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Iron deficiency after bariatric surgery: what is the real problem?

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The growing prevalence of obesity explains the rising interest in bariatric surgery. Compared with non-surgical treatment options, bariatric surgery results in greater and sustained improvements in weight loss, obesity associated complications, all-cause mortality and quality of life. These encouraging metabolic and weight effects come with a downside, namely the risk of nutritional deficiencies. Particularly striking is the risk to develop iron deficiency. Postoperatively, the prevalence of iron deficiency varies between 18 and 53 % after Roux-en-Y gastric bypass and between 1 and 54 % after sleeve gastrectomy. Therefore, preventive strategies and effective treatment options for iron deficiency are crucial to successfully manage the iron status of patients after bariatric surgery. With this review, we discuss the risks and the contributing factors of developing iron deficiency after bariatric surgery. Furthermore, we highlight the discrepancy in the diagnosis of iron deficiency, iron deficiency anaemia and anaemia and highlight the evidence supporting the current nutritional recommendations in the field of bariatric research. In conclusion, we advocate for more nutrition-related research in patient populations in order to provide strong evidence-based guidelines after bariatric surgery.

Iron deficiency: Bariatric surgery: Roux-en-Y gastric bypass: Sleeve gastrectomy

Six-hundred million adults around the world are suffering from obesity, defined as an abnormal or excessive fat accumulation that may impair health[(1)]. Worldwide, different prospective studies and meta-analyses observed that both overweight, defined as a BMI ≥25·0 kg/m^2, and obesity, defined as a BMI ≥30·0 kg/m^2, are associated with increased all-cause mortality[(2)]. More specific, every 5 kg/m^2 increase in BMI above 25 kg/m^2 is associated with an average increase in mortality of 30 %. Predominantly, the excess mortality is mainly the result of vascular diseases (e.g. IHD, stroke and other vascular diseases) and diabetes[(3)]. These factors, including the growing prevalence of obesity, the severity of associated comorbidities and the associated economic costs, explain the rising interest in preventive strategies with limited results so far[(4)]. Treatment of obesity is therefore imperative with lifestyle changes, dietary adjustments and increased physical activity as cornerstone[(5,6)]. Despite the ease of lifestyle modification, whether or not combined with pharmacological treatment, bariatric surgery results in greater and sustained improvements in weight loss, obesity-associated complications, all-cause mortality and quality of life compared with non-surgical treatment options[(7,8)]. These encouraging results explain the worldwide rising number of bariatric procedures as roughly half a million bariatric procedures were performed in 2013[(9)].

Abbreviations: ASMBS, American Society for Metabolic and Bariatric Surgery; IFSO, International Federation for the Surgery of Obesity and Metabolic Disorders; RYGB, Roux-en-Y gastric bypass; SG, sleeve gastrectomy; TSAT, transferrin saturation.
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Metabolic and bariatric surgery

Bariatric procedures are intended for patients suffering from morbid obesity where cornerstone treatment (e.g. lifestyle changes, dietary adjustments and increased physical activity) and/or pharmacological treatment produces insufficient weight loss. European and American guidelines recommend bariatric surgery for patients with a BMI ≥40 kg/m^2 or for patients with a BMI ≥35 kg/m^2 in combination with at least one obesity-associated comorbidity (e.g. type 2 diabetes, hypertension or obstructive sleep apnoea)[5,6]. Traditionally, bariatric surgery procedures are classified as restrictive, malabsorptive or a combination thereof. Restrictive procedures reduce the size of the stomach, which limits the energetic intake and triggers satiety, while malabsorptive procedures bypass a specific part of the intestine, which impedes the absorption of the ingested nutrients in the gastrointestinal tract. Combined procedures include both the aspects of restriction and malabsorption[10]. The positive effects of bariatric surgery extend beyond weight loss as the metabolic status of the patients is drastically improved after surgery. Accordingly, the concept of metabolic and bariatric surgery has emerged and gained acceptance over the years[11,12]. For the remainder of the review, metabolic and bariatric surgery will be referred to as bariatric surgery.

