Obesity, bariatric surgery, and iron deficiency: True, true, true and related

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Morbid obesity is a health problem that has been shown to be refractory to diet, exercise, and medical treatment. Surgeries designed to promote weight loss, termed bariatric surgery and typically involving a gastric bypass procedure, have recently been implemented to treat obesity with high success rates. However, long-term sequelae can result in micronutrient deficiencies. This review will focus on iron deficiency and its association with obesity and bariatric surgery. Iron deficiency develops after gastric bypass for several reasons including intolerance for red meat, diminished gastric acid secretion, and exclusion of the duodenum from the alimentary tract. Menstruating women, pregnant women, and adolescents may be particularly predisposed toward developing iron deficiency and microcytic anemias after bypass surgery. Preoperative assessment of patients should include a complete hematological work-up, including measurement of iron stores. Postoperatively, oral iron prophylaxis and vitamin C in addition to a multivitamin should be prescribed for bypass patients, especially for vulnerable populations. Once iron deficiency has developed, it may prove refractory to oral treatment, and require parenteral iron, blood transfusions, or surgical interventions. Bariatric surgery patients require lifelong follow-up of hematological and iron parameters since iron deficiency and anemia may develop years after surgery. Am. J. Hematol. 83:403–409, 2008. © 2007 Wiley-Liss, Inc.

Introduction

Morbid obesity is a health problem that has been shown to be refractory to diet, exercise, and medical treatment. According to the National Health and Nutrition Examination Survey conducted in 2003–2004, 32.3% of the US population is obese and 4.8% is morbidly obese [1]. Over the last few decades, bariatric surgery has been demonstrated to be an effective treatment for obesity [2,3]. There are several different procedures, including gastric bypass, laparoscopic adjustable gastric banding (LAGB), vertical banded gastroplasty (VBG), biliopancreatic diversion (BPD), and biliopancreatic diversion and duodenal switch (BPD-DS). The overall surgical mortality rate of these procedures has been generally less than 1%, and they have been successful in alleviating or mitigating obesity associated comorbidities [4]. However, bypass surgery itself may be associated with both short-term and long-term adverse events. Short-term complications include anastomotic leak, pulmonary embolism, wound infection, and incisional hernia [2]. Long-term sequelae include metabolic abnormalities and vitamin and mineral deficiencies such as iron, vitamin B_{12}, folate, calcium, and vitamin D. Iron deficiency and anemia can have a strong impact on quality of life [5], especially in menstruating women who make up a majority of bariatric surgery patients. The association between iron deficiency and bariatric surgery will be explored in this review.

History of Bariatric Surgery

The first bariatric surgery was performed in 1954, in which Kremen joined the proximal jejunum to the distal ileum, bypassing a large segment of the nutrient absorbing small intestine, a procedure known as jejunoileal bypass (JIB) [2]. Because of the malabsorption of carbohydrates, lipids, vitamins, and protein, the surgery resulted in serious long-term morbidities, including cirrhosis and liver failure in up to 7% of all patients [6,7]. These deleterious side effects led JIB to fall out of favor [8–12].

Since that time, two major versions of bariatric surgeries, bypass and banding procedures, have become popular for promoting weight loss without resulting in the serious sequelae associated with JIB. Gastric bypass procedures, including the Roux-en-Y gastric bypass (RYGBP; Fig. 1), biliopancreatic diversion, and biliopancreatic diversion and duodenal switch (BPD-DS, Fig. 2) induce weight loss through both restriction and malabsorption of food. In these bypass procedures, a portion of the small intestine, including the duodenum, is excluded from the digestive tract. The RYGBP entails the creation of a small gastric pouch (30 ml or less). This pouch is connected to a Roux limb (50–150 cm), a part of jejunum through which food travels. The duodenum and proximal jejunum, containing bile and pancreatic secretions, are initially excluded from this digestive tract but eventually join the Roux limb to form a common limb. BPD and BPD-DS are even more radical procedures, but have recently become popular for patients with BMIs >50 because of better weight loss outcomes [13]. Improved weight loss occurs because BPD and BPD-DS combine gastric restriction with a significantly greater degree of malabsorption than RYGBP, often excluding the entire jejunum from digestive continuity.

