Effect of laparoscopic sleeve gastrectomy on Nonalcoholic Fatty Liver Disease: A prospective study

George Abdelfady Nashed[1], Sameh Adel Aziz[1], Ahmed Mostafa Ghobashy[2], Fady Moris Abdallah[3*]

1 Professor of General Surgery, Faculty of Medicine, Cairo University.
2 Lecturer of General Surgery, Faculty of Medicine, Cairo University.
3 Assistant Lecturer of General Surgery, Faculty of Medicine, Cairo University
Email: drfadymaurice@gmail.com

Abstract

Background: Non-alcoholic fatty liver disease (NAFLD) prevalence is increasing, concomitant with the global obesity epidemic in many nations. Obesity, and other components of metabolic syndrome are all strongly correlated with NAFLD. Bariatric surgery is a highly reproducible and reliable management procedure for clinically severe obesity and its associated comorbidities. The aim of the current work was to assess the effect of Laparoscopic sleeve gastrectomy (LSG) on hepatic steatosis and fibrosis in patients with NAFLD. **Patients and methods:** This is a prospective observational study that was conducted on patients with obesity who were scheduled for LSG with fibroscan-proven NAFLD. Fibroscan-based steatosis (controlled attenuation parameter; CAP) and fibrosis (Liver stiffness measurement; LSM) measures were assessed preoperatively and 6-months postoperatively. **Results:** This study included 76 patients with NAFLD. At the Six-month post-surgery follow up, the patients showed significantly lower LSM and CAP than the baseline levels ($p<0.001$). The percentage of excess body weight loss (EBWL%) and the percentage of change in HDL (ΔHDL %) were significant predictors of the percentage of change in CAP scores (ΔCAP %) ($p=0.049$ and 0.05, respectively), which was the only significant predictor of the percentage of change in LSM scores (ΔLSM %) ($p<0.001$). **Conclusion:** Our findings emphasize the role of bariatric surgery as a successful management procedure for NAFLD. Whatever the factors determining hepatic steatosis in patients with NAFLD, it seems that the change in fibrosis scores is only influenced by the hepatic steatosis state.

Keywords: Non-alcoholic fatty liver disease (NAFLD), Obesity, Laparoscopic sleeve gastrectomy (LSG), fibroscan, steatosis, fibrosis

Introduction

Non-alcoholic fatty liver disease (NAFLD) is defined as the build-up of extra fat (greater than 5%) in the liver parenchyma in individuals who do not consume large amounts of alcohol or have secondary causes of hepatic steatosis [1]. NAFLD prevalence is increasing, concomitant with the global obesity epidemic in many nations. The Middle East (32%), North Africa (31%), and Asia (27%), respectively, have the highest incidence of NAFLD reported [2].

Non-alcoholic steatohepatitis (NASH) is at the more severe end of the spectrum and falls after non-alcoholic fatty liver (NAFL) and NAFLD, which are more benign disorders [3]. Hepatic fibrosis and cirrhosis, which are documented risk factors for developing hepatocellular carcinoma, can occur as consequences of NAFLD and NASH [4,5].

Modifiable risk factors for NAFLD include obesity, high-calorie intake, and a sedentary lifestyle. The most important modifiable risk factor for this disease, which is caused by an energy imbalance, is probably central obesity [6].

Obesity, type 2 diabetes mellitus (T2DM), and other components of metabolic syndrome are all strongly correlated with NAFLD. Bariatric surgery is a highly reproducible and reliable management procedure for clinically severe obesity and its associated comorbidities [7]. All mechanisms that contribute to the reduction of obesity and type 2 diabetes (T2DM) following bariatric surgery appear to be essential for the amelioration or resolution of NAFLD. By reducing body weight, bariatric surgery may also reduce hepatic fibrosis, fat build-up, and inflammation [8].

Laparoscopic sleeve gastrectomy (LSG) is one of the bariatric procedures that has been considered to improve the course of NAFLD [9]. It has been demonstrated that LSG leads to improved liver functions that were attributed to pathophysiologic mechanisms involved in the alleviation of inflammation and oxidative stress [10-12].

Transient elastography (fibroscan) is an ultrasound-based imaging modality used to assess the degree of steatosis and fibrosis in patients with NAFLD and NASH with high sensitivity and specificity [13]. The fibroscan probe induces vibrations of low frequency and mild amplitude that elicit elastic shear waves, which proceed through the parenchyma of the liver. Pulse-echo ultrasound acquisition is used to trail the shear wave propagation and to estimate its velocity that directly correlates with the tissue stiffness [14].

The aim of the current work was to assess the effect of LSG on hepatic steatosis and fibrosis in patients with NAFLD.

Subjects and Methods:

This is a prospective observational study that was conducted in the General Surgery Department of our institution. The study protocol was reviewed and permitted by the regional institutional research and ethics committee. The study was conducted per the Declaration of Helsinki.

