ELSEVIER

Surgery for Obesity and Related Diseases ▮ (2017) 00–00

SURGERY FOR OBESITY AND RELATED DISEASES

Original article

Patients with clinically metabolically healthy obesity are not necessarily healthy subclinically: further support for bariatric surgery in patients without metabolic disease?

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Received August 2, 2017; accepted November 29, 2017

Abstract

Background: Nonalcoholic fatty liver disease (NAFLD) increases the risk of liver cirrhosis and hepatocellular carcinoma and is also strongly correlated with extrahepatic diseases, including cardiovascular disease and type 2 diabetes. This risk of NAFLD among obese individuals who are otherwise metabolically healthy is not well characterized.

Objectives: To determine the prevalence and characteristics of NAFLD in individuals with metabolically healthy obesity.

Setting: A tertiary, academic, referral hospital.

Methods: All patients who underwent bariatric surgery with intraoperative liver biopsy from 2008 to 2015 were identified. Patients with preoperative hypertension, dyslipidemia, or prediabetes/diabetes were excluded to identify a cohort of metabolically healthy obesity patients. Liver biopsy reports were reviewed to determine the prevalence of NAFLD.

Results: A total of 270 patients (7.0% of the total bariatric surgery patients) met the strict inclusion criteria for metabolically healthy obesity. The average age was 38 ± 10 years and the average body mass index was 47 ± 7 kg/m^2. Abnormal alanine aminotransferase (>45 U/L) and asparate aminotransferase levels (>40 U/L) were observed in 28 (10.4%) and 18 (6.7%) patients, respectively. A total of 96 (35.5%) patients had NAFLD with NALFD Activity Scores 0 to 2 (n = 61), 3 to 4 (n = 25), and 5 to 8 (n = 10). A total of 62 (23%) patients had lobular inflammation, 23 (8.5%) had hepatocyte ballooning, 22 (8.2%) had steatohepatitis, and 12 (4.4%) had liver fibrosis.

Conclusion: Even with the use of strict criteria to eliminate all patients with any metabolic problems, a significant proportion of metabolically healthy patients had unsuspected NAFLD. The need and clinical utility of routine screening of obese patients for fatty liver disease and the role of bariatric surgery in the management of NAFLD warrants further investigation. (Surg Obes Relat Dis 2017;▮:00–00.)

Keywords: Bariatric surgery; Liver disease, Metabolically healthy obesity; Metabolic syndrome; Nonalcoholic fatty liver disease; Diabetes, Insulin resistance; Steatohepatitis

This study was presented at ObesityWeek 2017.

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https://doi.org/10.1016/j.soard.2017.11.032
1550-7289/

Obesity is endemic in the United States. In fact, nearly 40% of the population has a body mass index ≥30 kg/m^2 and approximately 200,000 people undergo bariatric surgery annually [1–4]. There is a known strong correlation between obesity and cardiometabolic co-morbidities, including cardiovascular disease, dyslipidemia, and diabetes [5,6]. In addition to an increased risk for cardiometabolic diseases, obesity is also associated with an increased risk for nonalcoholic fatty liver disease (NAFLD) [5,7]. NAFLD refers to the spectrum of fatty liver diseases, ranging from simple fatty liver to nonalcoholic steatohepatitis (NASH), which can progress to cirrhosis and liver failure [5,7].

NAFLD commonly co-occurs in obese patients who exhibit insulin resistance and metabolic syndrome [5,7–11]. In fact, because metabolic syndrome and NAFLD are intimately associated with insulin resistance, some have termed NAFLD the hepatic component of the metabolic syndrome [11]. Patients who are obese and exhibit features of the metabolic syndrome are referred to as metabolically abnormal obese patients, whereas patients who are obese and do not exhibit features of the metabolic syndrome are referred to as metabolically healthy obese (MHO) patients [12].