Banding procedures promote weight loss by purely restricting food intake, and therefore, malabsorption of nutrients is less of a concern. LAGB (Fig. 3), developed in 1993, is purely restrictive. An inflatable band is placed below the gastroesophageal junction, creating a pouch of 10–15 ml, which can be adjusted by adding or removing fluid through a subcutaneous port. Size of the pouch limits food intake and affects feelings of satiety [14]. VBG (Fig. 4)

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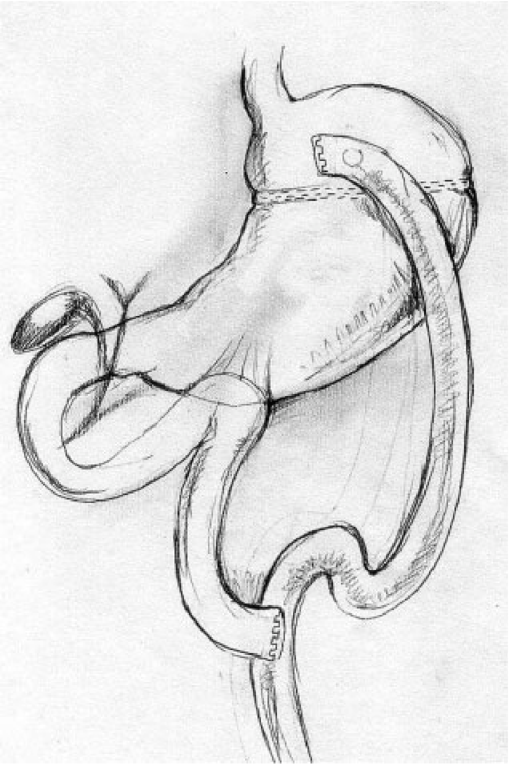

Figure 1. Roux-en-Y gastric bypass (RYGBP). Staples create a 30-ml or less gastric pouch. The jejunum is partitioned distal to the ligament of Treitz and the distal segment is anastomosed to the proximal stomach pouch.

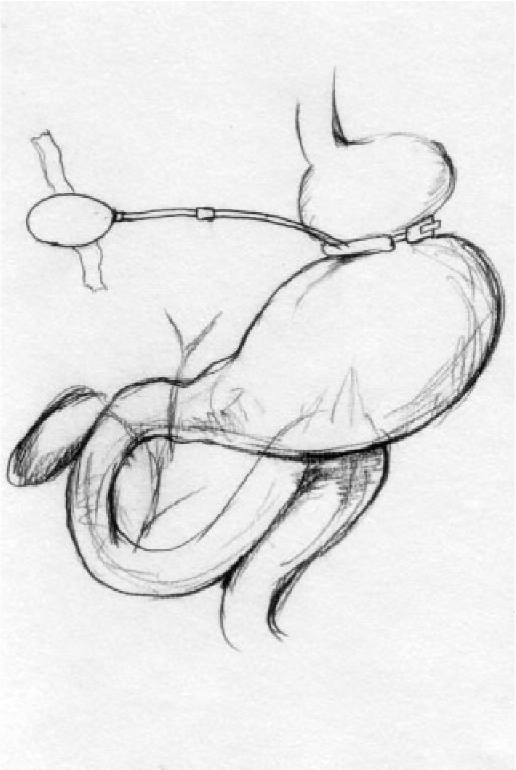

Figure 3. Laparoscopic adjustable gastric banding (LAGB). An inflatable band is placed below the gastroesophageal junction to create a 10–15-ml gastric pouch. The size can be adjusted via the subcutaneous port.

