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Original article

Use of noninvasive markers to predict advanced fibrosis/cirrhosis in severe obesity

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Abstract

Background: Nonalcoholic steatohepatitis is observed in 25%–55% of patients with severe obesity and in 2%–12% with bridging fibrosis or cirrhosis. There is currently no noninvasive test for the diagnosis of severe liver fibrosis before bariatric surgery.

Objective: To determine the best noninvasive test for predicting advanced liver disease in patients with severe obesity.

Setting: University tertiary care hospital, Brazil.

Methods: A cross-sectional retrospective study was conducted with 699 patients with severe obesity undergoing bariatric surgery: 568 without a biopsy (nonbiopsy cohort) and 131 patients who had undergone an intraoperative liver biopsy. The tissues were subjected to histologic diagnosis (Brunt criteria) and classified as advanced fibrosis (stages 3 and 4) or no significant fibrosis (absence of nonalcoholic steatohepatitis and stages 1 or 2). The following predictive indices of cirrhosis were calculated in all patients: aspartate aminotransferase/alanine aminotransferase ratio (AAR), age-platelet (AP) index, aminotransferase-to-platelet ratio index (APRI), cirrhosis discriminant score (CDS), and hepatitis C antiviral long-term treatment against cirrhosis (HALT-C). The cutoff values, sensitivity, specificity, and areas under the receiver operating characteristic curves (AUROCs) were calculated for patients with biopsies.

Results: The AUROC of the AAR, AP, APRI, CDS, and HALT-C model for predicting advanced fibrosis or cirrhosis were, respectively, .522, .88, .99, .905, and .921. The calculated cutoff values, sensitivity, and specificity, respectively, were as follows: AAR: .94, .7, .45; AP 5, .7, .93; APRI .44, 1.0, .97; CDS 6, .7, .97; and HALT-C: .76, 1.0, .77.

Conclusion: APRI index was the best predictor of advanced liver disease in patients with severe obesity. (Surg Obes Relat Dis 2015;▮:00–00.)

Keywords: APRI index; CDC; HALT-C; Liver cirrhosis; Severe obesity

Obesity is a chronic multifactorial disease defined as a pathologic increase in body fat mass, a low-intensity chronic inflammatory state [1], and associated co-morbidities such as cardiovascular disease, diabetes, cancer [2], and nonalcoholic fatty liver disease (NAFLD). NAFLD may be present in 10%–30% of the general population and in 84%–96% of the severe obesity population [3,4]. NAFLD presents a spectrum of histologic alterations characterized by steatosis, lobular inflammation, cell ballooning, and fibrosis [3]. Some studies suggest an association between obesity, NAFLD, and liver cirrhosis [5].

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Nonalcoholic steatohepatitis (NASH), the most severe form of NAFLD, is observed in 25%–55% of the severely obese population, with bridging fibrosis or cirrhosis in 2%–12% of patients [4]. It is estimated that 15%–20% of patients with NAFLD will progress to cirrhosis [6], for which the mortality is 30%–40% in 10 years [7].

Liver biopsy is considered the gold standard for the differential diagnosis between NAFLD, NASH, and cirrhosis [8]. However, biopsy presents several limitations: intra- and interobserver variation [9,10], low quantification of dynamic progression or regression of disease [11], and risks associated with an invasive procedure, especially in severe obesity [10]. The macroscopic appearance of the liver during bariatric surgery is also insufficient to establish a correct diagnosis of advanced NASH [12].

Several clinical predictors, such as age, female gender, obesity, diabetes mellitus, arterial hypertension, low platelet count, and elevated aspartate aminotransferase (AST), are associated with the presence of advanced liver fibrosis in severe obesity [10,13]. It is important to know if a patient has advanced liver disease before the operation because this can modify the preoperative care; choice of surgical procedure, such as sleeve gastrectomy rather than gastric bypass; or, in the presence of portal hypertension and gastric/esophageal varices, whether a bariatric procedure should be performed at all before liver transplantation [14].