While bariatric surgery is established to induce weight loss and/or improve the metabolic profile, several evolutions have occurred within the anatomical procedures[13]. Worldwide, the combined Roux-en-Y gastric bypass (RYGB) procedure is considered the gold standard of all bariatric procedures in view of its beneficial balance between the long-term efficacy and complication rate. However, the more recent, restrictive sleeve gastrectomy (SG) procedure is rapidly gaining popularity and has exceeded RYGB as the most commonly performed procedure within academic medical centres of the USA[14]. The alterations in the gastrointestinal anatomical architecture after RYGB and SG are visualised in Fig. 1. Briefly, the laparoscopic RYGB procedure involves the formation of a small gastric pouch and a gastric remnant using surgical staples. Afterwards, the small intestine is rearranged into a Y-configuration through the segmentation of the proximal part of the small intestine distal to the ligament of Treitz. The distal part of the small intestine is reconnected to the small gastric pouch through a gastrojejunostomy with the formation of the Roux limb, while the proximal part of the small intestine is reconnected to the Roux limb through a jejunojejunal anastomosis to facilitate the passage of secreted digestive enzymes and bile salts. The laparoscopic SG procedure involves the resection of the greater curvature of the stomach starting at the antrum between the pylorus and the end of the nerve of Latarjet up to the angle of His. A sleeve-like pouch is formed that connects the oesophagus to the small intestine[15,16]. These restrictive and malabsorptive alterations in the gastrointestinal anatomical architecture have a direct effect on the intake, digestion and absorption of nutrients, while additionally inducing changes in the levels of several gut peptides involved in the regulation of appetite and satiety. Taken together, both anatomical and physiological alterations contribute to the desired beneficial weight and metabolic effects[17].

Iron deficiency after bariatric surgery

The beneficial results of bariatric surgery with respect to weight loss and comorbidities come at a cost, namely the risk for postoperative complications. Among all complications, the frequency of nutritional complications is a worrying trend and clearly demands extra attention[18]. These deficiencies develop as a consequence of the alterations in the gastrointestinal anatomical architecture and the associated changes in the physiology of the gastrointestinal tract[19]. Particularly striking is the risk of developing iron deficiency as it impairs the normal physiological function of tissues such as blood, brain and muscles[20]. Different factors contribute to the development of iron deficiency after bariatric surgery including reduced iron intake, reduced secretion of hydrochloric acid and a reduction in the surface area for absorption (Fig. 2). Taken together, these factors contribute to the development of iron deficiency after bariatric surgery and will be further discussed in the review[19,21]. Furthermore, it should be emphasised that obese patients are already predisposed to develop iron deficiency. Inadequate iron intake, greater requirements due to a higher blood volume and the presence of low-grade chronic inflammation inhibits the absorption of iron, which may lead to iron deficiency in obese patients and can then persist or even worsen after bariatric surgery[22].

Iron intake after bariatric surgery

The contribution of iron intake to iron deficiency after bariatric surgery has been the topic of investigation in several studies. Tables 1 and 2 provide an overview of the studies to date that have evaluated iron intake after RYGB and SG. After surgery, iron intake was mostly lower or even inadequate compared with the available estimated average requirements or dietary reference intake for healthy individuals[23–35]. Postoperatively, the restricted dietary intake, increased satiety and reduced appetite contribute to the lower iron intake by means of a reduced intake of micronutrients[27]. Furthermore, the lower iron intake is partially the result of the low tolerance for red meat. Recent studies report a rate of intolerance ranging from 23 to 50 % after bariatric surgery. Differences in reporting methodology explain the variety in the reported prevalence. For instance, disparity within the definition for red meat intolerance is observed between the different studies. Nicoletti *et al.* defined red meat intolerance 'as an abnormal physiologic response (nausea and vomiting) after eating red meat', while Moize *et al.* defined red meat intolerance as 'nausea, vomiting, diarrhoea or abdominal discomfort following the ingestion of red meat'. Despite this variance, the