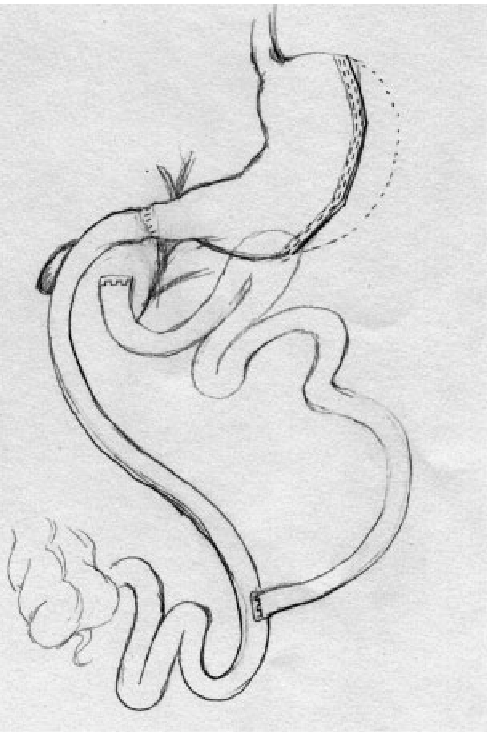

Figure 2. Biliopancreatic diversion with duodenal switch (BPD-DS). A limited gastrectomy creates a small gastric pouch. The proximal duodenum is anastomosed to ileum to form the alimentary tract while a long biliopancreatic limb is diverted. The distal part of the biliopancreatic limb is anastomosed to the ileum 50–200 cm from the ileocecal junction.

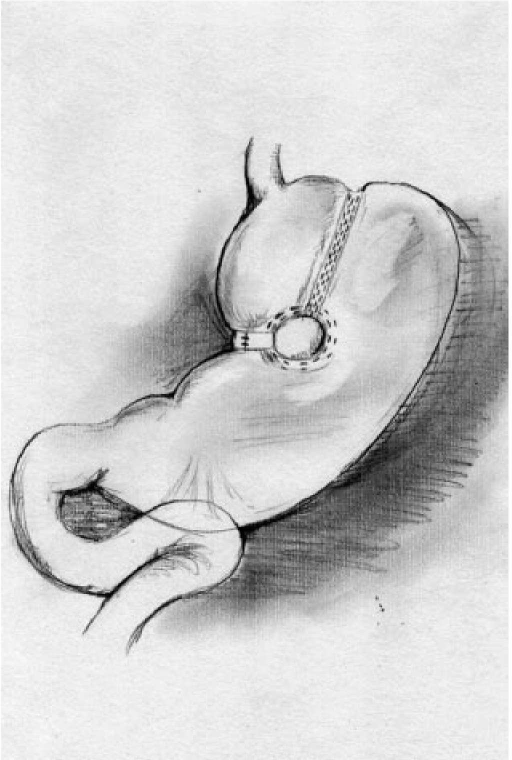

Figure 4. Vertical banded gastroplasty (VBG). A small upper gastric pouch is created via staples and gastric band.

involves stapling the stomach close to the gastroesophageal junction to create a small gastric pouch. A small outlet from the gastric pouch is created and reinforced by a gastric band, which results in slower emptying of gastric contents into the rest of the digestive tract. These banding techniques have somewhat poorer weight loss reduction outcomes [15].

Gastric Bypass, Iron Deficiency, and Anemia

Iron deficiency and iron deficiency anemia are particularly associated with gastric bypass surgery and are more prevalent with bypass rather than purely restrictive procedures [16–18]. The overwhelming majority of studies report iron deficiency, ranging from $\sim$6 to $\sim$50% within months to years of follow-up [19–21]. Case reports have even noted bypass patients experiencing pica, a condition that is associated with iron deficiency and defined by unusual cravings for ice, cornstarch, clay, or other substances [22,23].

There are several reasons why iron deficiency occurs in gastric bypass patients.

Avoidance of red meat

There are two bioavailable forms of iron: molecular iron and heme iron. Meat is a major source of heme and in Europe and North America, two-thirds of body iron stores are derived from heme rather than molecular iron [24].

Some evidence suggests that diminished intake of red meat after bypass surgery contributes to iron deficiency in bypass patients. Halverson et al. reported that 27 out of 69 patients seen on follow-up who had received gastric bypass were experiencing emesis after consuming high-fiber meats [25]. A study of 41 bypass patients by Crowley et al., which included a 24-hr food intake questionnaire and survey of vitamin supplementation, found that 90% of the patients consumed less than 70% of the recommended daily allowance of iron 6–9 years postoperatively [26]. A large retrospective study by Avinoah et al. examined the nutrient deficiencies of a group of bypass patients, with a mean follow-up of 6.7 years and found that those who were classified as meat-eaters (defined as eating beef, poultry, or fish more than one time per week) had higher mean serum iron values. Avinoah et al. also found that 50% of his bypass patients experienced chronic meat intolerance after surgery [27].