The association between metabolically abnormal obese patients, NAFLD, and the cardiometabolic benefits of bariatric surgery has been well established [13–16]. Nevertheless, the association between MHO patients, NAFLD, and the cardiometabolic benefits of bariatric surgery remain relatively unknown [9]. In fact, some studies have suggested that MHO patients have insulin sensitivity and liver fat deposition similar to nonobese individuals, while other studies have found an increased prevalence of NAFLD in MHO patients [9,17,18]. Therefore, the purpose of our study was to determine the prevalence and characteristics of NAFLD in a cohort of patients with severe but metabolic healthy obesity.

Methods

Inclusion and exclusion criteria

The institutional review board approved this study. Retrospective chart review was performed on all patients who underwent bariatric surgery at our institution from January 2008 through December 2015. All patients who underwent primary, elective, open, or laparoscopic bariatric surgery, including gastric banding, gastric plication, sleeve gastrectomy, Roux-en-Y gastric bypass, or duodenal switch were eligible for study inclusion. Patients who underwent emergency bariatric surgery and those patients who underwent revisional bariatric surgery were not eligible for study inclusion.

Identification of MHO patients

Strict criteria were used to ensure that only patients without signs of metabolic unhealthiness were included in our study. Metabolically healthy obesity was defined as patients with a body mass index ≥30 kg/m^2 without associated hypertension, dyslipidemia, or insulin resistance. The definitions used for these conditions were based on the standardized outcomes reporting published by the American Society for Metabolic and Bariatric Surgery.[19] Specifically, hypertension was defined as a systolic blood pressure ≥140 mm Hg, diastolic blood pressure ≥90 mm Hg, or the use of antihypertensive medications [19]. Dyslipidemia was defined as a fasting low-density lipoprotein level ≥130 mg/dL, high-density lipoprotein <40 mg/dL, triglycerides ≥150 mg/dL, or the use of lipid-lowering medication [19]. Finally, insulin resistance was defined as a fasting blood glucose level ≥100 mg/dL, glycosylated hemoglobin ≥5.7%, or the use of antidiabetic medications [19]. Patients were considered MHO if and only if they did not meet any of the listed criteria for hypertension, dyslipidemia, and insulin resistance.

Determining extent of liver disease

All patients undergoing bariatric surgery at our institution have preoperative laboratory blood work done within 30 days of surgery and undergo routine liver biopsy at the time of surgery. Therefore, the extent of liver involvement was determined by both laboratory blood evaluation and histologic evaluation of the liver. Abnormal blood asparate aminotransferase (AST) levels were defined as >40 U/L and abnormal blood alanine aminotransferase (ALT) levels were defined as >45 U/L per our institution's laboratory cut-points.

Routinely, a core needle biopsy is obtained from the left lobe of the liver at the time of bariatric surgery at our institution. A Tru-Cut soft tissue biopsy needle (Bard Max-Core, Covington, GA) is passed percutaneously from the anterior abdominal wall through the left lobe of the liver for tissue sampling under direct visualization. The liver tissue specimen is preserved in formalin and sent to the pathology department for analysis. Fatty liver disease is graded based on the presence or absence of steatosis, hepatocyte ballooning, and lobular inflammation.

To determine the extent of liver disease, 3 mechanisms were used: (1) the pathology results, (2) the NAFLD Activity Score (NAS), and (3) a NASH scoring algorithm [7]. NAFLD was defined as steatosis in at least 5% of hepatocytes on pathology. Liver steatosis was graded on a scale of zero to 3 (0–3), with zero corresponding to less than 5% steatosis, 1 corresponding to 5% to 33% steatosis, 2 corresponding to 34% to 66% steatosis, and 3 corresponding to >66% steatosis [7]. Hepatocyte ballooning was graded on a scale of zero to 2 (0–2) with zero corresponding to none, one corresponding to few, and 2 corresponding to many [7,20]. Lobular inflammation was graded on a scale of zero to 3 (0–3) with zero corresponding to none, 1 corresponding to <2 foci per high power field (hpf), 2