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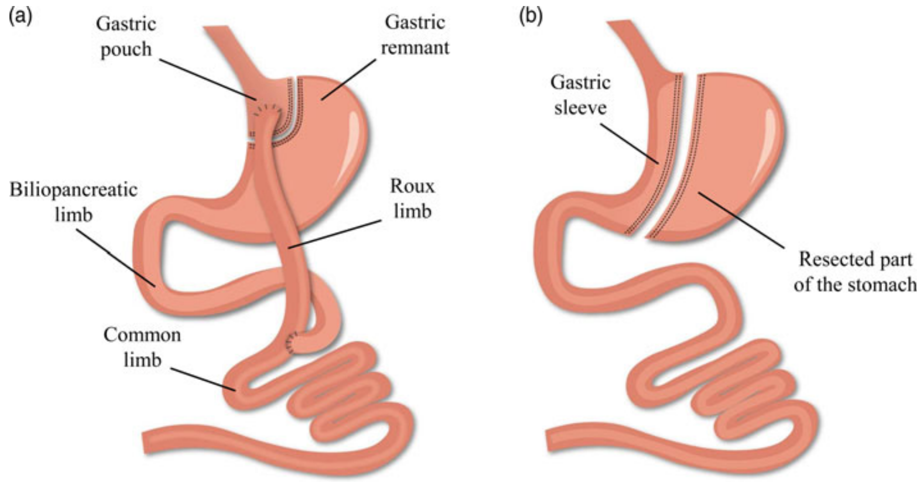

Fig. 1. (Colour online) Alterations in the gastrointestinal anatomical architecture after Roux-en-Y gastric bypass (a) and sleeve gastrectomy (b).

tolerance for red meat improves as time passes further from the bariatric procedure[36,37]. Finally, poor adherence to dietary guidelines provided by professionals, non-adherence to recommended supplementation or insufficient professional guidance further contribute to low iron intake. Adherence to the postoperative dietary recommendations has been reported to be inadequate, which tends to increase over time. Supplementation adherence tends to be lower in the late postoperative period compared with the early postoperative period[38]. Concerning professional guidance, accreditation standards from the American Society for Metabolic and Bariatric Surgery (ASMBS) and the International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO) recommend that patients receive postoperative follow-up[39,40]. Nonetheless, it has been reported that 47–90 % of patients do not receive nutritional advice after surgery[41].

Iron absorption after bariatric surgery

Low iron intake after surgery is not an exclusive explanation for the development of iron deficiency. The digestion and absorption of iron are affected by alterations in the gastrointestinal anatomical architecture as illustrated in Fig. 2. First, the reduced secretion of hydrochloric acid hinders the reduction of ferric iron into the absorbable ferrous form[42,43]. Secondly, the bypass of the duodenum and proximal part of the jejunum after RYGB reduces the intestinal absorption area for iron, which is mainly absorbed in the duodenum. Thirdly, the villi of the gastrointestinal tract are affected and potentially further contribute to the reduction of the intestinal absorption area for iron after surgery. Spak *et al.* and Casselbrant *et al.* found a decrease in villi height in the Roux limb after RYGB, while no studies have investigated potential changes in villi height after SG[44,45]. Taken together, bariatric surgery impedes the ability to absorb iron from both dietary sources and nutritional supplementation. To the best of our knowledge, five studies investigated the impact of bariatric surgery on iron absorption by comparing pre- and postoperative data[21,28,46–48]. Ruz *et al.* investigated the absorption of dietary iron after RYGB (*n* 36). Iron absorption tests were performed before and at 6, 12 and 18 months after RYGB using a standard diet containing 3 mg labelled iron. At each follow-up, iron absorption was significantly decreased to approximately 30 % of the preoperative baseline value[28]. To distinguish between haem- and non-haem iron, iron absorption tests were performed before and 12 months after RYGB (*n* 20) and SG (*n* 20) using a standard diet containing labelled ferric chloride and labelled haem iron. Iron absorption from both haem and non-haem iron decreased significantly after RYGB and SG, but the magnitude of reduced absorption for haem iron was greater compared with non-haem iron (haem absorption: 23·9 (SEM 22·2–25·8)% *v.* 6·2 (SEM 5·3–7·1)%; non-haem absorption: 11·1 (SEM 9·8–12·5)% *v.* 4·7 (SEM 3·1–5·5)%)[46].