Decreased dietary intake of iron, however, is not the sole explanation of iron deficiency. Bypass patients tend to have greater meat tolerance than banded patients, yet, a randomized controlled trial comparing bypass with banded patients demonstrated that only the bypass patients were iron deficient, despite having this better tolerance for eating red meat [17].

Diminished gastric acid secretion

Initial metabolism of molecular iron (Fe^{3+}) occurs in the stomach and is facilitated by gastric acid. Molecular iron is solubilized at the low pH of the stomach before it becomes available for absorption in the alkaline duodenum [24]. Any gastric surgery, such as gastric bypass, that involves separating the antrum from the proximal gastric pouch will result in a relative paucity of parietal cells. The diminished gastric acid secretion, in turn, hinders the solubilization of ferric iron and ultimately absorption of the reduced form, ferrous iron, in the duodenum. Bile reflux or achlorhyridia may also inhibit solubilization, resulting in iron deficiency.

Historically when peptic ulcer disease was treated with partial gastrectomies to reduce acid secretion, iron deficiency developed secondarily to surgery, with a reported incidence of 57% in men and 72.5% in women [28]. Similarly, gastric bypass patients experience decreased gastric acid production in their proximal pouch. Behrns et al. pre- and postoperatively evaluated the gastric acid secretion in eight patients who underwent bypass and found significant postsurgical decreases in acid secretion under both basal and pentagastrin stimulated conditions [29]. In contrast, banding procedures maintain digestive continuity with the antrum and duodenum, and not surprisingly, rates of nutritional deficiencies, and particularly iron deficiency, are lower than in bypass populations [30,31].

Exclusion of the duodenum

The duodenum is excluded from digestive continuity with gastric bypass. Although inorganic iron can be absorbed by the entire small intestine, most absorption of molecular iron and heme iron occurs across the apical and basolateral membranes of duodenal enterocytes [26]. When molecular iron reaches the duodenal brush border, the iron is reduced from the ferric to ferrous form by ferric reductase and transferred across the apical brush-border by the divalent metal transporter 1 (DMT) [32]. Once molecular iron has been imported into the enterocyte, the body's required iron is exported into the serum through the protein ferroportin while excess iron is retained in the duodenal cell as ferritin.

Absorption of heme is impaired by bypass in two important ways. First, gastric bypass delays interaction of pancreatic enzymes and biliary secretions with the food bolus, and effectively diminishes the ability to free the heme moiety from myoglobin and hemoglobin. Second, heme absorption occurs in the duodenum, and exclusion of the duodenum from the digestive continuity severely impacts the body's ability to absorb. In normal physiology, heme is imported, possibly by the proton-coupled folate transporter/heme carrier protein-1, into the duodenal enterocyte [33,34]. Iron is then separated from its protoporphyrin ring by a duodenal enzyme, possibly heme oxygenase, which is present in enterocytes. The liberated iron then joins the same metabolic pathway as inorganic iron and is exported by ferroportin.

Patients who have bypass surgery, a procedure that excludes the duodenum from food absorption, have significantly lower serum iron and hemoglobin concentrations than those who receive banding procedures, which preserves duodenal integrity [35]. The amount of jejunal absorptive surface, on the other hand, has little impact on iron absorption, suggesting that the rest of the small intestine cannot upregulate iron absorption sufficiently enough to compensate for the duodenal exclusion that occurs in bypass surgeries. In two different studies, Brolin et al. compared rates of iron deficiency among groups of superobese bypass patients who had differing lengths of defunctionalized jejunum and found no significant difference in iron deficiency between the groups [36,37]. A prospective comparison of patients who had Roux-en-Y gastric bypass (RYGP) versus patients with biliopancreatic diversion (BPD) found they had equivalent ferritin levels at 2-year postoperative follow-up ($P = 0.89$) despite differing common jejunal limb and absorptive surface lengths [38].

