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Original article

# Prevalence and characteristics of individuals without diabetes and hypertension who underwent bariatric surgery: lessons learned about metabolically healthy obese

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Abstract

**Background:** Recent studies describe a unique subset of obese individuals with normal metabolic profiles despite having excess weight called "metabolically healthy but obese (MHO)". Our aim was to determine the prevalence of individuals without diabetes and hypertension and risk factors associated with the MHO phenotype among bariatric surgery patients.

**Methods:** We conducted a retrospective study of 710 adults who underwent bariatric surgery at Johns Hopkins between 2008 and 2010. In the first analysis of 523 individuals, we identified 150 individuals without diabetes and hypertension; in the second analysis of 260 individuals, we identified 44 individuals without diabetes, hypertension and hypertriglyceridemia. We used multivariable logistic regression to examine the association between each group and potential risk factors including age, sex, race, body mass index, and presence of liver disease on liver biopsy.

**Results:** The prevalence of individuals without diabetes and hypertension was 28.7%; among these individuals 88.7% had liver steatosis, 7.3% nonalcoholic steatohepatitis (NASH), and 19.3% liver fibrosis. These individuals were significantly more likely to be white OR = 1.9 (95% CI: 1.1–3.1), younger OR = 4.1 (95% CI = 2.6–6.3), and female OR = 2.1, (95% CI = 1.2–3.6) and less likely to have liver steatosis OR = 0.4 (95% CI = 0.2–0.9) or NASH OR = 0.3 (95% CI = 0.2–0.6). **Conclusion:** Among bariatric surgery patients, almost a third of patients do not have diabetes and hypertension and could be probably considered "MHO" and were more likely to be white, young, female, and have less liver injury. The high prevalence of liver steatosis in MHO individuals among bariatric surgery patients challenges the notion of MHO as a truly metabolically healthy entity. (Surg Obes Relat Dis 2015;11:142–147.) © 2015 American Society for Bariatric Surgery. Published by Elsevier Inc. All rights reserved.

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The presence of metabolic complications varies widely among obese individuals. Recently, a unique subset of

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obese individuals with normal metabolic profiles (normal insulin sensitivity, absent hypertension, and favorable lipid and inflammation profiles) despite obesity has been described as "metabolically healthy obese (MHO)" [1,2]. Additionally, MHO individuals have been characterized by

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less visceral and ectopic fat in the liver and lower liver enzymes compared to non-MHO individuals [2-4].

The prevalence of MHO individuals varies between 10% and 40% depending on its definition [5]. The prevalence of MHO individuals among obese patients undergoing bariatric surgery is unknown. Similarly, there is little known about the characteristics behind the metabolically favorable profile of the MHO phenotype among morbidly obese or bariatric surgery patients. Preliminary data suggest that decrease in visceral fat distribution and increase in weight and adiponectin at birth may lead to MHO phenotype [2,6,7].

In this retrospective study, our objectives were to determine the prevalence of individuals without diabetes and hypertension and to identify potential risk factors associated with the MHO phenotype among bariatric surgery patients.

## Methods

### Study population

This is a single center, retrospective cross-sectional study. The study population includes 710 consecutive patients above the age of 18, presenting for bariatric surgery at The Johns Hopkins Center for Bariatric Surgery between July 2008 and June 2010. The study was approved by the Johns Hopkins Institutional Review Boards.

We excluded persons with frequent alcohol use, positive Hepatitis B surface antigen, Hepatitis C antibody, or detectable Hepatitis C viral RNA, hemochromatosis, autoimmune liver disease, Wilson's disease, alpha 1 antitrypsin deficiency, primary biliary cirrhosis, primary sclerosing cholangitis, and toxic liver, and pregnancy. Patients with missing data on diabetes status, hypertension status, race, smoking status, liver enzymes, liver biopsy, or those undergoing revisional bariatric surgeries were also excluded from analysis. We performed 2 analyses: 1) we analyzed 523 individuals with complete data on diabetes and hypertension status as well as covariates mentioned above and 2) we analyzed 260 individuals from the first analysis who had additional data on fasting serum triglycerides.

#### Data collection and definitions

A single clinical investigator reviewed all patient charts and recorded patient data collected within 6 months before surgery. Data collected included age, gender, ethnicity/race, body mass index (BMI kg/m<sup>2</sup>), blood pressure, fasting glucose (mg/dL), lipid panel, and hepatic aminotransferases (alanine aminotransferase [ALT] and aspartate aminotransferase [AST] U/L). Ethnicity and race were self-reported. One to 3 blood pressure measurements were recorded, and we used the average value or 1 reading value if only 1 was available. All patients underwent a routine intraoperative wedge liver biopsy at the start of bariatric surgery. Biopsy specimens were fixed and stained with hematoxylin and eosin and Masson's trichrome. Biopsy specimens were read by 1 expert hepatopathologist. For the current analyses, the following liver biopsy features were considered: steatosis, nonalcoholic steatohepatitis (NASH), any inflammation, and any fibrosis.

Diabetes was identified by self-report of prior diagnosis, diagnosis in the medical record, use of diabetes medications, or fasting glucose > 126 mg/dL. Similarly, we identified hypertension from self-report, diagnosis in the medical record, use of antihypertensive medications or measured systolic blood pressure > 130 mm Hg and diastolic blood pressure > 85 mm Hg.

We defined MHO phenotype as obesity without diabetes, hypertension and hypertriglyceridemia (serum triglycerides > 150 mg/dL).

#### Statistical analysis

The differences in characteristics between those with and without diabetes and hypertension in the first analysis and between MHO and non-MHO groups in the second analysis were evaluated with Chi-squared test or t test. We used multivariable logistic regression model to evaluate the independent correlates of absence of diabetes and hypertension in the first analysis and MHO in the second analysis and included the following variables as covariates: age, race, gender, steatosis and NASH. The model's fit was tested using likelihood-ratio test. Stratified analyses were performed by gender and race. Data were analyzed using STATA version 12.1 (College Station, Texas).

## Results

Among 523 patients included in the first analysis, 78% were female, 77% were white, and 48% were < 45 years old. A total of 28.7% of the patients did not have diabetes and hypertension and had a mean BMI of 49 kg/m<sup>2</sup>. The physical and metabolic characteristics of individuals with and without diabetes and hypertension are shown in Table 1. Gender, age, prevalence of NASH, liver fibrosis, and steatosis were significantly different between the 2 groups (P < .05). No differences were noted between the 2 groups for race, BMI, smoking status, or liver enzymes. The unadjusted results of the analyses examining the association between the potential correlates and absence of diabetes and hypertension are shown in Table 2. After multivariable adjustment, our results showed that white race, female gender, and younger age were factors independently associated with absence of diabetes and hypertension (Fig. 1 and Table 2): white race OR = 1.9 (95% CI = 1.1-3.1), female OR = 2.1 (95% CI = 1.2-3.6), and younger than 45 years old OR = 4.1 (95% CI = 2.6-6.3). In addition, patients with liver steatosis were 60% less likely (OR .4, 95% CI =0.2–0.9) and those with NASH 69% less likely (OR = 0.3, CI = 0.2-0.6) to be in this group of obese without diabetes and hypertension.

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