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ORIGINAL ARTICLE

Impact of bariatric surgery on non-alcoholic fatty liver disease

Authors' Contribution:
A–Study Design
B–Data Collection
C–Statistical Analysis
D–Data Interpretation
E–Manuscript Preparation
F–Literature Search
G–Funds Collection

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ABSTRACT:

Introduction: Up to 300 million people have the body mass index (BMI) greater than 30 kg/m2. Obesity is the cause of many serious diseases, such as type 2 diabetes, hypertension, and non-alcoholic fatty liver disease (NAFLD). Bariatric surgery is the only effective method of achieving weight loss in patients with morbid obesity.

Objectives: The aim of the study was to assess the impact of bariatric surgery on non-alcoholic fatty liver disease in patients operated on due to morbid obesity.

Material and Methods: We included 20 patients who were qualified for bariatric procedures based on BMI > 40 kg/m2 or BMI > 35kg/m2 with the presence of comorbidities. The average body weight in the group was 143.85kg, with an average BMI of 49.16kg/m2. Before the procedure, we evaluated the severity of non-alcoholic fatty liver disease in each patient using the Sheriff-Saadeh ultrasound scale. We also evaluated the levels of liver enzymes. Follow-up evaluation was performed twelve months after surgery.

Results: Twelve months after surgery, the average weight was 102.34 kg. The mean %WL was 33.01%, %EWL was 58.8%, and %EBMIL was 61.37%. All patients showed remission of fatty liver disease. Liver damage, evaluated with ultrasound imaging, decreased from an average of 1.85 on the Sheriff-Saadeh scale, before surgery, to 0.15 twelve months after surgery ($p < 0.001$). As regards liver enzymes, the level of alanine aminotransferase decreased from 64.5 (U/l) to 27.95 (U/l) ($p < 0.001$), and the level of aspartate aminotransferase decreased from 54.4 (U/l) to 27.2 (U/l).

Conclusions: Bariatric procedures not only lead to a significant and lasting weight loss, but they also contribute to the reduction of fatty liver disease and improve liver function.

KEYWORDS: non-alcoholic fatty liver disease, bariatric surgery, morbid obesity

INTRODUCTION

Worldwide, it is estimated that there are approximately 1 billion overweight people, and more than 300 million suffer from obesity (BMI > 30kg/m^2) [1]. Adipose tissue is a highly active metabolic and endocrine organ that contributes to the development of diabetes, metabolic syndrome, non-alcoholic fatty liver disease (NAFLD), and other conditions.

NAFLD is a broad term that encompasses many different disorders that range from fatty liver disease to inflammatory disease with fibrosis and cirrhosis. In NAFLD, the etiology of liver changes is not associated with alcohol consumption, despite a similar appearance to alcoholic liver disease. It is hypothesized that the disease is possibly related to lifestyle and genetic factors. [2] The disease was first diagnosed in the 1930s, described in 1950s, and characterized histopathologically in 1980s. However, only now has it been recognized as an important clinical problem. [3] NAFLD is characterized by lipid accumulation in the hepatocytes, and in NAFLD, lipids comprise more than 5% of the liver. NAFLD is believed to result from an increased flow of free fatty acids (FFA) through the liver. It may be caused by increased lipolysis, increased fat intake, mitochondrial dysfunction associated with insulin resistance, or by *de novo* lipogenesis. [7]

NAFLD is considered to be one of the main causes of chronic liver dysfunction in the developed world, afflicting 9–30% of the general population. There is a well-established association between NAFLD and excessive caloric intake that leads to obesity. Correlation between the severity of obesity and the degree of NAFLD is found in 90% of biopsies performed during bariatric procedures. [4]

Currently, there are no unequivocal guidelines regarding the treatment of NAFLD. Weight loss, achieved through lifestyle changes and exercise, offers some improvement. In patients with morbid obesity, if these methods are ineffective, bariatric surgery seems to be the most appropriate treatment. Even though weight loss is the most visible effect of bariatric surgery, its most important goal is the treatment of life-threatening comorbidities. The influence of surgical procedures on NAFLD is poorly documented compared to other comorbidities, like diabetes or hypertension.

AIM OF THE STUDY

To estimate the influence of bariatric procedures on the natural course of non-alcoholic fatty liver disease.

MATERIAL AND METHODS

As regards the indications for surgical treatment, we used the recommendations of the Section of Metabolic and Bariatric Surgery of the Polish Surgeon Society, as follows, body mass index (BMI) ≥ 35 kg/m^2 with comorbidities or BMI ≥ 40 kg/m^2 with or without comorbidities. The inclusion criteria were as follows, informed consent to participate in the study, age between 18-65 years, and fulfilment of eligibility criteria for bariatric treatment [laparoscopic sleeve gas-

trectomy (LSG) or laparoscopic Roux-en-Y gastric bypass (LRYGB)]. We excluded patients who were lost to follow-up after 12 months, patients diagnosed with mental diseases, patients diagnosed with alcohol or drug dependence, and patients who had undergone different bariatric procedures. In total, 20 patients were included in the study. All patients underwent laparoscopic bariatric procedures in the 2nd Department of General Surgery, Jagiellonian University Medical College. Among the patients, there were 12 women (60%) and 8 men (40%). The mean age was 39.55 years. The mean body mass was 143.85kg, and the mean BMI was 49.16kg/m^2. Sixteen patients had either diabetes or glucose tolerance impairment. Currently, there are guidelines regarding the choice of surgery method is patients with diabetes, and it is believed that LRYGB is more effective in patients with a long history of diabetes. Five patients underwent LSG, and 15 patients underwent LRYGB.