Conversely, the BPD with duodenal switch (BPD-DS), a gastric bypass procedure that may preserve some function of the proximal duodenum, may offer protection from iron deficiency. A large cross-sectional study ($n = 717$) comparing patients receiving BPD, which excludes the duodenum with those receiving BPD-DS, which may maintain some duodenal function, found that those with the duodenal switch had significantly higher serum ferritin levels ($P < 0.001$) [39]. A smaller more recent cross-sectional study ($n = 103$) comparing BPD with BPD-DS, however, found no significant difference ($P = 0.26$) in serum iron levels between the two groups, but serum ferritin, a more specific marker for iron deficiency, was not reported in the study [40]. Retrospective follow-up of 589 BPD-DS patients at 3 years confirmed the first cross-sectional study and found that no patients developed iron deficiency as measured by mean serum iron levels [41].

Other factors

Iron deficiency after surgery may be due to increased blood loss. Rats with surgically created blind intestinal loops manifest gastrointestinal bleeding [42]. Bypass patients, who also have loops of bowel excluded from the digestive tract, may similarly experience gastrointestinal blood loss. Other sources of blood loss include marginal ulcers, which are known to occur at the anastomosis site of the proximal jejunum and gastric pouch. Gastric bypass patients may also experience an iron-losing enteropathy. Bypass patients can have an overgrowth of intestinal bacteria, especially in their blind, bypassed loop of bowel, resulting in the damage and excretion of intestinal epithelial cells and their free iron stores [42].

In most studies, it is impossible to tease out whether rapid weight loss contributed to the iron deficiency since serum iron or ferritin was initially measured more than 1 year after the surgery, often at the nadir of patient weight loss. Thus, low serum iron levels could be due to rapid weight loss and malnutrition as well as chronic poor absorption of iron through the small intestine.

Limited evidence, however, suggests that the amount of weight lost and weight loss velocity has minimal influence on the degree of iron deficiency. Brown et al. [43] conducted a postoperative dietary survey of 12 women and found that the mean iron intake at the 3-month mark had decreased from 18 ± 2 mg per day (preoperatively) to 3 ± 0.4 mg (postoperatively) with a mean weight loss of 17% of preoperative weight. However, serum iron levels did not yet reflect this decreased dietary iron intake. Rather, patients actually had higher serum iron levels 3 months postoperatively than they did preoperatively. While serum iron is not the best assessment of iron stores, this limited study suggests that weight loss and rate of weight loss do not have an immediate impact on iron levels. Avinoah et al. further explored a possible correlation between degree of weight loss, velocity of weight loss, and iron saturation and found that a correlation did not exist. Rather, iron saturation steadily declined throughout the 96-month study period, even as patients regained previously lost weight [27]. Furthermore, there is limited data on whether hormones which impact iron metabolism, such as TSH, T3, and T4, are affected by weight loss surgery. Abnormal thyroid function tests have been used as exclusion criteria from studies; however, thyroid function tests are not typically recommended as part of standard postoperative laboratory testing [44,45].

Iron Deficiency and Anemia in Special Populations

Within the bariatric surgery population, certain groups of patients are particularly at risk for iron deficiency.

Women

Menstruating women are at high risk for iron deficiency and anemia postbypass and the complications that may ensue post-bypass, including hospitalization and transfusion [20,36,46–48]. Lower preoperative iron stores may partially explain why women may be more likely to exhibit iron deficiency than men in studies with limited follow-up and why the onset of postsurgical iron deficiency is so variable, from months to years.

The resumption of menstruation postoperatively may also contribute to increased rates of iron deficiency in women. A study evaluating the gynecological changes of 109 reproductive age morbidly obese women who underwent bariatric surgery found that preoperatively, 40.4% experienced menstrual irregularities, decreasing to 4.6% after massive postoperative weight loss [49], suggesting that bariatric surgery may correct the anovulatory and insulin resistant state associated with obesity and polycystic ovarian syndrome.

The predisposition of menstruating women to develop iron deficiency holds true even when different bariatric surgeries are compared. A study comparing bypass and banding techniques found that menstruating women, no matter the surgical procedure that they received, had significantly lower postsurgical hemoglobin and serum iron levels than nonmenstruating women. There were no significant differences between the hemoglobin and serum iron levels for nonmenstruating women [50]. Within this study, the iron deficiency anemia became so severe that 10% of menstruating women with bypass and 5% with banded procedures subsequently required hysterectomy because of persistent dysfunctional uterine bleeding. A retrospective case series of gastric bypass showed that low iron levels were significantly less common ($P < 0.02$) in women who had a total abdominal hysterectomy prior to surgery [51].