Based on the study of Agarwal et al. [15] who used fibroscan to assess the impact of bariatric surgery on NAFLD, and assuming an alpha risk of 5% and a power of 80%, the minimum sample size needed was 77 patients.

Patients with obesity who were scheduled for LSG according to the institution strategy and per 2020 update of the Clinical practice guidelines of the European Association for Endoscopic Surgery (EAES), endorsed by the International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO) [16] during the period from March 2020 to November 2021, underwent complete history taking, clinical and laboratory examination, and fibroscan assessment. Consecutive adult patients with fibroscan-proven NAFLD or NASH were eligible for the study. Patients with a history of alcohol or hepatotoxic drug intake, fatty liver or insulin sensitization-inducing drug intake such as amiodarone, estrogens, or methotrexate, more than three-fold elevated liver enzymes, seropositive tests of viral hepatitis, or any metabolic or auto-immune disease affecting the liver were excluded from the study. Informed written consent was obtained from each included patient.

Data concerning the patients' demographics, anthropometric measures, comorbidities, laboratory investigations (liver function tests and lipid profile), abdominal ultrasound examination, and fibroscan were registered.

Fibroscan assessment was performed using FibroScantouch 502 (Echosens, Paris, France) machine. Liver stiffness measurement (LSM) between 2 and 6 kPa is considered normal. Fibrosis was staged from 0 to 4: F0 (absence of fibrosis), F1 (perisinusoidal or portal), F2 (perisinusoidal and portal/periportal), F3 (septal or bridging fibrosis), and F4 (cirrhosis) [17].

Using the fibroscan, ultrasound-based controlled attenuation parameter (CAP) was measured to determine the degree of steatosis with stages of S0 (no steatosis); a median CAP value of 205 dB/m (180–227 dB/m), which corresponds to a percentage of <5% hepatic steatosis, S1 (mild steatosis); a median cap value of 245 dB/m (231– 268 dB/m), which corresponds to a percentage of 5–33% hepatic steatosis, S2 (moderate steatosis); a median cap value of 299 dB/m (268–323 dB/m), which corresponds to a percentage of 34-66% hepatic steatosis, and S3 (severe steatosis); a median cap value of 321 dB/m (301–346 dB/m), which corresponds to a percentage of >67% hepatic steatosis [18].

Laparoscopic sleeve gastrectomy was performed as standardized over 36Fr bougie with resection from the His angle to about 3-4 cm proximal to the pylorus. No stable line reinforcement was performed [19].

After routine postoperative care, the study patients received follow-up schedules at 3 and 6 months postoperatively, during which they were subjected to complete clinical, laboratory, and fibroscan assessments.

The percentage of total weight loss (TWL%) and excess body weight loss (EBWL%) were calculated as previously described [20]. Comorbidity remission was judged per the standardized outcome reporting published by the American Society for Metabolic and Bariatric Surgery [21].

Study outcomes

The primary outcome of our study was the effect of LSG on hepatic steatosis and fibrosis, as shown by fibroscan assessment, in patients with NAFLD. The secondary outcome was the potential predictors of this effect.

Statistical analysis

The analysis of patients' data was performed using the SPSS statistical software (IBM Corp., Armonk, NY, USA), version 28. Categorical values were presented as frequencies and percentages. Cochran's Q test was used for paired categorical comparisons. Numerical values were tested for normality, and a paired t- was performed accordingly. Linear regression analysis was performed to assess change in fibrosis scores. A p-value less than 0.05 was considered statistically significant.

Results

This prospective study included 76 patients who were scheduled for LSG and had NAFLD as shown in abdominal ultrasound and proven by fibroscan. The patient's ages ranged from 19 to 50 years with a mean of 36 ± 7.21 years. Males constituted 59.2% of the study patients (n=45). The baseline BMI ranged from 37 to 58.6 kg/m^2 with a mean of 45.44 ± 4.43 kg/m^2. The excess body weight (EBW) ranged from 56.25 to 81 kg, with a mean of 71.1 ± 5.46 kg.

The baseline patients' comorbidities were dyslipidemia in 100% of patients, diabetes mellitus in 46.05% of patients (n=35), and hypertension in 31.6% of patients (n=24).

The fibroscan assessment revealed a baseline LSM ranging from 1.55 to 12.00 kPa, with a mean of 6.87 ± 1.55 kPa, and CAP ranging from 235.00 to 400.00 dB/m, with a mean of 332.17 ± 51.37 dB/m. According to the patients' LSM, four patients (5.3%) were in S1, twenty-one patients (27.6%) were in S2, and the remaining fifty-one patients (67.1%) were in S3. As for the CAP measures, forty-five patients (59.2%) had an F1 grade, thirty-one patients (39.5%) had an F2 grade, and one patient (1.3%) had an F3 grade (Table 2).

