2.127)	0.919	1.844(0.804–4.229)	0.149
Preoperative AST				
≤ 40	Ref.		Ref.	

ALT alanine aminotransferase, AST aspartate aminotransferase, RYGB Roux-en-Y gastric bypass, SG sleeve gastrectomy, SGJB sleeve gastrectomy with jejunal bypass, OR odds ratios, CI confidence intervals

Related factors	ALT		AST	
	OR(95%CI)	P value	OR(95%CI)	P value
40–80	0.905(0.430–1.903)	0.793	1.457(0.682–3.114)	0.331
> 80	0.374(0.077–1.803)	0.220	0.271(0.033–2.194)	0.221
Uric acid	1.749(0.937–3.267)	0.079	1.734(0.886–3.393)	0.108
Triglyceride	1.266(0.684–2.345)	0.453	1.435(0.741–2.781)	0.284
Total cholesterol	1.384(0.655–2.926)	0.395	1.193(0.535–2.656)	0.666
Fasting blood-glucose	1.369(0.723–2.594)	0.335	1.591(0.809–3.131)	0.178
Folic acid				
≤ 4.2	Ref.		Ref.	
4.2–19.8	0.518(0.244–1.099)	0.087	0.495(0.227–1.080)	0.077
> 19.8	0.265(0.027–2.612)	0.255	0.375(0.038–3.715)	0.402
Vitamin B12				
≤ 197	Ref.		0.800(0.066–9.669)	0.861
197–771	1.152(0.204–6.485)	0.873	1.622(0.437–6.020)	0.470
> 771	0.727(0.094–5.633)	0.760	Ref.	
Waist circumference				
≤ 110	0.100(0.034–0.297)	< 0.001	0.101(0.031–0.326)	< 0.001
110–120	0.440(0.197–0.984)	0.046	0.360(0.154–0.840)	0.018
120–130	1.100(0.425–2.847)	0.844	0.668(0.254–1.761)	0.415
> 130	Ref.		Ref.	
ALT alanine aminotransferase, AST aspartate aminotransferase, RYGB Roux-en-Y gastric bypass, SG sleeve gastrectomy, SGJB sleeve gastrectomy with jejunal bypass, OR odds ratios, CI confidence intervals				

Ethical Approval. The study was approved by the Medical Ethics Committee of Chengdu Third People's Hospital (2019S-46).

Informed consent. Informed consent has been taken from all participants associated with this research. All patients signed the informed consent form, and were performed in accordance with the Declaration of Helsinki.

Results

Changes in ALT and AST in the two groups after BS. Among the 177 patients who underwent BS, 63 patients had abnormally elevated ALT (35.59%) and 49 patients had abnormally elevated AST (27.68%) one month after surgery. There was no difference in ALT and AST levels between the study group and the control group before the operation ($P>0.05$). The elevation of ALT and AST in the study group after the operation was statistically significant ($P<0.05$). Also, ALT was significantly improved in the control group after surgery ($P<0.05$) (Table 1).

Screening of candidate risk factors. Univariate logistic regression analysis showed that sex, BS method, body mass index (BMI), and waist circumference (WC) were significant risk factors for abnormally elevated ALT and AST one month after BS ($P<0.05$). However, other factors, such as age, ALT, and AST levels before surgery, and diabetes, were not correlated with the abnormal increase in liver enzymes ($P>0.05$) (Table 2).

Independent risk factor analysis. The above four indicators were included in the multivariate logistic regression analysis, and the results showed that WC was an independent risk factor for abnormally elevated ALT and AST one month after BS ($P<0.05$) (Fig.1 and Fig.2). The Hosmer-Lemeshow test showed a good fit of the model (ALT: $\chi^2 = 5.177$, $P = 0.638$; AST: $\chi^2 = 2.249$, $P = 0.945$).

Discrimination of prediction models. The area under the ROC curve (AUC) for WC was 0.712 for abnormally elevated ALT (95% CI: 0.64-0.79; $P<0.0001$) (Fig.3A), and was 0.707 for AST (95% CI: 0.63-0.79; $P<0.0001$) (Fig.3B). It suggested that WC could predict abnormal increases in ALT or AST after BS and had certain discrimination. The cutoffs of WC for ALT and AST were 117.35 cm (sensitivity, 0.746; specificity, 0.623) and 113.65 cm (sensitivity, 0.878; specificity, 0.477), respectively (Fig.3).

Discussion

Abnormal elevations of ALT and AST indicate abnormal liver chemistry and potential liver damage³. Besides, elevated ALT levels were associated with increased liver-related mortality^{7,8}. We observed a moderate incidence of early transient abnormally elevated ALT and AST levels in patients undergoing BS (ALT: 35.59%; AST 27.68%), although these levels gradually recovered during subsequent follow-up. Sex, different BS methods, BMI, and WC were all associated with the phenomenon. However, WC before BS was an independent risk factor and was a good predictor of early postoperative liver injury (cutoff: ALT, 117.35 cm; AST, 113.65 cm).

