Impact of bariatric surgery on non-alcoholic fatty liver disease

Piotr Major, Michał Pędziatr, Mateusz Rubinkiewicz, Maciej Stanek, Anna Głuszewska, Magdalena Pisarska, Piotr Małczak, Andrzej Budzyński, Piotr Budziński

INTRODUCTION

Worldwide, it is estimated that there are approximately 1 billion overweight people, and more than 300 million suffer from obesity (BMI > 30kg/m²) [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/m² with comorbidities or BMI ≥ 40 kg/m² 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-
The mean BMI one year after the procedure was 36.42kg/m² (down from 49.16kg/m²). The mean body mass was 102.34 kg (down from 143.85 kg). 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

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/m² (down from 49.16kg/m²). The mean body mass was 102.34 kg (down from 143.85 kg). The %WL was 33.01%, %EWL was 58.8%, and %EBMIL was 61.37%.

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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
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 28 kg/m², 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. Haaf ez 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 our 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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**REFERENCES**

1. WHO: The World Health Report 2002 – Reducing Risks, Promoting Healthy Life 2009. Available from: http://www.who.int/whr/2002/en/, Access 20.06.2014

2. Farrel GC. Non-alcoholic fatty liver and non-alcoholic steatohepatitis. In: Textbook of hepatology. From basic science to clinical practice. 3rd Edn. Oxford: Blackwell Publishing 2007, 1195–1207.

3. Zelman S. The liver in obesity. A.M.A Archives of Internal Medicine, vol. 90, pp. 141–156, 1952.

4. Pirvuulescu I, Gheorghe I., Csiki I et al. Noninvasive Clinical Model for the Diagnosis of Nonalcoholic Steatohepatitis in Overweight and Morbidly Obese Patients undergoing to Bariatric Surgery. Chirugia(2012) 107: 772–779

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**Tab. 1. The Sheriff-Saadeh scale**

| GRADE | 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 |
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5. Saadeh S, Younossi ZM, Remer EM et al. The utility of radiological imaging in nonalcoholic fatty liver disease. Gastroenterology. 2002 Sep;123(3):745–50
6. Picot J, Jones J, Colquitt JL et al. The clinical effectiveness and cost-effectiveness of bariatric (weight loss) surgery for obesity: a systematic review and economic evaluation. Health Technol Assess. 2009 Sep;13(41):1–190, 215–357, iii–iv. doi: 10.3310/hta13410
7. Seung Hoi Koo. Nonalcoholic fatty liver disease: molecular mechanisms for the hepatic steatosis Clinical and Molecular Hepatology 2013;19:210–215
8. Tsuneto, A., Hida, A., Sera N et al. 2010. Fatty liver incidence and predictive variables. Hyper Res. 33: 638–643
9. Matteoni CA, Younossi ZM, Gramlich T et al. Nonalcoholic fatty liver disease: a spectrum of clinical and pathological severity. Gastroenterology 1999;116:1413–1419
10. Cohen J, Horton J, Hobbs H. Human Fatty Liver Disease: Old Questions and New Insights. Science 2011 June 24; 332(6037): 1519–1523
11. Loría P, Carulli L, Bertolotti M et al. 2009. Endocrine and liver interaction: the role of endocrine pathways in NASH. Nat. Revs. 6:236–247,
12. McHutchison J, Poynard T, Abdal N. Fibrosis as an end point for clinical trials in liver disease: a report of the international fibrosis group. Clin Gastroenterol Hepatol. 2006 Oct;4(10):1214–1220.
13. Gilmore IT, Burroughs A, Murray-Lyon IM et al. Indications, methods, and outcomes of percutaneous liver biopsy in England and Wales: an audit by the British Society of Gastroenterology and the Royal College of Physicians of London. Gut. 1995 March; 36(3): 437–441
14. Palmeri ML, Wang MH, Rouze NC et al. Noninvasive Evaluation of Hepatic Fibrosis using Acoustic Radiation Force-Based Shear Stiffness in Patients with Nonalcoholic Fatty Liver Disease. J Hepatol. 2011 Sep;55(3):666–72.
15. Foucher J, Castera L, Berhard PH. Prevalence and factors associated with failure of liver stiffness measurement using FibroScan in a prospective study of 2114 examinations. European Journal of Gastroenterology and Hepatology. 2006;18:411–412
16. Nobili V, Manco M, Devito R et al. Lifestyle intervention and antioxidant therapy in children with nonalcoholic fatty liver disease: a randomized, controlled trial. Hepatology. 2008 Jul;48(1):119–28.
17. Attar BM, Van Thiel DH. Current concepts and management approaches in nonalcoholic fatty liver disease. ScientificWorldJournal. 2013;2013:481893.
18. Vargas V, Allende H, Lecube A et al. Surgically induced weight loss by gastric bypass improves non alcoholic fatty liver disease in morbid obese patients. World J Hepatol. 2012 Dec 27;4(12):382–8.
19. Hafeez S, Ahmed MH. Bariatric surgery as potential treatment for nonalcoholic fatty liver disease: a future treatment by choice or by chance? J Obes. 2013;2013:839275.
20. Weingarten TN, Swain IM, Kendrick ML et al. Nonalcoholic steatohepatitis (NASH) does not increase complications after laparoscopic bariatric surgery. Obes Surg. 2011 Nov;21(11):1714–20.
21. Aguilar-Olivos, Nancy E, Almeda-Valdes, et al. The role of bariatric surgery in the management of nonalcoholic fatty liver disease and metabolic syndrome. Metabolism: clinical and experimental 2016, 65, 8, 1196-207.
22. Hannah WN Jr, Harrison SA Effect of Weight Loss, Diet, Exercise, and Bariatric Surgery on Nonalcoholic Fatty Liver Disease, Clin Liver Dis. 2016, May;20(2):339-50,

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Corresponding author: Piotr Major, 2nd Department of General Surgery, Jagiellonian University Medical College, Kopernika 21 St,31-501, Kraków, Poland, e-mail: majorpiotr@gmail.com

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