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Original article

Inflammation and iron status in bariatric surgery candidates

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Abstract

Background: Iron homeostasis is disturbed by the systemic inflammation commonly encountered in morbid obesity. However, inflammatory markers have seldom been considered in studies investigating the prevalence of iron deficiency (ID) in bariatric surgery (BS) candidates. The objective of this study was to evaluate the prevalence of ID and anemia with ID in BS candidates, accounting for inflammatory status as measured using high sensitivity C-reactive protein (hs-CRP), and to further characterize indices of iron status in BS candidates with systemic inflammation.

Patients and Methods: On the basis of ferritin, hemoglobin, and hs-CRP levels, iron status was categorized in 803 (85%) of 947 consecutive BS candidates. Ferritin <12 ng/mL in females and <15 ng/mL in males irrespective of hs-CRP level was classified as absolute-ID, whereas ferritin between those thresholds and 100 ng/mL was categorized as functional-ID (FID) if hs-CRP >3 mg/L. Anemia was defined as hemoglobin <12 or <13 g/dL in females and males, respectively. Additional iron and hematological indices were assessed in patients with FID.

Results: Prevalence of absolute- and functional-ID was 8.7 and 52.5%, respectively. Anemia was found in 11.2% of the cohort, 80% of which were associated with ID. Among patients with FID, transferrin saturation (T-Sat) <20% was common (70.0%) and associated with larger impairment of hematological indices.

Conclusion: The data show that when hs-CRP as inflammatory marker and ferritin as iron index are considered, impaired iron status could be identified in approximately two thirds of BS candidates. Furthermore, T-Sat <20%, especially along with ferritin <30 ng/mL, appear to be practical cut-offs to identify patients with FID with larger iron status impairment. (Surg Obes Relat Dis 2015;■:00–00.) © 2015 American Society for Metabolic and Bariatric Surgery. All rights reserved.

Keywords:

Gastric bypass; Sleeve gastrectomy; Iron; Iron deficiency; Anemia; Ferritin; Obesity; Inflammation; Bariatric surgery

Iron deficiency (ID) with or without anemia is amongst the most commonly reported nutritional deficiencies in bariatric surgery (BS) [1–3]. Of note, poor preoperative iron status has been associated with increased likelihood of postsurgical ID [3]. Thus, proper evaluation and

management of iron status before BS has been recommended to minimize its worsening after surgery, because the procedure is known to alter iron intake and absorption [2,4,5].

Laboratory classification of iron status in the BS candidate is complicated by the low-grade systemic inflammation frequently present in morbid obesity [6–8]. Iron homeostasis is disturbed in the presence of systemic inflammation [8–11]. However, plasma inflammatory markers have seldom been considered in studies investigating the prevalence

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of ID in BS candidates [2,11–15]. Circulating ferritin levels, the most commonly reported measurement in the assessment of ID in the field of BS [9], have been found to be elevated in the presence of systemic inflammation [8,10,16]. In this scenario, despite apparently adequate body iron stores, insufficient incorporation of iron into erythroid precursors may occur and has been defined as functional ID [8]. Serum ferritin levels <12 ng/mL have been established as indicative of absent iron stores irrespective of the presence of inflammation [8]. However, in non-dialyzed patients, a serum ferritin concentration up to 100 ng/mL has been associated with a high likelihood of ID in the presence of inflammation [8].

Against this background, study aims were (1) to evaluate the prevalence of ID, anemia, and anemia with ID in BS candidates when considering high-sensitivity C-reactive protein (hs-CRP) as marker of systemic inflammation, (2) to further characterize indices of iron status in BS candidates with systemic inflammation, and (3) to evaluate the clinical characteristics of BS candidates associated with ID and anemia with ID.