Six-month post-surgery follow up

At the end of the follow-up, the mean patients' BMI was 33.34 ± 2.92 kg/m2, with a statistically significant reduction compared to the baseline measures ($p<0.001$). The percentage of excess body weight loss (EBWL%) ranged from 48.5 to 97.9%, with a mean of 79.13 ± 15.93%. the percentage of total weight loss (TWL%) ranged from 21.05 to 46.24% with a mean of 34.73 ± 6.19% (Table 2).

Concerning patients' comorbidities, there was complete resolution in 95.6% of patients with dyslipidemia (n=66), 74.3% of patients with diabetes mellitus (n=26), and 69.2% of patients with hypertension (n=18). Improvement was shown in 5 patients with diabetes mellitus (14.3%) and all the remaining patients with hypertension (31.8%).

Fibroscan assessment demonstrated significantly lower LSM and CAP ($p<0.001$), with a mean LSM of 4.77 ± 0.93 kPa and a mean CAP of 262.45 ± 41.65 dB/m. This significant improvement was also manifested in statistically significant changes in the S ($p<0.001$) and F ($p=0.001$) categories, with twenty patients (26.3%) reversed to S0 grade, sixteen patients (21.1%) in S1 grade, twenty-nine patients (38.2%) in S2 grade, and eleven patients (14.5%) in S3 grade. The number of patients having F1 grade increased to 75 (98.7%), while only one patient (1.3%) was of F2 grade, and no patients remained of F3 grade (0%) (Table 2).

No statistically significant changes were shown in the liver function tests, while there was a statistically significant improvement in the lipid profile parameters ($p<0.001$).

Multivariate linear regression analysis showed that the EBWL% and the percentage of change in HDL (ΔHDL %) were significant predictors of the percentage of change in CAP scores (ΔCAP %) (p=0.049 and 0.05, respectively), which was the only significant predictor of the percentage of change in LSM scores (ΔLSM %) (p<0.001) (Figure 1).
During the follow-up period, no cases of major complications or mortality were encountered.

Table 1: Baseline demographic data of the study patients

		Study patients (n=76)	
		Mean ± SD	**Range**
Age (year)		36 ± 7.21	19 - 50
Baseline weight (Kg)		129.08 ± 10.6	110 - 152
Baseline Height (cm)		168.51 ± 6.6	150 - 180
Baseline BMI (Kg/m^2)		48.80 ± 7.83	37 – 58.6
EBW(Kg)		71.1 ± 5.46	56.25 - 81
		Count	**%**
Sex	**Male**	45	59.2%
	Female	31	40.8%
Comorbidities			
Type 2 diabetes mellitus		35	46.05%
Hypertension		24	31.6%
Dyslipidemia		69	90.8%

Table 2: Laboratory and fibroscan data of the study patients (n=76)

	Preoperative		**6-months Postoperative**		**p-value**
	Mean ± SD	**Range**	**Mean ± SD**	**Range**	
Total bilirubin (mg/dL)	0.51 ± 0.18	0.1 – 0.96	0.48 ± 0.1	0.1 – 0.9	0.08
AST (U/L)	30.79 ± 11.6	10 - 52	29.01 ± 9.99	10 - 45	0.29
ALT (U/L)	35.58 ± 9.7	10 - 70	32.58 ± 9.26	8 - 62	0.072
TG (mg/dL)	184.55 ± 38.9	98 - 287	127.46 ± 31.3	79 - 200	<0.001*
Δ TG% (Mean ± SD)	- 30.6 ± 10.1				
LDL (mg/dL)	133.82 ± 25.03	81 - 206	104.41 ± 19.08	62 - 142	<0.001*
Δ LDL% (Mean ± SD)	- 21.7 ± 6.7				
HDL (mg/dL)	40.76 ± 9.33	23 - 61	63.29 ± 8.81	34 - 79	<0.001*
Δ HDL% (Mean ± SD)	61.3 ± 34.9				
CAP (dB/m)	332.17 ± 51.4	235 - 400	262.45 ± 41.7	150 - 385	<0.001*
Δ CAP% (Mean ± SD)	- 20.5 ± 9.3				
LSM (kPa)	6.87 ± 1.55	4.2 - 12	4.77 ± 0.39	3.1 – 7.3	<0.001*
Δ LSM% (Mean ± SD)	- 29.3 ± 11.3				
	Count	**%**	**Count**	**%**	
Steatosis categories					
S0	0	0.0%	20	26.3%	<0.001*
S1	4	5.3%	16	21.1%	
S2	21	27.6%	29	38.2%	
S3	51	67.1%	11	14.5%	
Fibrosis categories					
F1	45	59.2%	75	98.7%	0.001*
F2	30	39.5%	1	1.3%	
F3	1	1.3%	0	0.0%	