All patients included in this study underwent an evaluation of liver function and structure in order to document the presence and severity of NAFLD. In order to assess liver function impairment, a standard set of blood liver enzymes was assessed, including aspartate aminotransferase (AST) and alanine aminotransferase (ALT). In order to evaluate liver structure and its impairment in the course of NAFLD, we performed ultrasound examinations. The Sheriff-Saadeh scale was used to assess the severity of steatohepatitis. The details of the Sheriff-Saadeh scale are shown in Table 1. [5] All ultrasonographic examinations were performed by the same experienced physician. The General Electric LOGIQ 7 system with a 3.5–5.5MHz convex probe was used for all examinations.

Follow-up evaluations were performed one year after surgery. During follow-up visits, we evaluated the effectiveness of bariatric procedures in terms of weight loss and reduction of comorbidities. A detailed medical history was taken, and physical examinations were conducted. Body weight was determined using the Tanita BC-420S MA device. The percentage weight loss (%WL), the percentage loss of excessive weight (%EWL), and the percentage loss of excessive BMI (%EBMIL) were used to evaluate the reduction in body mass. To evaluate NAFLD regression, follow-up ultrasound examinations were performed by the same person, according to the Sheriff-Saadeh scale, and the same laboratory tests as before surgery, including AST and ALT levels, were carried out The patients were referred for psychological or dietary advice, if they reported any problems in those areas.

The Statistica 10 software was used for statistical analysis, and the Student's t-test was used to the differences in AST and ALT levels before surgery and on follow-up. The Wilcoxon signed-rank test was performed for the Sheriff-Saadeh scale evaluation.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was approved by the Bioethics Committee of the Jagiellonian University. The study was registered under NCT02828579 (ClinicalTrials.gov)

RESULTS

We observed a reduction in the body mass index in all patients who underwent surgery. The mean BMI one year after the procedure was 36.42kg/m^2 (down from 49.16kg/m^2). The mean body mass was 102.34 kg (down from 143.85kg). The %WL was 33.01%, %EWL was 58.8%, and %EBMIL was 61.37%.

Out of all 20 patients, 14 (70%) had diabetes, and 2 (10%) had impaired glucose tolerance. Four patients required insulin administration, while the remaining patients took oral anti-diabetic drugs. Seventeen patients (85%) were diagnosed with hypertension, and 17 patients (85) also had hyperlipidemia. None of patients had obstructive sleep apnea.

In terms of concomitant diseases, we observed an improvement in diabetes control. Of all patients who were initially treated with anti-diabetic medications, 16 (80%) went into remission and did not require further diabetic treatment. Three patients continued to require insulin injections; however, their daily insulin intake dropped from a mean of 102.0 units per day to 37.6. units per day. We achieved normalization of blood pressure in 4 patients. Thirteen patients (65%) continued to require antihypertensive drugs. Ten patients (50%) had normalization of the lipid profile one year after bariatric surgery.

Before surgery, the mean Sheriff-Saadeh score in patients undergoing the procedure was 1.85 ± 1.08. One year after surgery, the mean score on the Sheriff-Saadeh scale dropped to 0.15, which was statistically significant ($p < 0.001$).

The mean AST level was 60.8 ± 36.5 U/l, and the average ALT level was 49.05 ± 47.6 U/l. We observed a statistically significant reduction in both ALT and AST levels to 27.7U/l for ALT ($p = 0.00$), and 54.4 U/l for AST ($p = 0.02$).

DISCUSSION

Over the past years, surgery has gained acceptance as a treatment method for morbid obesity. It leads to body weight reduction to an extent that is unobtainable with dietary modifications alone. It has been proven that both laparoscopic sleeve gastrectomy and laparoscopic Roux-en-Y gastric bypass surgery are both efficient and safe.[6]

NAFLD is a disease that is very strongly associated with obesity. [21, 22] The Dallas Heart Study also suggests that the prevalence of NAFLD varies with the ethnicity. In that study, NAFLD was diagnosed in 45% of Latinos, 33% of Caucasians, and 24% of African Americans. [8] Among patients with NAFLD, 10–20% suffer from non-alcoholic steatohepatitis (NASH), and 8–26% of patients with NASH develop liver cirrhosis. [9] It has been proven that some genetic defects related to VLDL synthesis may have an influence on morbidity. [10] There are several conditions that may contribute to the development of this disease, e.g., type 2 diabetes, metabolic syndrome, obesity, dyslipidemia, hypogonadism, hypothyroidism, polycystic ovarian syndrome, and even specific bacterial flora in the intestine [11].

