Does Neutrophil-Lymphocyte Ratio Correlate with the Improvement of Hepatosteatosis after Laparoscopic Sleeve Gastrectomy?

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Abstract
Introduction: Obesity is a disease that shortens life expectancy and predisposes to many diseases such as severe hepatosteatosis. Hepatosteatosis is characterized by inflammatory infiltration of the portal space. Bariatric surgery has improvement effect on hepatosteatosis and degree of inflammation. Laparoscopic sleeve gastrectomy is an effective and most common therapeutic option for obesity. Neutrophil-lymphocyte ratio is a parameter associated with inflammatory disease. This study aimed to investigate if there is any correlation between improvements in hepatosteatosis and biochemical parameters especially neutrophil-lymphocyte ratio and ultrasonographic findings 1 year after the laparoscopic sleeve gastrectomy. Methods: The files of 66 patients who underwent laparoscopic sleeve gastrectomy between May 2017 and April 2020 were retrospectively reviewed. Preoperative and postoperative 1-year demographic data, biochemical and inflammatory parameters, and ultrasonographic reports of the liver were reviewed. Results: A statistically significant improvement in hepatosteatosis was demonstrated by ultrasonography 1 year after laparoscopic sleeve gastrectomy. A significant decrease was also observed in neutrophil-lymphocyte ratio. No correlation was found between the decrease of neutrophil-lymphocyte ratio and improvement in hepatosteatosis. There was also significant difference between the preoperative and postoperative BMI, biochemical and inflammatory parameters. Conclusion: However, we found laparoscopic sleeve gastrectomy is associated with significant improvement in hepatosteatosis and inflammatory parameters; no correlation between the improvement in hepatosteatosis and NLR was seen at 1 year.

Introduction

Obesity is recognized as a global health problem [1]. It is a disease that shortens life expectancy and predisposes patients to other diseases, such as severe hepatosteatosis. Proinflammatory markers released from fatty tissue and various cytokines may play a role in the pathogenesis of hepatosteatosis [2, 3].
Laparoscopic sleeve gastrectomy (LSG) is an effective and common therapeutic procedure for obesity [4, 5]. For morbidly obese patients, LSG has a beneficial effect on nonalcoholic fatty liver disease. Endo et al. [6] reported improvement in nonalcoholic fatty liver disease after LSG was performed on obese Japanese patients. Batman et al. [7] demonstrated that LSG is associated with a significant improvement in liver steatosis.

The neutrophil-lymphocyte ratio (NLR) is a simple and readily available predictor of inflammation obtained from the white blood cell (WBC) count. The NLR is more easily quantified than other inflammatory factors, such as C-reactive protein (CRP), tumor necrosis factor α, apolipoprotein A-1, interleukin (IL)-6, and IL-1 [8, 9]. Neutrophils represent the active nonspecific inflammatory response opening the first line of defense, whereas lymphocytes signify the regulatory machinery that adjusts the inflammatory response [10]. The relationship between NLR and inflammatory diseases, cancers, and many liver diseases has been demonstrated [11].

The NLR has been studied to predict complications following major surgical procedures and bariatric surgery [12–14]. Farias et al. [15] demonstrated an improvement in the inflammatory profile and an increase in anti-inflammatory markers after obesity surgery.

The gold standard for the diagnosis of hepatosteatosis is liver biopsy. However, complications can occur with this procedure and result in pain, bleeding, or even death. Abdominal ultrasonography (USG) is a low-cost, noninvasive, and reliable imaging technique widely used in the clinical diagnosis of hepatosteatosis [16, 17].

The correlation between improvement in hepatosteatosis and change in NLR after LSG has not been previously studied. This study was conducted to investigate whether there is any correlation between improvements in the inflammatory profiles of obese patients who had undergone LSG and their reduced severity of hepatosteatosis. We aimed to find any correlation between NLR and hepatosteatosis 1 year after LSG and to evaluate the changes in biochemical and inflammatory parameters and body mass index (BMI).