***: statistically significant**

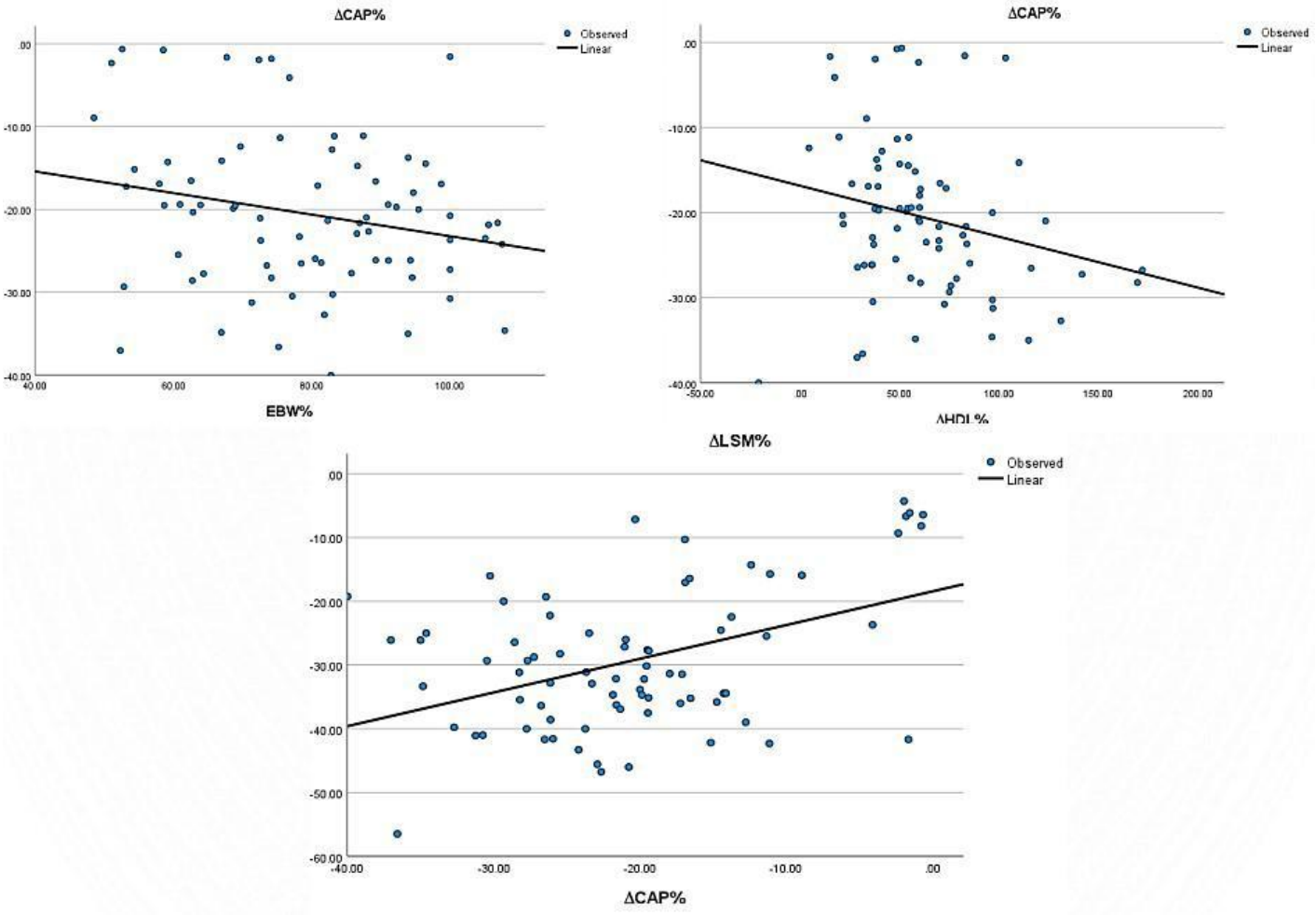

Figure 1: Multivariate linear regression analysis

Discussion

Non-alcoholic fatty liver (NAFL), non-alcoholic steatohepatitis (NASH), NASH-related cirrhosis, and hepatocellular carcinoma are the four clinical-pathological characteristics that often follow the course of NAFLD. Obesity has been connected to both the early stages of these conditions as well as their advancement, which propose a higher mortality risk [22]. Bariatric surgery can reduce hepatic fat deposition as a consequence of its resultant weight loss, metabolic effect, and chronic inflammation reduction [23].

This study aimed to determine the effect of LSG on nonalcoholic fatty liver disease. There is numerous research addressing the effect of bariatric surgery on patients with NAFLD. However, a few of them were prospective studies that assessed patients undergoing LSG and adopted the use of fibroscan in determining hepatic steatosis and fibrosis, more particularly in our geographical region.

Liver biopsy has not been implemented as a routine approach during bariatric surgery in our institution. Hence, fibroscan was used in this study. Although the gold standard for NAFLD diagnosis is liver biopsy, it is limited by being an invasive procedure. In addition, it is impacted by the small size of the obtained sample and the restricted biopsy region, which lead to sampling variability [24]. Moreover, it is not feasible to perform repeated biopsies to depict the changes in hepatic steatosis and/or fibrosis. Numerous non-invasive approaches have been proposed for the assessment of liver fibrosis, such as laboratory indices, NAFLD and BARD scores, and elastography methods including magnetic resonance elastography (MRE) and transient elastography (FibroScan). Fibroscan has been demonstrated to be a reliable technique to diagnose hepatic steatosis and fibrosis [25-28]. Garg et al. [29] compared fibroscan to liver biopsy and reported that fibroscan-

based assessment of hepatic steatosis and fibrosis in patients with morbid obesity has shown feasibility and accuracy.