Pregnancy

Bariatric surgery improves women's fertility [49,52]. However, it potentially aggravates the rate of iron deficiency in reproductive age women, especially since iron requirements increase during pregnancy. It is reassuring that one study of 79 consecutively enrolled, previously banded pregnant patients demonstrated only one case of anemia [53]. However, the gastric bypass patient population may be at greater risk for iron deficiency and anemia since it is generally a more common and refractory problem for these patients. In one case report, a woman with a history of gastric bypass and prepregnancy iron deficiency anemia developed severe anemia (nadir Hb 5.1 g/dl at 30 weeks, nadir mean cell volume of 59.6 fl at 27 weeks), requiring blood transfusions during her third trimester [54].

Anemia not only poses a risk for the mother, but also for the baby. Literature suggests that iron deficient mothers may be more likely to have preterm and low-birth weight infants [55]. Therefore, at a minimum, prenatal and perinatal iron tablets along with multivitamin, folate, and B_{12} supplementation are important. Gurewitsch et al. even proposed that female gastric bypass patients of childbearing age undergo preoperative and/or preconception treatment with parenteral iron to avoid the risks of transfusion therapy during pregnancy [54]. Banding procedures, which preserve iron absorption through the duodenum, may also be a better option than gastric bypass for some women who plan to have children after surgery.

Pediatrics

Obesity among adolescents is increasing at an alarming rate and obese adolescents, in particular, may face increased adult morbidity and mortality [56]. A consensus of pediatric surgeons and pediatricians who treat obese children and adolescents recommend that bariatric surgery should only be considered for adolescents who possess skeletal maturity (generally $\geq$13 years of age for girls and $\geq$15 years of age for boys) and who have a BMI $\geq$ 40 and comorbidities that might be corrected by surgery. At least 6 months of an organized weight loss program should have also been attempted [57].

Obese children and adolescents may be at increased risk for iron deficiency preoperatively. A cross-sectional study of obese pediatric patients demonstrated that mean serum iron levels were significantly lower for both male and female obese children than for normal weight children. This may be due to increased iron requirements from the increased surface area [58]. In addition to rapid growth, the proposed mechanisms for iron deficiency in adolescents include genetic influences, poor diet, and menstrual blood loss [59].

Gender plays an important role in adolescent iron status just as it does in adults. A study, which analyzed NHANES III data, not only found that iron deficiency increased as weight increased among children, but also that most of the iron deficiency was found among females. Subgroup analyses here too demonstrated a trend toward higher levels of iron deficiency in overweight adolescent females than normal weight adolescent females ($P < 0.07$) [59].

Surgeons are now performing gastric bypass and banding procedures on adolescents with low mortality rates and improvement in quality of life [60–62]. One major drawback to surgery, however, is that it may result in long-term nutrient deficiencies, including iron deficiency. Fewer iron reserves in the female adolescent population raises concerns that bypass and banding surgeries could aggravate a preexisting condition. Strauss et al. retrospectively reviewed data on 10 adolescents who underwent gastric bypass surgery and found that iron deficiency anemia occurred in 5 of 7 girls but no boys. All cases were corrected with mineral supplementation [63].

Diagnosis and Treatment

Classic laboratory findings for iron deficiency include anemia, a low MCV, a low serum iron, a high TIBC, and/or a low serum ferritin level. The reticulocyte counts will be low, reflecting a hypoproliferative anemia, while the serum soluble transferrin receptor levels will be elevated. A blood smear will show microcytic hypochromic red cells. Clinically, there may be feelings of fatigue and decreased exercise tolerance, pica and on examination they may have pale conjunctiva, koilonychia (spoon nails), atrophic glossitis, and rarely, esophageal webs (Plummer-Vinson syndrome).