Liver-related complications, such as elevated liver enzymes, thrombocytopenia, and impaired coagulation parameters, have been reported after BS. Severe ascites, hepatorenal syndrome, and liver failure also occur^{5,9,10}. The occurrence of hepato-related complications after BS is mainly seen in surgeries with a bypass length that is too long, and the mechanism may be related to malnutrition caused by an alimentary/common limb that is too short¹⁰⁻¹². However, most of the transiently elevated liver enzyme

levels recovered gradually during the follow-up⁴. In addition, we observed elevated liver enzymes after nonbypass surgical procedures, suggesting that other mechanisms may be involved.

Multivariate logistic regression analysis showed that waist circumference was an independent risk factor for early postoperative liver injury. Clinical studies have found that increased waist circumference, rather than weight, promotes liver enzymes, and increases the risk of NAFLD¹³⁻¹⁵. Excessive preoperative waist circumference often results in excessive visceral adipose tissue, which can damage liver cells by secreting inflammatory factors and related metabolites^{15,16}. As a result, the compensatory function of liver cells decreased in the early postoperative period, and liver enzymes increased abnormally for a short time. Also, it has been reported that surgery can stimulate the liver and lead to oxidative stress reactions, thus affecting early postoperative liver function¹⁷.

A large WC before BS is more likely to lead to early postoperative liver enzyme elevation and liver injury, but most can recover on their own. Spivak H et al¹² found that liver enzymes were also abnormally increased one year after BS. Omega-loop gastric bypass (OLGB), a method of BS, is a risk factor predicting liver enzyme elevation. This may be due to liver injury caused by different mechanisms; that is, excessive waist circumference and fat content, as previously mentioned, may lead to early liver injury and to long-term liver injury caused by influencing nutrient absorption by contrast bypass. Therefore, attention should be paid to long-term follow-up evaluation of the liver after BS, especially in patients with an enlarged WC and bypass surgery, to reduce liver-related surgical complications.

The advantage of our study lies in the screening of risk factors for the early elevation of ALT and AST after BS and the preliminary analysis combined with data from the reported literature. Also, in the context of increasing attention to the improvement of NAFLD after BS, attention to liver chemistry, and hepatocyte status during follow-up is needed. The limitations of our study were the small number of included patients. Moreover, we did not measure visceral fat parameters, so we could not determine the direct relationship between liver enzyme elevation and visceral fat content. However, waist circumference is currently an effective indicator for the assessment of abdominal obesity, and it remains to be seen whether other methods are always superior to waist circumference in visceral adipose tissue estimation¹⁸.

Conclusion

In brief, self-healing liver injury may occur early after BS. WC before BS was an independent risk factor for liver enzyme elevation. Long-term liver-related follow-up is necessary after BS, especially for patients with larger WCs and those who undergo bypass surgery.

Declarations

Data availability

All data generated or analysed during this study are included in this published article and its Supplementary Information files.

Author contributions

The study design was prepared by Y.Z. and H.Y. Data analysis, interpretation and manuscript drafting were written by Y.Z. and H.Y. The data was extracted by H.Y. and D.Z. Figures were prepared by X.L. and C.X. The manuscript was revised by T.Z. and Y.L. All authors read and approved the final version of the manuscript.

Competing interests

The authors declare no competing interests.

Additional information

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Figures

Figure 1

Multivariable logistic regression of abnormally elevated ALT one month after BS. WC was statistically significant ($P < 0.05$). RYGB Roux-en-Y gastric bypass, SG sleeve gastrectomy, SGJB sleeve gastrectomy with jejunal bypass, OR odds ratios, CI confidence intervals, ALT alanine aminotransferase, BS bariatric surgery, WC waist circumference

Figure 2

Multivariable logistic regression of abnormally elevated AST one month after BS. WC was statistically significant ($P<0.05$). RYGB Roux-en-Y gastric bypass, SG sleeve gastrectomy, SGJB sleeve gastrectomy with jejunal bypass, OR odds ratios, CI confidence intervals, AST aspartate aminotransferase, BS bariatric surgery, WC waist circumference

Figure 3

ROC curve of WC in predicting abnormally elevated ALT and AST after BS. (a) ROC curve of WC as a predictor of abnormal ALT elevation after BS. The AUC is 0.712 (95 % confidence interval: 0.64-0.79; $P < 0.0001$). The cutoff is 117.35 cm (sensitivity, 0.746; specificity, 0.623). (b) ROC curve of WC as a predictor of abnormal AST elevation after BS. The AUC is 0.717 (95 % confidence interval: 0.63-0.79; $P < 0.0001$). The cutoff is 113.65 cm (sensitivity, 0.878; specificity, 0.477). AUC area under curve, ROC receiver operating characteristic, WC waist circumference, ALT alanine aminotransferase, AST aspartate aminotransferase, BS bariatric surgery

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