In addition to the absorption of dietary iron, the alterations in the gastrointestinal anatomical architecture potentially interfere with the dissolution and absorption of iron supplements. In 1999, Rhode *et al.* investigated the absorption of 50 mg ferrous gluconate 3·2 years after RYGB (*n* 55). After surgery, 65 % of the included patients appeared to have normal iron absorption, defined as more than 100 % change in serum iron concentration over 3 h after administration. In the patients with normal absorption, a higher incidence of anaemia and lower levels of ferritin concentration were observed[47]. Additionally, two studies investigated the response to iron sulphate. Rosa *et al.* performed iron tolerance tests with 15 mg elemental iron originating from ferrous sulphate before and at 3 months after RYGB (*n* 9). Despite a delayed response in the first hour, no significant differences were observed in iron response after surgery, although six of the nine patients demonstrated a mean decrease of 50 % in area under the curve[48].

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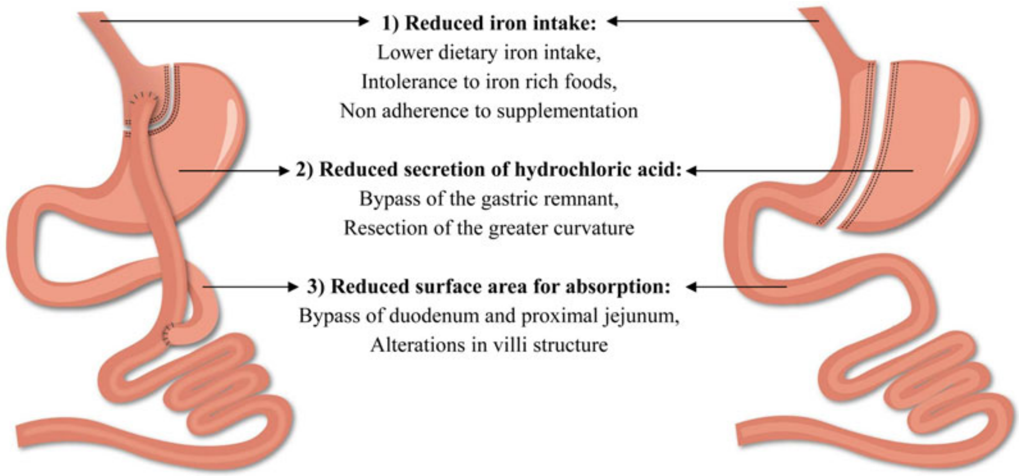

Fig. 2. (Colour online) Factors contributing to the development of iron deficiency after Roux-en-Y gastric bypass and sleeve gastrectomy.

Nonetheless, Gesquiere *et al.* performed iron challenges with 100 mg ferrous sulphate in iron-deficient patients after RYGB (*n* 23). One patient had sufficient absorption, defined as an increase in serum iron concentration larger than 80 µg/dl[21]. Based on these three studies, it is impossible to compare the level of iron absorption due to differences in study design, type of iron, dosage and formulation of the supplement. Iron absorption studies assessing the erythrocyte incorporation using stable iron isotopes would provide more convincing data on the effectiveness of iron supplementation after bariatric surgery[49].

Iron status after bariatric surgery

In light of the risk to develop iron deficiency, different studies have examined the preoperative and post-operative nutritional status of iron after RYGB and SG. Postoperatively, the prevalence of iron deficiency varies between 18·0 and 53·3 % during a follow-up of maximal 11·6 years after RYGB, while the prevalence of anaemia ranges between 6·0 and 63·6 %[30,31,50–68]. To elucidate the contribution of iron deficiency to the development of anaemia, two studies evaluated the prevalence of iron deficiency anaemia during a follow-up of maximal 10 years after RYGB. Within these studies, the prevalence of iron deficiency anaemia ranged between 6·6 and 22·7 % after RYGB[56,67]. In comparison, the prevalence of iron deficiency varies between 1 and 54·1 % during a follow-up of maximal 5 years after SG. Additionally, the prevalence of anaemia ranges between 3·6 and 52·7 % after SG[69–79]. According to a prospective cohort study of Hakeam *et al.*, iron deficiency anaemia occurred in 1·6 % of the patients 1 year after SG[71]. Remarkably, the prevalence of iron deficiency, anaemia and iron deficiency anaemia varies widely both after RYGB and SG. Inconsistency within the definition of deficiencies and differences in bariatric procedure, follow-up, dietary guidance and nutritional supplementation clarify the extent of variation.