Postbypass, patients require careful follow-up of their hematological parameters, including complete blood count with MCV, serum iron, ferritin, and TIBC. After the first year, these values should continue to be checked on a biyearly or yearly basis. In an attempt to prevent nutritional deficiencies, most surgeons now prescribe a multivitamin to all patients, but they may not provide enough daily iron to prevent iron deficiency or anemia. Brolin et al. found that 24 of 79 of his patients who took multivitamins still developed iron deficiency postoperatively [46]. Adherence was also assessed in this study, and although it correlated with serum folate and B_{12} levels, it did not correlate with iron status.

With the realization that menstruating women are at increased risk for developing iron deficiency and anemia after bypass surgery, a majority of surgeons prescribe iron supplementation in addition to a multivitamin [64]. A prospective, double-blind randomized study comparing iron prophylaxis with placebo found that placebo-treated patients had a significant drop in their ferritin levels 2 years postoperatively as opposed to those treated with 320 mg (twice daily) of iron [65].

Treatment for iron deficiency in bypass patients has changed over the years. In earlier studies, when oral iron prophylaxis was not routine, most practitioners prescribed oral iron supplementation for the treatment of iron deficiency, and it was shown to be reasonably effective [25,26,46]. More recent studies have been less promising and demonstrate that recalcitrant, unresponsive iron deficiency anemia can be a significant problem for these patients [36,46,48].

It is reasonable to initially attempt to correct iron deficiency in patients with hemoglobin levels $\geq$10 g/dl with oral iron supplementation. Since ferrous iron formulations are more readily absorbed, only ferrous salts should be used. Sustained release formulations should be avoided because they reduce the amount of iron that is present for absorption in the small intestine. Iron deficient patients can typically absorb 50–100 mg of iron daily; however, this may be diminished in gastric bypass patients. There are several ferrous salt supplements available that can be used to improve iron status. Ferrous sulfate (325 mg, hydrated) and ferrous fumarate (200 mg) provide $\sim$65 mg of iron per tablet. Patients should be instructed to take 1–2 tablets per day as prophylaxis to prevent iron deficiency or 3–4 tablets per day to restore iron deficient patients. If iron parameters do not improve within several months of starting therapy, the dosage may need to be increased. In menstruating females, up to six tablets per day has been required to correct iron deficiency anemia [66].

Ideally, oral iron should be taken on an empty stomach. However, this may increase its unpleasant side effects, including nausea, epigastric discomfort, abdominal cramps, and constipation, and consequently, patient compliance may be poor. A liquid preparation may be tried when oral tablets are not tolerated. The dose can be decreased, but the time required to correct iron stores (4 months minimum) will take longer. Evidence suggests that certain foods impair iron absorption, and if possible, should not be taken along with ingestion of the iron supplements. These include tea, bran and cereal, and calcium-rich foods [24].

The addition of vitamin C to oral iron supplementation may help prevent and treat iron deficiency [67]. Vitamin C increases the acidity of the gastrointestinal tract so that iron can be reduced to its ferrous form and more readily absorbed. Rhode et al. tested this hypothesis [68]. Twenty-nine patients, who had undergone gastric bypass 3.2 ± 2 years earlier and who were noted to be iron deficient (here defined as ferritin <29 μg/l), were given oral iron for 1 month and then oral iron and vitamin C for the second month, thus serving as their own controls. Hemoglobin levels corrected during the first month with only oral iron but during the second month, there was a more significant rise in hemoglobin and ferritin levels when compared with the first month, suggesting that vitamin C enhanced absorption.

Patients who remain refractory to oral supplementation or are noncompliant with their oral supplementation may require parenteral iron treatments, especially if they are symptomatic and/or have hemoglobin levels less than 10 g/dl [17,36,69]. Brolin et al. observed in a prospective study that no patient with severe anemia (defined as a hemoglobin $<$10 g) responded to oral treatment alone [51]. There are different formulations of parenteral iron, including iron dextran (50 mg elemental iron/ml), iron-sucrose complex (Venofer, 20 mg elemental iron/ml), and iron sodium gluconate complex (Ferrlecit, 12.5 mg/ml). All can either be administered intramuscularly or intravenously, though intravenously may be preferred because it is less painful and will not cause brown discoloration at the injection site. Since there is a risk of anaphylaxis with the administration of parenteral iron, a small test dose should be given first with the physician at bedside to monitor vital signs. Repletion dosing can be calculated as

$$\text{Iron (mg)} = [0.3 \times \text{patient's weight (lbs)} \times 100\ (14.8 - \text{patient's hemoglobin})]/14.8$$

Most iron deficient adults require 1–2 g of replacement iron, or 20–40 ml of iron dextran. Patients with large BMIs will require more. The dose is typically administered diluted in normal saline over 1–2 hr. Some patients may experience arthralgias several days after therapy, which is often relieved with NSAIDS, but pretreatment with methylprednisolone (60 mg) is another option. Patients may require the administration of intravenous iron several times a year in order to maintain iron stores [45].