This prospective study showed that 6 months after LSG, there was a significant reduction in the hepatic steatosis and fibrosis parameters that coincided with the comorbidities' remission and lipid profile improvement.

In accordance with our findings, the recent meta-analysis conducted by Lee et al. [30] to investigate the effect of bariatric surgery on patients with biopsy-diagnosed NAFLD revealed the resolution of steatosis and fibrosis in 66% and 40% of patients, respectively. Algooneh et al. [31], in their retrospective study, reported complete resolution of NAFLD, as diagnosed by abdominal ultrasound, in 56% of the studied cases after LSG. Concerning using fibroscan for patients'assessment, in similarity with our findings, Jimenez et al. [32], Nickel et al. [33], and Cazzo et al. [34] found a reduction in fibrosis scores after bariatric surgery in patients with NAFLD. This was confirmed in the study of Garg et al. [29] who reported a decline in LSM from 8.6 to 6.0 kPa and CAP values from 322 dB/m to 251 dB/m one year after bariatric surgery. Reduction of LSM one-year after surgery was also shown in the study of Naveau et al. [35] to be 5.37 after a mean baseline value of 6.95. These values are comparable with the current study figures, where the mean LSM declined from 6.87 to 4.77 kPa and the mean CAP reduced from 332.17 to 262.45 dB/m.

Although several studies have shown that bariatric surgery improves fibrosis, the evidence is still inconclusive; a meta-analysis study conducted by Laursen et al. [36] reported that numerous studies showed fibrosis improvement after bariatric surgery, whereas others found worsened fibrosis. The recent study by Seeberg and colleagues [37] demonstrated worsened fibrosis scores. These contradictory results could be attributed to the variation in study design, methods to assess fibrosis, and follow-up time.

The promising effect of bariatric surgery on NAFLD could be presumed when an in-depth look at the pathogenetic mechanisms involved in the development of NAFLD is taken. Indeed, these mechanisms are not completely understood, in spite of the considerable evolution that has occurred recently. It has been proposed that the injury of the hepatic tissue is initiated by the accumulation of triglycerides, which trigger inflammatory mediators and oxidative stress. This disruption would be followed by steatohepatitis and fibrosis [38]. Moreover, free fatty acids (FFAs), which show greater influx to the liver as a consequence of insulin resistance, are a mainstay in promoting liver damage [39]. Thus, it is plausible that bariatric surgery causes NAFLD resolution not only via weight loss but also through mechanisms involved in the improvement of glucose homeostasis, lipid metabolism, and reduced inflammatory activity, all involved in NAFLD pathophysiology [36]. In the context of LSG, Cabré et al. [40] illustrated that LSG led to a significant elevation in the hepatic levels of STAT-3, a cytoplasmic protein that, upon phosphorylation, initiates transcription of genes that promote cellular proliferation and protective effects. Furthermore, Salman et al. [12] found that LSG-induced weight loss was paralleled with an elevation in serum adiponectin levels, which is documented to enhance fatty acid oxidation and glucose uptake in skeletal muscles. It inhibits gluconeogenesis, lipogenesis, and hepatic steatosis [41].

Notably, this study showed significant comorbidity remission and lipid profile improvement after LSG. This aligns with most previous studies [29,42-44]. The current study, however, demonstrated a non-significant difference in the hepatic function markers. The plausible explanation is that most of our patients had normal baseline levels of liver enzymes. This is consistent with Seeberg et al. [37] who assumed that the levels of liver enzymes might not be sufficient to evaluate the alteration in hepatic steatosis after bariatric surgery and Laursen et al. [36] who found that transaminases exhibit limited accuracy for the prediction of NASH severity. Abelson et al. [45] and Matter et al. [46] also found non-significant changes in ALT and AST levels at different follow-up periods.

Interestingly, the present work demonstrated that the EBWL% and the Δ HDL% were significant predictors of the changes in hepatic steatosis (Δ CAP%), which was the only significant predictor of Δ LSM%. Other studies identified predictors of the NAFLD course. The study of Algooneh et al. [31] reported a significant resolution of NAFLD among the patients who attained > 50% excess weight loss. Salman et al. [47] found that weight loss amount was a predictor of fibrosis reversal in patients with NASH-related cirrhosis.

