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Original article

Nonalcoholic fatty liver disease in patients with different baseline glucose status undergoing bariatric surgery: analysis of intraoperative liver biopsies and literature review

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Abstract

Background: Bariatric surgery has been investigated as a treatment option for obese patients with nonalcoholic fatty liver disease (NAFLD). Because patients with NAFLD and type 2 diabetes show accelerated progression from liver disease to cirrhosis, it has been suggested that surgery could be indicated for patients with lower degrees of obesity and type 2 diabetes.

Objective: To analyze the degree of tissue damage in liver biopsies obtained from patients undergoing bariatric surgery, correlating histopathologic findings with their baseline glucose status.

Setting: General hospital in the public health system.

Methods: Intraoperative liver biopsies were obtained from 521 obese patients undergoing bariatric surgery. Patients were divided into 3 study groups according to their preoperative glucose levels: 167 (32.05%) type 2 diabetic, 132 (25.33%) prediabetic, and 222 (42.61%) normoglycemic patients. Tissue samples were classified in accordance with Brunt and Clinical Research Network Non-alcoholic Steatohepatitis criteria.

Results: Prevalence of NAFLD was 95%. Higher rates of hepatic fibrosis were observed in diabetic patients (56.4%) compared with prediabetic (29.2%), and normoglycemic patients (28.6%) ($P < .001$). Nonalcoholic steatohepatitis was diagnosed in 59.4% of the diabetics, in 49.2% of the prediabetics, and in 36% of the normoglycemic obese ($P < .001$). Only 1.5% of the diabetics had no histologic hepatic alterations.

Conclusion: NAFLD is markedly more severe in diabetic patients. Our data suggest that intraoperative liver biopsy should be considered for diabetic patients undergoing bariatric surgery. Early bariatric surgery should be investigated as a means to prevent progression of NAFLD. (Surg Obes Relat Dis 2017;■:00–00.) © 2017 American Society for Metabolic and Bariatric Surgery. All rights reserved.

Keywords: NAFLD; Bariatric surgery; Type 2 diabetes; Obesity

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The worldwide obesity epidemic is directly correlated with the rising prevalence of nonalcoholic fatty liver disease (NAFLD) [1], which represents the most common cause of hepatic disease in adults [2]. The disease spectrum ranges

from steatosis to nonalcoholic steatohepatitis (NASH), fibrosis, and cirrhosis [2–4]. NAFLD is usually detected during routine tests for other conditions, being found in up to 20% to 30% of the population [5]. While the prevalence in nonobese individuals is 10% to 15%, it can affect up to 85% of the morbidly obese individuals [1,6–8].

NAFLD is a known risk factor for type 2 diabetes (T2D), systemic hypertension, and chronic kidney disease. Steatosis progresses to NASH, fibrosis, and cirrhosis in approximately 5% to 6% of patients [5]. Patients with NAFLD and DM have a worse prognosis, showing an accelerated progression from liver disease to cirrhosis, and higher risk of hepatocellular carcinoma [9,10].

Clinico-biochemical parameters as well as scores of hepatic damage have been used to predict development of liver fibrosis in patients with NAFLD.⁵ Although the so-called NAFLD fibrosis score (NFS) is used as a routine test in most healthcare services [11,12], the only reliable method to diagnose NAFLD is liver biopsy, which accurately demonstrates the degree of steatosis and differentiates between NASH necroinflammatory lesions and fibrosis [13,14].

It has been demonstrated that bariatric surgery results not only in significant and sustained weight loss in obese patients, but also in improvement in clinical and metabolic parameters, decrease in insulin resistance and reduction in cardiovascular events [4,10,15]. Nevertheless, the role of bariatric surgery as a viable option for the treatment for NAFLD in the obese population is still not defined to this date [4,16]. The aim of this study was to assess the degree of liver damage through intraoperative liver biopsy in obese patients undergoing bariatric surgery, correlating their histopathologic findings with preoperative glucose status.

Methods

We analyzed a large series of patients undergoing bariatric surgery at the Class III Obesity Center within a General Hospital (Public Health System) from 2001 to 2016. Data were obtained through a retrospective review of their medical records.

Patients were selected for bariatric surgery according to the criteria of the National Institutes of Health Consensus Statement [17]: body mass index (BMI) ≥ 40 kg/m² or ≥ 35 kg/m² associated with one or more co-morbidities, age between 18 and 65 years, and failure of clinical treatment for more than 2 years. Patients with T2D and a BMI of 30 to 35 were considered eligible for the surgical treatment. Exclusion criteria were age < 18 years, history of alcohol abuse or dependence, history of viral hepatitis or viral markers positive for hepatitis B or C, hemochromatosis, and the use of hepatotoxic drugs. The patients underwent different types of surgery, including Roux-en-Y gastric bypass, vertical sleeve gastrectomy, and duodenal switch. Because the Brazilian Public Health System does not provide remuneration for laparoscopic bariatric surgeries,

all procedures had to be performed via laparotomy. Informed consent was obtained from all patients before inclusion in the study. The Research Ethics Committee of our institution approved the study.

Clinical variables

Several preoperative demographic, clinical, and laboratory characteristics of the patients were analyzed. Metabolic syndrome was diagnosed according to the 2005 International Diabetes Foundation consensus [18]: presence of abdominal obesity and at least 2 of the following characteristics: triglycerides ≥ 150 mg/dL, high-density lipoprotein cholesterol ≤ 40 mg/dL in men or ≤ 50 mg/dL in women, blood pressure $\geq 130/85$ mm Hg or use of blood pressure medication, and blood glucose ≥ 100 mg/dL or use of oral antidiabetic agents. Because the body mass index (BMI) in all patients was > 35 kg/m², abdominal obesity was presumed and abdominal circumference was not measured [18]. Diabetes and prediabetes were diagnosed according to the criteria of the American Diabetes Association [19]. Complete remission of T2D was defined as fasting blood glucose < 100 mg/dL and glycated hemoglobin (HbA1C) $< 5.7\%$, in the absence of pharmacotherapy [20]. Laboratory data included serologic hepatitis C and hepatitis B tests, aspartate aminotransferase, alanine aminotransferase, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and non-high-density lipoprotein cholesterol, triglycerides, albumin, hemogram, platelets, uric acid, fasting blood sugar and HbA1C, and fasting insulin. Insulin resistance was calculated using the homeostasis model assessment of insulin resistance with the following formula: (fasting blood sugar mg/dL \times insulin μ U/L) / 405 [21]. Additionally, the NFS was calculated using the formula proposed by Angulo et al. [11]: NFS = $1.675 + 0.037 \times \text{age (yr)} + .094 \times \text{BMI (kg/m}^2) + 1.13 \times \text{prediabetes/diabetes (Yes = 1, No = 0)} + .99 \times \text{aspartate aminotransferase/alanine aminotransferase} - .013 \times \text{platelets (} \times 10^9 / 1) - .66 \times \text{albumin (g/dL)}$ [11]. The NFS cutoff point to categorize fibrosis was < -1.455 ; -1.455 to $.676$ and $> .676$ for low, indeterminate, and high probability of advanced fibrosis, respectively.

Histologic analysis

Liver biopsies were performed during bariatric surgery through a wedge excision immediately after opening the abdominal cavity. Approximately 2 cm of tissue were obtained. The histopathologic findings of all 521 were stratified according to Brunt criteria [22]. A specialized pathologist who was blind to the clinical characteristics of the patients conducted the analysis. The biopsy material was stained with hematoxylin and eosin and PicroSirius red.

Of the 521 initial cases, 393 paraffin-embedded tissue blocks were still available for a second histologic analysis.

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