Blood transfusions or surgical interventions have also been successfully utilized in patients with hemoglobin levels $<$10 g/dl, when oral and parenteral therapies have failed [17,36,51,69]. Hysterectomies have been performed on menstruating women with refractory anemia [35,51] and reversal of gastric bypass is another surgical option. In a retrospective review of 153 patients, Reinhold found that six menstruating women required reversal of gastric bypass and conversion to gastroplasty (a purely restrictive procedure similar to banding) to increase absorptive surface and correct a treatment-resistant iron deficiency [48]. Erythropoietin in a severely anemic and decompensated patient may also be considered and may be preferable to transfusion or surgery in spurring a brisk early response.

Long-term correction of anemia remains problematic. It is important to exclude other etiologies for a persistent anemia, and in some studies, up to 50% of cases may not be attributable solely to iron deficiency [51]. In Brolin's prospective, double blind, randomized controlled trial testing the effectiveness of prophylactic iron supplementation, he found that vitamins and oral iron supplements corrected iron deficiency, but did not protect many women in the treatment arm from developing anemia from factors other than iron deficiency. Other sources of anemia may include chronic disease, endocrinological causes, or concomitant B_{12} and folate deficiency [19,25,26,46]. The macrocytic cell and increased cell volume indices typical of these deficiencies may not be evident in bariatric surgical patients [19].

Confounding Factors and Limitations

There are few randomized, controlled trials studying iron deficiency in bariatric surgery. This has meant that much of the material for this review was, by necessity, drawn from more descriptive case series or retrospective data. Some studies did not assess or report preoperative levels of iron and hemoglobin, making the degree of change difficult to evaluate. Patient ethnicity/race was not typically reported.

Assessment of iron deficiency was also problematic. Earlier studies relied on serum iron levels, which are easily influenced by recent dietary intake, rather than serum ferritin, a more sensitive yet still problematic test of iron stores. Serum transferrin receptor levels were rarely performed and no bone marrow examinations were reported. The average length of follow-up of patients, when stated, varied, from months to years and a significant number of patients were lost to follow-up, especially between 1 and 3 years of their operation. Since differing amounts of preoperative iron stores influence the time to onset of low iron levels and anemia, iron deficiency and other micronutrient deficiencies may be underestimated in studies with limited follow-up.

Summary

As obesity and bariatric surgery rates continue to climb, anemia will become an ever-increasing concern for this patient population, especially for menstruating females. Preoperative assessment of patients should include a complete hematological work-up, including measurement of iron stores, B_{12}, and folate. Postoperatively, oral iron prophylaxis and vitamin C in addition to a multivitamin should be prescribed for bypass patients, especially for menstruating women. Pregnant women and adolescents who have undergone bariatric surgery may also be at high risk of developing iron deficiency, and these patients may require aggressive oral iron supplementation.

Patients who have received purely restrictive procedures, such as VBG and LABG, may be less likely to develop iron deficiency, and additional iron supplementation can be decided between health care provider and patient. Once iron deficiency has developed, however, it may prove refractory to treatment. In some cases, parenteral iron, blood transfusions, and surgical measures to stop sources of bleeding may be warranted. Even when iron deficiency is corrected, further work-up should include assessment of B_{12} and folate stores.

Bariatric surgery patients require lifelong follow-up of hematological and iron parameters, since iron deficiency and anemia may develop years after surgery.

Methods

The articles were found via PubMed using different search terms including "bariatric surgery, anemia," "obesity, adolescent, iron deficiency," "pediatric bariatric surgery," and "pregnancy, bariatric surgery." The bibliographies of studies found during the PubMed searches were also examined and additional relevant articles were reviewed.

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