Diagnosis of iron deficiency, anaemia and iron deficiency after bariatric surgery

One of the major challenges to diagnose patients as iron deficient concerns the definition of iron deficiency. The proportion of patients affected by iron deficiency depends on the proposed iron status markers and their reference ranges. Malone *et al.* investigated the proportion of patients affected by iron deficiency after RYGB using three different definitions (*n* 125). First, iron deficiency was defined as serum ferritin <15 ng/ml (male) or <12 ng/ml (female) or as transferrin saturation (TSAT) <20 % (male) or <16 % (female). Secondly, iron deficiency was based on a combination of serum iron <40 µg/dl and serum ferritin <35 ng/ml. Thirdly, iron deficiency was based on serum ferritin <20 ng/ml. Based on the first definition, 28·3 % of the ferritin values and 47·8 % of the TSAT values fulfilled the criteria for iron deficiency. Based on the combination of serum iron and ferritin, 57·5 % of the patients were suffering from iron deficiency, while 43·4 % of the patients were suffering from iron deficiency, based on the third definition[80]. These data strengthen the clinical significance of combining different iron status markers to assess the prevalence of iron deficiency.

In Table 3, an overview of the iron status markers and cut-off values used in the afore-mentioned studies is given for iron deficiency, anaemia and iron deficiency anaemia[30,31,50–79]. Low levels of serum iron concentration are frequently used to diagnose iron deficiency after surgery[61,71,72,76,77,79]. However, serum iron concentration is not an absolute diagnostic marker for iron deficiency due to its diurnal variation and external influences[81]. Additionally, diagnosis of iron deficiency is sometimes merely based on serum ferritin

Table 1. Overview of studies reporting iron intake after Roux-en-Y gastric bypass

Ref.	Sample size and follow-up (months/year)	Methods	Total iron intake	Iron supplementation
Colossi *et al.*[23]	Patients: 1 month (189), 3 months (182), 6 months (158), 9 months (187), 12 months (147), 18 months (164) and 24 months (193) after surgery	24 h dietary recall	Iron intake was inadequate compared with the DRI	NR
De Torres *et al.*[24]	Patients: ± 3·4 years after surgery (44), controls: healthy subjects (38)	4-d food record	Iron intake was lower compared with controls and inadequate compared with the EAR	Recommended, but not reported or included in total iron intake
Mercachita *et al.*[25]	Patients: before (60), 1 year (45) and 2 years (17) after surgery	24 h dietary recall	Iron intake was lower after surgery and inadequate compared with the DRI	Recommended and reported, but not included in total iron intake
Miller *et al.*[26]	Seventeen patients: before, 3 weeks, 3, 6 and 12 months after surgery	4-d food record	Iron intake was lower after surgery and inadequate compared with the EAR	Recommended but not reported or included in total iron intake
Moizé *et al.*[27]	294 patients: before, 6, 12, 24, 48 and 60 months after surgery	3-d food record	Iron intake was lower after surgery and inadequate compared with the DRI	Recommended, but not reported or included in total iron intake
Ruz *et al.*[28]	Patients: before (67), 6 months (58), 12 months (56) and 18 months (51)	3-d food record	Iron intake was significantly lower at 6 and 12 months after surgery	Recommended and reported, but not included in total iron intake
Wardé-Kamar *et al.*[29]	Sixty-two patients: 30 ± 8 months after surgery	24 h recall	Iron intake was at or above RDA recommendations after surgery	Recommended and reported, but not included in total iron intake
Gesquiere *et al.*[30]	Patients: before (54), 1 month (54), 3 months (50), 6 months (46) and 12 months (42) after surgery	2-d food record	Iron intake was lower until 6 months and increased at 12 months. At 1 year, 14·3 % had a dietary iron intake below the EAR	Recommended and reported, but not included in total iron intake
Aron-Wisnewsky *et al.*[31]	Fourteen patients: before, 1 and 3 months after surgery	24 h food record	Iron intake was adequate after surgery compared with the French recommendations	Recommended, reported and included in total iron intake
Bavaresco *et al.*[32]	Forty-eight patients: before, 1, 3, 6, 8 and 12 months after surgery	24 h dietary recall	Iron intake was lower after surgery and inadequate (recommendations not specified)	Recommended, but not reported or included in total iron intake
Menegati *et al.*[33]	Twenty-five patients: 6–64 months after surgery, thirty-three controls: weight-matched subjects	FFQ	Iron intake was lower compared with controls	NR

Ref., reference; NR, not reported; DRI, dietary reference intake; EAR, estimated average requirements.