**Materials and Methods**

A total of 160 patients underwent LSG by a single surgeon between May 2017 and April 2020. Bariatric surgery is not performed if patients have chronic liver disease, viral hepatitis, autoimmune hepatitis, drug-induced liver disease, biliary obstruction, chronic kidney disease, coagulation disorders, or severe complications related to congestive heart failure.

Subjects were included in the study if they were at least 18 years of age and had a BMI of more than 40 kg/m² or 35 kg/m² with co-morbid conditions (e.g., taking oral antidiabetic drugs, hypertension, obesity-related joint problems, obstructive sleep apnea). Patients who had undergone bariatric surgery for a second time and patients who did not attend the first-year follow-up were excluded from the study.

A total of 66 patients met the inclusion criteria for the study. Demographic data (age, gender, height, weight, and BMI), biochemical parameters (aspartate aminotransferase [AST], alanine aminotransferase [ALT], gamma glutamyl transferase [GGT], lactate dehydrogenase [LDH], high-density lipoprotein [HDL], low-density lipoprotein [LDL], albumin, total protein, total cholesterol, and triglycerides [TG]), inflammatory parameters (NLR, CRP levels, and WBC count), and liver USG reports were obtained before LSG. All patients were invited to a laboratory test 1 year after LSG.

Laboratory measurements of patients were obtained through venous blood samples that were collected after at least 12 h of fasting and arrived at the laboratory within 2 h. Blood samples were centrifuged for at least 10 min at 5,000 rpm/min.

All participating patients underwent LSG under general anesthesia with endotracheal intubation using five trocars in the supine position by the same surgeon, who applied a pneumoperitoneum with a pressure of 18 mm Hg. Gastric resection was performed using a 39-Fr bougie.

The same radiologist performed grayscale USG examinations on patients using a 3.5-MHz convex probe and a Samsung RS80A device after they had fasted for at least 8 h. The degree of steatosis in the liver was classified as normal (grade 0), mild (grade 1), moderate (grade 2), or severe (grade 3) based on the degree of increased echo of the liver parenchyma and whether the echo of the intrahepatic vascular structures and diaphragm was clearly seen in the fatty liver with increased echo [7].

**Statistical Analysis**

Data analysis was performed using SPSS version 22. First, the quantitative variables' frequencies, number of observations, and percentages were presented, as well as descriptive statistics for the quantitative variables. Comparisons of the laboratory data and hepatosteatosis degree rate were performed between the preoperative group and the postoperative first-year follow-up group. Paired samples, T tests, and F tests of analysis of variance were used for normally distributed variables, and the Wilcoxon test was used for non-normally distributed variables. In addition, the marginal homogeneity test was conducted to determine the effect of obesity surgery on the degree of hepatosteatosis. The obtained values were given as mean ± standard deviation, and p values of less than 0.05 were considered statistically significant.

**Results**

There were 66 patients in the study, of which 23 (34.8%) were male and 43 (65.2%) were female. The ages of the patients ranged from 18 to 67 years, and the mean age was 40 years. The mean BMI of the patients before surgery was 43.3 and decreased to a mean of 24.8 1 year after LSG. This change was statistically significant.
The differences between the preoperative and postoperative mean NLRs and WBC counts were statistically significant, but the difference in CRP levels was not significant. There were also significant differences between preoperative and postoperative ALT, GGT, LDH, LDL, albumin, total protein, and total cholesterol levels. No significant differences were found in AST, HDL, or TG (Table 1).

A significant effect of LSG on the degree of hepatosteatosis was observed. No patient had grade 3 hepatosteatosis 1 year after LSG, although the rate was 10.6% before surgery. The rate of grade 2 hepatosteatosis decreased from 45.5% to 3.1% after LSG (Table 2).