Regarding Δ HDL%, our findings are consistent with the fact that HDL has a documented role in the prevention of inflammation, platelet activation, oxidation, and crucially, the transport of cholesterol from peripheral tissues to the liver to be excreted in bile via the reverse cholesterol transport pathway. Altered HDL levels are seen in disorders associated with systematic inflammation or insulin resistance characterized by altered HDL functions [48]. Thus, the overt alleviation of the inflammatory status and insulin resistance after bariatric surgery should have an effect on HDL levels as well as hepatic steatosis. Our findings denote that, whatever the factors determining hepatic steatosis, it seems that, in patients with NAFLD, the change in fibrosis scores is only influenced by the hepatic steatosis state.

The current study findings need to be validated in a large sample study with a longer period of follow-up.

CONCLUSION

This study adds new evidence concerning the ameliorating effect of LSG on steatosis and fibrosis in patients with NAFLD as well as remission of comorbidities and resolution of the dyslipidemic state. Our findings emphasize the role of bariatric surgery as a successful management procedure for NAFLD. Whatever the factors determining hepatic steatosis in patients with NAFLD, it seems that the change in fibrosis scores is only influenced by the hepatic steatosis state.

STATEMENTS AND DECLARATIONS

- **Acknowledgements:** None.
- **Authors' Contributions:** All authors equally contributed to this work.
- **Funding:** None.
- **Statement for informed consent:** Informed consent was obtained from all individual participants included in the study.
- **Statement for conflict of interest:** The authors declare that they have no conflict of interest.
- **Ethical approval:** This study has been approved by the appropriate institutional research ethics committee.

References

1. Benedict M, Zhang X (2017) Non-alcoholic fatty liver disease: An expanded review. World J Hepatol 9:715–732. https://doi.org/10.4254/wjh.v9.i16.715
2. Wong MCS, Huang JLW, George J, et al (2019) The changing epidemiology of liver diseases in the Asia–Pacific region. Nat Rev Gastroenterol Hepatol 16:57–73. https://doi.org/10.1038/s41575-018-0055-0
3. Pouwels S, Sakran N, Graham Y, et al (2022) Non-alcoholic fatty liver disease (NAFLD): a review of pathophysiology, clinical management and effects of weight loss. BMC Endocr Disord 22:63. https://doi.org/10.1186/s12902-022-00980-1
4. Ahmed A, Wong RJ, Harrison SA (2015) Nonalcoholic Fatty Liver Disease Review: Diagnosis, Treatment, and Outcomes. Clinical Gastroenterology and Hepatology 13:2062–2070. https://doi.org/10.1016/j.cgh.2015.07.029
5. Machado MV, Diehl AM (2016) Pathogenesis of Nonalcoholic Steatohepatitis. Gastroenterology 150:1769–1777. https://doi.org/10.1053/j.gastro.2016.02.066
6. Polyzos SA, Kountouras J, Mantzoros CS (2019) Obesity and nonalcoholic fatty liver disease: From pathophysiology to therapeutics. Metabolism - Clinical and Experimental 92:82–97. https://doi.org/10.1016/j.metabol.2018.11.014
7. Younossi Z, Anstee QM, Marietti M, et al (2018) Global burden of NAFLD and NASH: trends, predictions, risk factors and prevention. Nat Rev Gastroenterol Hepatol 15:11–20. https://doi.org/10.1038/nrgastro.2017.109
8. Madsbad S, Dirksen C, Holst JJ (2014) Mechanisms of changes in glucose metabolism and bodyweight after bariatric surgery. The Lancet Diabetes & Endocrinology 2:152–164. https://doi.org/10.1016/S2213-8587(13)70218-3
9. Głuszyńska P, Lemancewicz D, Dzięcioł JB, Razak Hady H (2021) Non-Alcoholic Fatty Liver Disease (NAFLD) and Bariatric/Metabolic Surgery as Its Treatment Option: A Review. J Clin Med 10:5721. https://doi.org/10.3390/jcm10245721
10. Nobili V, Carpino G, De Peppo F, et al (2018) Laparoscopic Sleeve Gastrectomy Improves Nonalcoholic Fatty Liver Disease-Related Liver Damage in Adolescents by Reshaping Cellular Interactions and Hepatic Adipocytokine Production. J Pediatr 194:100-108.e3. https://doi.org/10.1016/j.jpeds.2017.10.036
11. Cabré N, Luciano-Mateo F, Fernández-Arroyo S, et al (2019) Laparoscopic sleeve gastrectomy reverses non-alcoholic fatty liver disease modulating oxidative stress and inflammation. Metabolism 99:81–89. https://doi.org/10.1016/j.metabol.2019.07.002
12. Salman AA, Sultan AAEA, Abdallah A, et al (2020) Effect of weight loss induced by laparoscopic sleeve gastrectomy on