Table 2. Overview of studies reporting iron intake after sleeve gastrectomy

Ref.	Sample size and follow up (months/year)	Methods	Total iron intake	Supplementation
Moizé *et al.*[27]	Sixty-one patients: before, 6, 12, 24, 48 and 60 months after surgery	3-d food record	Iron intake was lower after surgery and inadequate compared with the DRI	Recommended, but not reported or included in total iron intake
Chou *et al.*[35]	Forty patients: 5 years after surgery	FFQ	Iron intake was inadequate compared with the DRI and the ASMBS recommendations	NR

Ref., reference; NR, not reported; DRI, dietary reference intake; ASMBS, American Society for Metabolic and Bariatric Surgery.

concentration[31,51,54,56,60]. Low levels of serum ferritin imply the presence of depleted iron stores. Nonetheless, concentration of ferritin might be increased as inflammation increases the production of this acute phase protein. As a result, measuring inflammatory markers (e.g. C-reactive protein or α_1-acid glycoprotein) could help to interpret ferritin measurements[82,83]. Another marker regularly used as a standalone determinant of iron deficiency is TSAT, which is calculated by dividing serum iron concentration with serum transferrin concentration[58,62,65,66,70]. Again, low TSAT is not an absolute marker, but is characteristic for iron deficiency[81]. Which iron status markers should then be used to diagnose iron deficiency after bariatric surgery? As no single iron status marker is an absolute determinant of iron deficiency, the preferred screening approach is a combination of markers. These markers should include at least ferritin concentration, which is relevant in the absence of underlying inflammation, and TSAT, which provides more reliable information in the presence of underlying information. Furthermore, assessing hepcidin and/or the soluble transferrin receptor concentration would provide additional important information regarding iron homeostasis. Nonetheless, the utility of these markers may somehow be limited in clinical practice due to associated costs and availability issues[84–86].

In contrast to diagnosing iron deficiency, one marker is sufficient to detect the presence of anaemia. According to the WHO, Hb concentration below 130 g/l for men aged 15 years or above and a concentration below 120 g/l for non-pregnant females aged 15 years or above is representative for anaemia[87]. Although the credibility of these cut-off values has been discussed in literature in light of differences in ethnicity. Therefore, new age, sex and ethnic-specific cut-off values have been proposed[88,89]. The disparity in cut-off values for diagnosing anaemia could explain the variety in reference ranges used within the afore-mentioned studies as illustrated in Table 3[30,31,50–79]. As stated earlier, the prevalence of anaemia reaches an upper limit of approximately 50 % after SG and 65 % after RYGB. These high rates of anaemia may reflect a variety of vitamin or mineral deficiencies, but are predominantly the result of iron deficiency. To distinguish between the different causes, the mean corpuscular volume of erythrocytes can be measured. Microcytic and hypochromic erythrocytes are considered the hallmark finding of iron deficiency anaemia[83,90]. Clearly, there is a need to standardise the definition of iron deficiency, anaemia and iron deficiency anaemia based on the most relevant iron status markers and their reference range.

Nutritional recommendations after bariatric surgery

Throughout the years, different organisations have published guidelines on clinical and nutritional guidance of patients before and after bariatric surgery. Table 4 summarises the available guidelines and updates proposed by the ASMBS and the IFSO concerning nutritional screening for deficiencies, preventive postoperative vitamin and mineral supplementation and postoperative supplementation for the treatment of iron deficiency. To prevent iron deficiency, pre- and postoperative nutritional screening in combination with multivitamin and mineral supplementation is recommended. In case of iron deficiency, oral or parenteral iron administration is required. To rate the quality of their recommendations, both organisations adopted grading systems (IFSO: Oxford centre for evidence-based medicine classification system; ASMBS: the protocol for standardised production of clinical practice guidelines provided by the American Association of Clinical Endocrinologists). However, these grading systems illustrate the lack of strong evidence supporting the preventive postoperative vitamin and mineral supplementation guidelines. In Table 4, the quality of evidence supporting the current recommendations for nutritional screening for deficiencies, preventive postoperative vitamin and mineral supplementation and postoperative supplementation for the treatment of iron deficiency is provided[5,6,91,92]. The absence of strong evidence might also explain the difficulty of patients to adhere to the proposed guidelines as patients experience clinical burden despite preventive strategies. According to a recent study in 16 620 French post-bariatric patients, the number of patients that received reimbursement for a nutritional iron supplement decreased significantly in the first 5 years after surgery[93]. These data confirm the poor adherence to the international guidelines and advocate for more nutritional research in order to provide strong evidence-based guidelines after bariatric surgery.

