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Original article

Derivation and validation of a scoring system for predicting nonalcoholic steatohepatitis in Taiwanese patients with severe obesity

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Abstract

Background: Nonalcoholic steatohepatitis (NASH) is common in severely obese Asians and may progress to advanced liver disease. Although invasive, liver biopsy is the gold standard for NASH NASdiagnosis. Scoring systems for predicting NASH in obese Asians are scarce.

Objectives: To develop and validate a scoring system to predict NASH in Taiwanese patients with severe obesity.

Setting: University hospital, Taiwan.

Methods: Preoperative clinical and laboratory data were obtained from 180 severely obese patients who underwent bariatric surgery. NASH was evaluated by liver histopathology. Patients were divided into 2 groups: a derivation cohort (n = 120) and a validation cohort (n = 60).

Results: Of the 180 patients, 91 (50.6%) had NASH. Multivariate analysis identified body mass index (BMI), alanine aminotransferase (ALT), and triglyceride as independent predictors for NASH in the derivation group. A weighted sum of the score was: [(1 for presence of 45 kg/m^2 ≦ BMI > 40 kg/m^2) or (2 for presence of BMI > 45 kg/m^2)+(2 for presence of ALT > 40 IU/L)+(1 for presence of triglyceride > 140 mg/L)]. The area under the receiver operating characteristic curve of this model was .80 and .82 in derivation and validation cohort, respectively. Patients were further divided into low- and high-risk for NASH by using a cutoff score of 3. Diagnostic accuracy was 74% and 80% in derivation and validation cohorts, respectively.

Conclusion: We developed and subsequently validated a simple clinical scoring system incorporating BMI, ALT, and triglyceride to predict NASH in Taiwanese patients with severe obesity. (Surg Obes Relat Dis 2016;▮:00–00.)

Keywords: Scoring system; Nonalcoholic steatohepatitis; Nonalcoholic fatty liver disease; Obesity; Bariatric surgery

With the progressive epidemics of obesity and nonalcoholic fatty liver disease (NAFLD), prevalence is increasing in Western countries and Asia. NAFLD has become the most common chronic liver disease worldwide

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[1,2] NAFLD includes a spectrum of syndromes, ranging from simple steatosis, nonalcoholic steatohepatitis (NASH) to fibrosis, cirrhosis, and hepatocellular carcinoma. Disease progression to NASH and cirrhosis appears to be very slow [3,4]. Infiltration of inflammatory cells characterizes NASH. This characteristic contributes to the progression of hepatitis, fibrosis, cirrhosis, and HCC [5]. Between 10% and 29% of patients with NASH develop cirrhosis within 10 years [6]. Obesity is one of the most important risk factors for NAFLD and NASH. The prevalence of NAFLD and NASH in morbidly obese patients is 91% and 37%, respectively [7].

It is important to distinguish simple steatosis from NASH. Although liver biopsy is presently the gold standard for the diagnosis of NASH [8], it is an invasive procedure and is associated with complications such as hemorrhage (.32%) and even mortality (.01%) [9]. In addition, this procedure is also challenging in obese patients. Radiological modalities such as ultrasound, computed tomography, and magnetic resonance imaging can detect hepatic steatosis but are unable to distinguish NASH from simple steatosis [10,11]. Therefore, developing simple and noninvasive tests that can allow accurate diagnosis of NASH is necessary.

Development of NASH has been reportedly associated with obesity, diabetes, insulin resistance (IR), and metabolic syndrome (MS). In addition, contributing factors may include chronic inflammation, oxidative stress, and adipokine dysregulation [12–14]. Accuracy of using a single factor to predict the presence of NASH is usually poor. Therefore, clinical scoring systems have been proposed, combining clinical features and laboratory investigations for identifying NASH in morbidly obese patients from Western countries. However, the reported results are inconsistent, and some studies have not been validated [15–20]. In addition, as the prevalence of NASH may differ with race and ethnicity, no existing data has been obtained from the Asian population. Therefore, this study aimed to develop and validate a scoring system for predicting NASH in an Asian population with severe obesity.

Methods

Eligible patients

Severely obese Taiwanese patients with a body mass index (BMI) > 37 kg/m^2 or a BMI > 32 kg/m^2 with obesity-related co-morbidities were evaluated by a multidisciplinary team at the E-Da Hospital, in Kaohsiung, Taiwan. Those patients unable to reduce their weight via dieting, behavior modification, or pharmacologic therapy were considered for bariatric surgery [21].

This cross-sectional study consecutively enrolled 242 obese patients between November 2007 and August 2009 who agreed to undergo bariatric surgery and intraoperative liver biopsy. Exclusion criteria included age <20 years; alcohol consumption > 140 g/wk; use of hepatotoxic drugs; presence of liver diseases such as Wilson's disease, hemochromatosis, α1-antitrypsin deficiency, or autoimmune hepatitis; and malignant diseases. All patients were negative for hepatitis B and C viral markers. To avoid potential effects of medications on NAFLD, patients on glucose-lowering drugs were also excluded. The study was approved by the ethical committee of E-Da Hospital, and written informed consent was obtained from each participant.

Sixty-two patients were excluded from this study from the original enrolled 242 patients. This included 33 patients with hepatitis B, 7 patients with hepatitis C, 12 patients with alcohol consumption, and 10 patients taking glucose-lowering drugs. A total of 180 patients were enrolled in the final analysis. The patients were then divided into 2 groups: the first 120 patients (derivation cohort) and the remaining 60 patients (validation cohort).

Preoperative assessment

Preoperative data were collected, consisting of demographic information (age and sex), coexisting medical diseases (type 2 diabetes or T2D and hypertension) and anthropometric measurements (weight and body height). The BMI was calculated as the weight in kilograms divided by the square of height in meters (kg/m^2). Measured biochemical data levels included aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma glutamyl transpeptidase (GGT), bilirubin, blood glucose, fasting insulin, total cholesterol, triglyceride, HDL-cholesterol, LDL-cholesterol, uric acid, ferritin, and high sensitivity C-reactive protein (hsCRP). The homeostasis model assessment of insulin resistance (HOMA-IR) was calculated using glucose and insulin in a fasting state. The equation is the following: HOMA-IR = (insulin × glucose) / 22.5, where insulin was expressed in μU/mL and glucose in mmol/L [22].

Serum was frozen at −80°C for later measurement of adiponectin and leptin. Serum adiponectin concentration was measured using a commercially available enzyme immunoassay kit (Phoenix Pharmaceuticals, Inc., Burlingame, CA, USA), and the serum leptin concentration was measured using a commercially available radioimmunoassay kit (LINCO Research, St. Charles, MO, USA).

Histologic examination

Wedge liver biopsy specimens, about 2 cm × 2 cm, obtained at the beginning of bariatric surgery were routinely stained with hematoxylin and eosin. All biopsy specimens were evaluated by an experienced pathologist (J.C. Hwang). Histopathology was assessed according to the diagnostic criteria for NASH established by Brunt et al. [23] and the