Patients and methods

Participants in this cross-sectional study were selected among the 947 BS candidates evaluated at the authors' institution between 2005 and 2009. Eligibility criteria included age 18 years or older. Exclusion criteria included prior BS ($n = 43$), estimated glomerular filtration rate ≤ 30 mL/min/1.72 m² ($n = 7$), or lack of availability of hs-CRP, ferritin, or hemoglobin (Hb) determinations obtained at the same time point and determined at the Center for Biological Diagnosis at the authors' institution during presurgical evaluation ($n = 115$). The local ethics committee approved this study, and written informed consent was obtained from all participants.

Presurgical parameters included in the current analysis encompass clinical, anthropometric, biochemical, hematological, and fibrogastroscopic findings. Weight, height, and waist circumference (WC) were measured as previously described [3]. Diagnosis of type 2 diabetes mellitus, hypertension, dyslipidemia, sleep apnea syndrome, metabolic syndrome (MetSd) [17], and tobacco use was based on medical history and laboratory data. Results on the fibrogastroscopy, routinely performed during presurgical evaluation, were reviewed and categorized as positive or negative for the presence of *Helicobacter pylori* and inflammatory or ulcerative lesions in the esophagus, stomach, or duodenum.

High-sensitivity CRP was measured as previously reported, and values >3 mg/L were considered indicative of inflammation [18,19]. Biochemical markers of iron status included ferritin, transferrin saturation (T-Sat), and soluble transferrin receptor (sTfR), and the ratio sTfR/(log ferritin) was calculated [7,8]. Iron, ferritin, and sTfR were measured as previously reported [3,20], and transferrin was measured

by immunoturbidimetry. A ferritin <12 ng/mL in females or <15 ng/mL in males was considered indicative of absolute ID irrespective of hs-CRP levels [8]. If hs-CRP >3 mg/L, a ferritin concentration between those thresholds and 100 ng/mL was considered as functional iron deficiency (FID) [8]. Transferrin saturation (T-Sat) <20%, sTfR >1.8 mg/L, and sTfR/(log ferritin) >1.8 were considered as indicative of ID based on published literature [8,11,21]. Hematological parameters included Hb, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and percentage of hypochromic red cells (%HRC) and were measured using an Advia 2400 analyzer (Siemens, Barcelona, Spain). Anemia was defined as Hb <12 or <14 g/L in females and males, respectively [22]. The MCV, MCH, and %HRC cut-offs indicative of impaired red cell production secondary to iron deficiency were based on published literature [11]. Serum vitamin B12 (vitB12) and folic acid were measured as previously reported [3].

Statistical analysis

All data are expressed as mean \pm SD or percentages unless stated otherwise. Differences between groups were evaluated using parametric or nonparametric test as appropriate (chi-squared or Fisher's test for categorical variables, and ANOVA and Bonferroni statistics as post hoc analysis for quantitative variables). Sensitivity, specificity, positive and negative predictive values, and overall accuracy indices were calculated from cross-tabs. Predictive factors of ID and anemia with ID were ascertained by logistic regression analysis. The SPSS 20.0 statistical package was used, and significance was set at a P value of <.05.

Results

The main clinical characteristics of the 803 study participants are shown in Table 1. A hs-CRP <3 mg/L was found in 96 (12.0%) patients, of whom 8 (8.3%) presented with absolute ID (ferritin <12 or <15 ng/dL, respectively in females and males). Of 707 (88%) patients with hs-CRP >3 mg/L, a ferritin level below these thresholds was found in 62 (8.8%), and a ferritin level between these cut-offs and 100 ng/dL was found in 423 (59.8%). Thus, on the basis of set criteria, absolute ID was identified in 8.7% of the study participants, but an additional 52.5% of the cohort presented with FID. Comparison of patients with ID or FID combined versus those with normal iron stores showed a greater frequency of ID in females and in individuals who had slightly younger age, a smaller WC, and absence of hypertension, dyslipidemia, sleep apnea syndrome, or MetSd (Table 1). Indeed, logistic regression analysis with gender, age, and diagnosis of MetSd as covariates confirmed these were independent predictors of ID before surgery: female gender: odds ratio (OR) 10.362

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