F tests of analysis of variance showed no correlation between the improvement in hepatosteatosis and the mean NLR values 1 year after LSG (Table 3). The subgroup analysis is shown in Figure 1.

**Table 1.** Laboratory data of patients before and 1 year after LSG

| Variables | Preoperative | | One year after surgery | | p value |
|-----------|--------------|---|------------------------|---|--------|
|           | mean | standard deviation | mean | standard deviation | |
| NLR       | 2.92  | 1.18 | 1.48 | 0.85 | **0.000** |
| WBC       | 8.77  | 1.81 | 6.54 | 1.64 | **0.000** |
| CRP       | 1.05  | 3.04 | 0.59 | 0.87 | 0.071 |
| BMI       | 43.43 | 5.93 | 24.83 | 2.33 | **0.000** |
| AST       | 22.05 | 10.55 | 19.33 | 6.14 | 0.220 |
| ALT       | 31.13 | 17.39 | 20.53 | 8.88 | **0.000** |
| GGT       | 35.89 | 22.09 | 23.60 | 16.46 | **0.000** |
| LDH       | 202.95 | 41.25 | 168.14 | 32.75 | **0.000** |
| Albumin   | 4.50  | 0.28 | 4.41 | 0.43 | **0.005** |
| Total protein | 7.53  | 0.46 | 7.11 | 0.44 | **0.000** |
| Total cholesterol | 203.06 | 47.27 | 172.43 | 29.41 | **0.000** |
| HDL       | 47.97 | 12.34 | 50.27 | 10.27 | 0.243 |
| LDL       | 127.88 | 40.84 | 109.90 | 28.22 | **0.001** |
| TG        | 161.77 | 144.52 | 117.62 | 63.82 | 0.080 |

**Table 2.** Hepatosteatosis degree rate of the patients before and 1 year after LSG

| Hepatosteatosis degree | Before the surgery | One year after the surgery | Test | p value |
|------------------------|-------------------|----------------------------|------|---------|
| Grade 1                | 25                | 22                         | MH = 95,000 | **0.000** |
| Grade 2                | 30                | 3                          |      |         |
| Grade 3                | 7                 | –                          |      |         |
| Normal                 | 4                 | 41                         |      |         |

MH, marginal homogeneity test.

**Table 3.** Correlation between hepatosteatosis and mean NLR values 1 year after LSG

| Hepatosteatosis degree | Test and p value |
|------------------------|------------------|
| normal | grade 1 | grade 2 |
| X SDSS | X SDSS | X SDSS |
| Mean NLR level at 1 year | 1.34 | 1.70 | 1.8 |
| SD 0.85 | SD 1.35 | SD 0.01 |

F, analysis of variance (ANOVA) F test.
Discussion

In this study, a significant improvement in hepatosteatosis was observed through USG 1 year after LSG. A significant decrease in NLR and BMI was also observed. The correlation between improvement in hepatosteatosis and change in NLR after LSG has not been previously studied. However, no correlation was found between the decrease in NLR and improvement in hepatosteatosis.

Nonalkolik steatohepatit is the most common chronic liver disease, with a prevalence rate of up to 90% in morbidly obese people. It can progress to liver fibrosis and even cirrhosis [7, 18, 19]. Liver biopsy is the gold standard technique in the diagnosis of hepatosteatosis; however, it is an invasive method [20]. Abdominal USG is a low-cost, noninvasive, and reliable imaging modality widely used for diagnosing hepatosteatosis. Wu et al. [17] showed that USG had 86% sensitivity and 81% diagnostic accuracy in detecting hepatosteatosis, comparing preoperative USG and liver biopsy findings in patients undergoing bariatric surgery. Mottin et al. [16] reported a high positive predictive value (95.4%), suggesting USG usage as a diagnostic tool for hepatosteatosis in morbidly obese patients.