Recently, Fujii et al. [15] reported that 5 noninvasive tests (AST/alanine aminotransferase ratio [AAR], age-platelet index [AP index], AST-to-platelet ratio index [APRI], cirrhosis discriminant score [CDS], and hepatitis C antiviral long-term treatment against cirrhosis [HALT-C]) used to predict cirrhosis in patients with hepatitis C virus (HCV) were also useful in patients with NASH. CDS and HALT-C model were the best tests to predict the risk of cirrhosis with sufficient reliability in patients with NASH.

Nevertheless, to the best of our knowledge, there is currently no noninvasive test recommended for the diagnosis of severe liver fibrosis before bariatric surgery. The aim of our study was to determine the best noninvasive test to predict advanced liver disease in patients with severe obesity.

Methods

Electronic medical records of patients undergoing bariatric surgery between 2005 and 2013 in the Metabolic and Bariatric Unit, Hospital das Clinicas, University of São Paulo Medical School, were retrospectively studied. The present study was performed according to the ethical recommendations of the Declaration of Helsinki, and it was approved by the Hospital das Clinicas Ethical Committee.

Nine hundred three patients who underwent bariatric surgery were identified, and 712 individuals had complete laboratory data (AST, alanine aminotransferase, platelets count, and international normalized ratio) for all index calculations before surgery. Patients with other causes of liver disease, including hepatitis B (n = 2), hepatitis C (n = 5), hemochromatosis, Wilson's disease, autoimmune liver diseases (n = 1), or excessive alcohol consumption (20 g/d; n = 5), were excluded, leaving 699 patients in the study: 568 without a biopsy (nonbiopsy cohort) and 131 patients who had undergone an intraoperative liver biopsy.

The predictive indices of cirrhosis (AAR, AP index, APRI, CDS, and HALT-C) previously described and calculated in all patients are described in Table 1.

Liver biopsies were performed during bariatric surgery under direct vision using a 16-gauge Tru-cut needle (CareFusion, Vernon Hills, IL, USA) according to the surgeon's statement. All liver biopsy specimens had the minimal requirements and were fixed in formalin after the biopsy. Representative liver sections were stained with hematoxylin and eosin, Masson's trichrome, and periodic acid–Schiff stain. The liver tissues were subjected to histologic diagnosis according to the degree of fibrosis by the criteria of Brunt et al. [22]. The 4 histologic fibrosis stages were as

Table 1
Predictive indices of cirrhosis and calculation formulas

Index	Formula
AAR [16,17]	AST/ALT
AP index [18]	Sum of age score in yr* + platelet count (10^3/mm^3) score†
APRI [19]	AST/upper limit of the normal × 100/platelets (10^3/mm^3)
CDS [20]	Sum of platelet count (10^3/mm^3) score‡ + AST/ALT ratio score§ + INR score¶
HALT-C [21]	Exp (log odds) / 1 + exp (log odds)‖

AAR = AST/ALT ratio; ALT = alanine aminotransferase; AP = age-platelet index; APRI = AST-to-platelet ratio index; AST = aspartate aminotransferase; CDS = cirrhosis discriminant score; HALT-C = hepatitis C antiviral long-term treatment against cirrhosis; INR = international normalized ratio.

* < 30 = 0; 30–39 = 1; 2 = 40–49; 3 = 50–59; 60–69 = 4; > 70 = 5.

† > 225 = 0; 200–224 = 1; 175–199 = 2; 150–174 = 3; 125–149 = 4; < 125 = 5.

‡ > 340 = 0; 280–339 = 1; 220–279 = 2; 160–219 = 3; 100–159 = 4; 40–99 = 5; < 40 = 6.

§ > 1.7 = 0; 1.2–1.7 = 1; 0.6–1.19 = 2; < 0.6 = 3.

¶ < 1.1 = 0; 1.1–1.4 = 1; > 1.4 = 2.

‖ Log odds (predicting cirrhosis) = –5.56 – .0089 × platelet count (10^3/mm^3) + 1.26 × AST/ALT + 5.27 × INR.