liver histology and serum adipokine levels. J Gastroenterol Hepatol 35:1769–1773. https://doi.org/10.1111/jgh.15029
13. Kwok R, Tse Y-K, Wong GL-H, et al (2014) Systematic review with meta-analysis: non-invasive assessment of non-alcoholic fatty liver disease – the role of transient elastography and plasma cytokeratin-18 fragments. Alimentary Pharmacology & Therapeutics 39:254–269. https://doi.org/10.1111/apt.12569
14. Wong GL-H (2013) Update of liver fibrosis and steatosis with transient elastography (Fibroscan). Gastroenterol Rep (Oxf) 1:19–26. https://doi.org/10.1093/gastro/got007
15. Agarwal L, Aggarwal S, Shalimar, et al (2021) Bariatric Surgery in Nonalcoholic Fatty Liver Disease (NAFLD): Impact Assessment Using Paired Liver Biopsy and Fibroscan. OBES SURG 31:617–626. https://doi.org/10.1007/s11695-020-04977-4
16. Di Lorenzo N, Antoniou SA, Batterham RL, et al (2020) Clinical practice guidelines of the European Association for Endoscopic Surgery (EAES) on bariatric surgery: update 2020 endorsed by IFSO-EC, EASO and ESPCOP. Surg Endosc 34:2332–2358. https://doi.org/10.1007/s00464-020-07555-y
17. Xiao G, Zhu S, Xiao X, et al (2017) Comparison of laboratory tests, ultrasound, or magnetic resonance elastography to detect fibrosis in patients with nonalcoholic fatty liver disease: A meta-analysis. Hepatology 66:1486–1501. https://doi.org/10.1002/hep.29302
18. Petta S, Wong VW-S, Cammà C, et al (2017) Improved noninvasive prediction of liver fibrosis by liver stiffness measurement in patients with nonalcoholic fatty liver disease accounting for controlled attenuation parameter values. Hepatology 65:1145–1155. https://doi.org/10.1002/hep.28843
19. Ferrer-Márquez M, Belda-Lozano R, Ferrer-Ayza M (2012) Technical controversies in laparoscopic sleeve gastrectomy. Obes Surg 22:182–187. https://doi.org/10.1007/s11695-011-0492-0
20. van de Laar AWJM, Acherman YIZ (2014) Weight loss percentile charts of large representative series: a benchmark defining sufficient weight loss challenging current criteria for success of bariatric surgery. Obes Surg 24:727–734. https://doi.org/10.1007/s11695-013-1130-9
21. Brethauer SA, Kim J, el Chaar M, et al (2015) Standardized outcomes reporting in metabolic and bariatric surgery. Surg Obes Relat Dis 11:489–506. https://doi.org/10.1016/j.soard.2015.02.003
22. Perumpail BJ, Khan MA, Yoo ER, et al (2017) Clinical epidemiology and disease burden of nonalcoholic fatty liver disease. World J Gastroenterol 23:8263–8276. https://doi.org/10.3748/wjg.v23.i47.8263
23. Truong E, Noureddin M (2022) Improvement in nonalcoholic fatty liver disease through bariatric surgery. Clinical Liver Disease 20:13–17. https://doi.org/10.1002/cld.1229
24. Bedossa P, Dargère D, Paradis V (2003) Sampling variability of liver fibrosis in chronic hepatitis C. Hepatology 38:1449–1457. https://doi.org/10.1016/j.hep.2003.09.022
25. Wong VW-S, Vergniol J, Wong GL-H, et al (2010) Diagnosis of fibrosis and cirrhosis using liver stiffness measurement in nonalcoholic fatty liver disease. Hepatology 51:454–462. https://doi.org/10.1002/hep.23312
26. Wong VW-S, Vergniol J, Wong GL-H, et al (2012) Liver stiffness measurement using XL probe in patients with nonalcoholic fatty liver disease. Am J Gastroenterol 107:1862–1871. https://doi.org/10.1038/ajg.2012.331
27. Petta S, Maida M, Macaluso FS, et al (2015) The severity of steatosis influences liver stiffness measurement in patients with nonalcoholic fatty liver disease. Hepatology 62:1101–1110. https://doi.org/10.1002/hep.27844
28. Cassinotto C, Boursier J, de Lédinghen V, et al (2016) Liver stiffness in nonalcoholic fatty liver disease: A comparison of supersonic shear imaging, FibroScan, and ARFI with liver biopsy. Hepatology 63:1817–1827. https://doi.org/10.1002/hep.28394
29. Garg H, Aggarwal S, Shalimar null, et al (2018) Utility of transient elastography (fibroscan) and impact of bariatric surgery on nonalcoholic fatty liver disease (NAFLD) in morbidly obese patients. Surg Obes Relat Dis 14:81–91. https://doi.org/10.1016/j.soard.2017.09.005
30. Lee Y, Doumouras AG, Yu J, et al (2019) Complete Resolution of Nonalcoholic Fatty Liver Disease After Bariatric Surgery: A Systematic Review and Meta-analysis. Clin Gastroenterol Hepatol 17:1040-1060.e11. https://doi.org/10.1016/j.cgh.2018.10.017
31. Algooneh A, Almazeedi S, Al-Sabah S, et al (2016) Non-alcoholic fatty liver disease resolution following sleeve gastrectomy. Surg Endosc 30:1983–1987. https://doi.org/10.1007/s00464-015-4426-0
32. Jimenez LS, Mendonça Chaim FH, Mendonça Chaim FD, et al (2018) Impact of Weight Regain on the Evolution of Non-alcoholic Fatty Liver Disease After Roux-en-Y Gastric Bypass: a 3-Year Follow-up. Obes Surg 28:3131–3135. https://doi.org/10.1007/s11695-018-3286-9
33. Nickel F, Tapking C, Benner L, et al (2018) Bariatric Surgery as an Efficient Treatment for Non-Alcoholic Fatty Liver Disease in a Prospective Study with 1-Year Follow-up : BariScan Study. Obes Surg 28:1342–1350. https://doi.org/10.1007/s11695-017-3012-z
34. Cazzo E, Jimenez LS, Pareja JC, Chaim EA (2015) Effect of Roux-en-Y gastric bypass on nonalcoholic fatty liver disease evaluated through NAFLD fibrosis score: a prospective study. Obes Surg 25:982–985. https://doi.org/10.1007/s11695-014-1489-2