LSG is the most common bariatric procedure around the world [21–23]. Improvement of hepatosteatosis has been reported with a decrease in BMI after LSG [6, 7, 24]. Esquivel et al. [25] showed that all the participating patients reversed or reduced the stage of hepatosteatosis 1 year after LSG.

Obesity and obesity-related diseases are related to inflammation. The adipose tissue contributes to both the initiation and maintenance of systemic inflammation [9, 26]. Obesity shows a low grade of chronic inflammation due to a loss of balance between pro- and anti-inflammatory signals [9]. Elevated levels of several inflammatory markers have been associated with an increased risk of several obesity-related diseases, including cardiovascular disease, type 2 diabetes, and nonalkolik steatohepatit [2, 3].

The NLR is more sensitive for evaluating inflammatory conditions than CRP levels. The NLR allows for a better prediction of clinical outcomes in patients with systemic inflammation [9]. The NLR has been studied several times following bariatric surgery [9, 13, 14]. Bulur et al. [27] showed that the NLR decreased after surgery in a proportional reduction in adipose tissue. Da Silva et al. [13] demonstrated that postoperative day 1 NLR was independently associated with 30-day outcomes following bariatric surgery. Zubiaga and Ruiz-Tovar [9] studied metabolic parameters in patients undergoing sleeve gastrectomy and showed that preoperative NLR had an inverse correlation with excess weight loss and a direct correlation with fasting glucose 5 years post-operation.

In this study, preoperative and postoperative hepatosteatosis were evaluated using USG. A significant improvement in hepatosteatosis was observed 1 year after LSG. The difference between the preoperative and postoperative mean NLR values was also significant. To analyze the predictive value of NLR with outcomes, preoperative and postoperative 1-year NLR was studied with improvement in hepatosteatosis. However, no correlation was found between the improvement in hepatosteatosis and the change in NLR after LSG.

In addition to NLR, CRP levels and WBC counts were studied to evaluate the inflammatory response of the LSG. A significant difference was found between the preoperative and postoperative WBC counts, but the difference in CRP levels was not significant. Similar findings to our results have been reported. Ramalho et al. [28] observed a decrease in CRP levels and WBC counts after LSG that was not statistically significant. Chiappetta et al. [29] reported significantly decreased CRP levels, but the change in WBC count was not significant after bariatric surgery. The changes in biochemical parameters in this study were similar to those of previous studies [30].

This study had some limitations as it was a retrospective study that included a small number of cases. Only the NLR, WBC count, and CRP levels were evalu-

![Fig. 1. Subgroup analysis of the improvement of hepatosteatosis.](image)
lated as chronic inflammation markers. Inflammatory factors that have been studied before, such as tumor necrosis factor α, apolipoprotein A-1, IL-6, and IL-1, would most likely support our findings [8, 9]. However, WBC counts and CRP levels represent the standard biochemical parameters usually studied in daily clinical practice.

Conclusions

LSG has an anti-inflammatory effect by decreasing the NLR. Improvements in hepatosteatosis after LSG did not correlate with the mean NLR decrease, but prospective studies with greater patient participation and additional inflammatory parameters may support the findings of the present study.

Statement of Ethics

The Institutional Review Board of Istinye University approved the present study (approval No. 21-63), which conformed to the principles of the Declaration of Helsinki. Patient consent for participation was obtained using the opt-out method.

Conflict of Interest Statement

The authors declare that they have no conflicts of interest.

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Author Contributions

Kadir Yildirim, Ilhan Karabacak, and Recep Aktimur designed the original concept of this study. Zafer Malazgirt and Mahmut Fikret Gursel wrote the initial draft of the manuscript. Kadir Yildirim, Ilhan Karabacak, and Esra Kayahan Ulu reviewed and edited the manuscript. All other authors contributed to data collection and interpretation and critically reviewed the manuscript. All authors approved the final version of the manuscript and agreed to be accountable for all aspects of the work, ensuring that questions relating to the accuracy or integrity of any part of the work were appropriately investigated and resolved.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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