In order to diagnose NAFLD, a history of alcohol use must be ruled out, along with other chronic disorders that may lead to chronic liver disease. In the course of the disease, elevated liver function tests (LFT) and a decreased level of adiponectin in peripheral blood may be observed. Other tests that may be useful in diagnosing NAFLD include ultrasound (US), magnetic resonance

Tab. I. The Sheriff-Saadeh scale

GRADE	0	1	2	3
Description	Normal echogenicity	Slight, diffuse increase in fine echoes in liver parenchyma with normal visualization of diaphragm and intrahepatic vessel borders	Moderate, diffuse increase in fine echoes with slightly impaired visualization of intrahepatic vessels and diaphragm	Marked increase in fine echoes with poor or non-visualization of the intrahepatic vessel boarder, diaphragm, and posterior right lobe of the liver

imaging (MRI), computed tomography (CT) of the abdomen, and liver elastography. With respect to ultrasound, low cost, safety, and lack of radiation exposure make it the first-line method for the diagnosis and follow-up of NAFLD.

Liver biopsy remains the gold standard in the diagnosis of NAFLD. [12] It is the most conclusive method that can be used to exclude steatohepatitis, which is a condition that can lead to liver fibrosis and eventually cirrhosis. However, the procedure is invasive and carries a risk of complications, which may affect up to 20% of patients. [13] The rising incidence of NAFLD in Western countries underscores the necessity of developing a less invasive diagnostic test for distinguishing NAFLD from steatohepatitis. The use of liver elastography allows for the evaluation of increased liver stiffness in hepatic fibrosis. [14] This technique is very difficult to apply in bariatric patients, since in patients with a BMI greater than 28kg/m^2, there is a high possibility of misdiagnosis. [15] According to the authors, liver biopsy can be avoided in 75% of patients.

There are several ultrasound scales to assess the severity of NAFLD. The ultrasonographic scale developed by Sheriff and Saadeh is an easy tool for detecting and monitoring the disease. However, this scale, by itself, does not distinguish between steatosis and steatohepatitis. Nevertheless, we are convinced that this simple tool is very useful in the monitoring of liver status and indicating which patients should undergo liver biopsy.

There is strong evidence that the most effective way to diminish liver steatosis is body mass reduction. Promrat et al., who studied lifestyle modification as a treatment option, have shown that a minimum body weight loss of 7% causes improvement in liver histology. Dietary modification, together with physical activity, improves lipid levels and aminotransferases and mitigates insulin resistance. [16] Research on the pharmacological treatment of NAFLD also offers some hope. A few drugs seem to be potentially useful, including metformin, alpha-tocopherol, vitamin C, and thiazolidinediones. However, none of these agents has been proven effective in decreasing the level of liver steatosis. [16] Surprisingly, regular consumption of coffee provides some protection against liver fibrosis. [17] Although lifestyle modification should be the treatment of choice in all cases of NAFLD, it is not a practical solution in patients with morbid obesity. The long-term results of conservative treatment of obesity and related comorbidities in this study group are very disappointing. So far, surgery is the only method that has well-documented and lasting results.

NAFLD may be found in up to 98% of patients undergoing bariatric surgery. However, it is not associated with a higher risk of perioperative morbidity, even if the patient suffers from non-alcoholic steatohepatitis (NASH), which is an advanced phase of NAFLD that is defined by the presence of inflammatory infiltration in the liver tissue.

Our study suggests that bariatric surgery promotes regression of hepatic steatosis. We observed significant improvement not only in liver function tests but also in Sheriff-Saadeh scores that dropped significantly, proportionally to the reduction in BMI. Our findings are similar to those from other trials that have evaluated NAFLD status after bariatric surgery. Vargas et al. revealed that the Roux-en-Y gastric by-pass not only leads to body weight reduction but also improves liver function through regression of liver steatosis. [18] Hady et al., who investigated the influence of laparoscopic sleeve gastrectomy on the metabolic status of patients, proved that it causes changes in the levels of AST and ALT; however, these changes were not statistically significant. Nevertheless, the surgery was associated with a significant decline in lipid levels. Haafez et al. compared vertical band gastroplasty and adjustable gastric banding in terms of forward regression of liver steatosis in patients who underwent bariatric surgery. [19] Moreover, according to Weingarten et al., NAFLD and NASH are not contraindications to bariatric surgery and do not increase the perioperative complication rate. [20] A limitation of our study is a small study sample; however, this is one of few available studies in the European population and the first study in the Polish population. Moreover, to out knowledge, this is the only study that has investigated the feasibility of ultrasound scales as the sole diagnostic method without the need of liver biopsy.

CONCLUSIONS

Lifestyle modification should be the first-line treatment in NAFLD; however, bariatric surgery should be considered as a treatment option in patients with severe and complex obesity.

Ethical approval: The study was approved by the Bioethics Committee of the Jagiellonian University.

Competing interest: No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

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