35. Naveau S, Lamouri K, Pourcher G, et al (2014) The diagnostic accuracy of transient elastography for the diagnosis of liver fibrosis in bariatric surgery candidates with suspected NAFLD. Obes Surg 24:1693–1701. https://doi.org/10.1007/s11695-014-1235-9
36. Laursen TL, Hagemann CA, Wei C, et al (2019) Bariatric surgery in patients with non-alcoholic fatty liver disease - from pathophysiology to clinical effects. World J Hepatol 11:138–149. https://doi.org/10.4254/wjh.v11.i2.138
37. Seeberg KA, Borgeraas H, Hofsø D, et al (2022) Gastric Bypass Versus Sleeve Gastrectomy in Type 2 Diabetes: Effects on Hepatic Steatosis and Fibrosis. Ann Intern Med 175:74–83. https://doi.org/10.7326/M21-1962
38. Arab JP, Arrese M, Trauner M (2018) Recent Insights into the Pathogenesis of Nonalcoholic Fatty Liver Disease. Annu Rev Pathol 13:321–350. https://doi.org/10.1146/annurev-pathol-020117-043617
39. Pierantonelli I, Svegliati-Baroni G (2019) Nonalcoholic Fatty Liver Disease: Basic Pathogenetic Mechanisms in the Progression From NAFLD to NASH. Transplantation 103:e1–e13. https://doi.org/10.1097/TP.0000000000002480
40. Cabré N, Luciano-Mateo F, Fernández-Arroyo S, et al (2019) Laparoscopic sleeve gastrectomy reverses non-alcoholic fatty liver disease modulating oxidative stress and inflammation. Metabolism 99:81–89. https://doi.org/10.1016/j.metabol.2019.07.002
41. Berg AH, Combs TP, Du X, et al (2001) The adipocyte-secreted protein Acrp30 enhances hepatic insulin action. Nat Med 7:947–953. https://doi.org/10.1038/90992
42. Abelson JS, Afaneh C, Dolan P, et al (2016) Laparoscopic Sleeve Gastrectomy: Co-morbidity Profiles and Intermediate-Term Outcomes. Obes Surg 26:1788–1793. https://doi.org/10.1007/s11695-015-2002-2
43. Lira NS, Macedo CES, Belo GM, et al (2018) Analysis of the lipid profile of patients submitted to sleeve gastrectomy and Roux-en-Y gastric bypass. Rev Col Bras Cir 45:e1967. https://doi.org/10.1590/0100-6991e-20181967
44. Zaki MKS, Al-Jefri OH, Kordi RE, et al (2021) Correlation of Bariatric Surgery Effect on Lipid Profile Among Obese Patients. Cureus 13:e18118. https://doi.org/10.7759/cureus.18118
45. Mattar SG, Velcu LM, Rabinovitz M, et al (2005) Surgically-induced weight loss significantly improves nonalcoholic fatty liver disease and the metabolic syndrome. Ann Surg 242:610–617; discussion 618-620. https://doi.org/10.1097/01.sla.0000179652.07502.3f
46. Praveen Raj P, Gomes RM, Kumar S, et al (2015) The effect of surgically induced weight loss on nonalcoholic fatty liver disease in morbidly obese Indians: "NASHOST" prospective observational trial. Surg Obes Relat Dis 11:1315–1322. https://doi.org/10.1016/j.soard.2015.02.006
47. Salman MA, Mikhail HMS, Nafea MA, et al (2021) Impact of laparoscopic sleeve gastrectomy on fibrosis stage in patients with child-A NASH-related cirrhosis. Surg Endosc 35:1269–1277. https://doi.org/10.1007/s00464-020-07498-4
48. McCullough A, Previs SF, Dasarathy J, et al (2019) HDL flux is higher in patients with nonalcoholic fatty liver disease. Am J Physiol Endocrinol Metab 317:E852–E862. https://doi.org/10.1152/ajpendo.00193.2019