Apart from the guidelines of international organisations, some researchers have provided updates or even

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Table 3. Iron status markers and cut-off values used to diagnose iron deficiency, anaemia or iron deficiency anaemia

Ref.	Iron deficiency	Anaemia	Iron deficiency anaemia	Ref.	Iron deficiency	Anaemia	Iron deficiency anaemia
Salgado *et al.*[50]	Fer < 30 ng/ml and CRP < 0·5 mg/dl; or TSAT < 20 %	♂: Hb < 13 g/dl ♀: Hb < 12 g/dl	NR	Cable *et al.*[64]	NR	♂: Hb < 14 g/dl ♀: Hb < 12 g/dl	NR
Kotkiewicz *et al.*[51]	Fer < 10 ng/ml	♂: Hb < 14 g/dl ♀: Hb < 12 g/dl	NR	Karefylakis *et al.*[65]	♂: TSAT < 20 % ♀: TSAT < 10 %	♂: Hb < 134 g/l ♀: Hb < 120 g/l	NR
Worm *et al.*[52]	NR	♂: Hb < 8·3 mmol/l ♀: Hb < 7·3 mmol/l	NR	Vargas-Ruiz *et al.*[66]	TSAT < 15 %	♂: Hb < 14 g/dl ♀: Hb < 13 g/dl	NR
Skroubis *et al.*[53]	NR	♂: Hb < 13·5 g/dl ♀: Hb < 12·5 g/dl	NR	Rojas *et al.*[67]	≥2 abnormal markers: MCV < 80 fl, ZPP>70 µg/dl, TSAT < 15 % or Fer < 12 µg/l	Hb < 12 g/dl	Hb < 12 g/dl plus ≥2 abnormal markers: MCV < 80 fl, ZPP>70 µg/dl, TSAT < 15 % or Fer < 12 µg/l
Kim *et al.*[54]	Fer < 15 ng/ml	♂: Hb < 13 g/dl ♀: Hb < 12 g/dl	NR	Von Drygalski *et al.*[68]	NR	♂: Hb < 13 g/dl ♀: Hb < 12 g/dl	NR
Avgerinos *et al.*[55]	NR	♂: Hb < 11 g/dl ♀: Hb < 10 g/dl	NR	Gjessing *et al.*[69]	NR	♂: Hb < 13·4 g/dl ♀: Hb < 11·7 g/dl	NR
Obinwanne *et al.*[56]	Fer < 50 ng/ml	♂: Hb < 13·6 g/dl ♀: Hb < 11·8 g/dl	Fer < 50 ng/ml and Hb < 13·6 g/dl (♂) or < 11·8 g/dl (♀)	Al-Sabah *et al.*[70]	TSAT < 20 %	♂: Hb < 130 g/l ♀: Hb < 120 g/l	NR
Yu *et al.*[57]	NR	♂: Hb < 13 g/dl ♀: Hb < 12 g/dl	MCV < 80 fl, MCHC < 27 g/dl and Fer < 30 ng/ml	Hakeam *et al.*[71]	♂: Fer < 13 µg/l, ♀: Fer < 30 µg/l or sTfR>1·76 mg/l or Fe < 8 µmol/l with TSAT < 16 %	♂: Hb < 13 g/dl ♀: Hb < 12 g/dl	♂: Hb < 13 g/dl, ♀: Hb < 12 g/dl with ♂: Fer < 13 µg/l, ♀: Fer < 30 µg/l or sTfR > 1·76 mg/l or Fe < 8 µmol/l with TSAT < 16 %
Ledoux *et al.*[58]	TSAT < 20 %	Hb < 11·5 g/dl	NR	Zarshenas *et al.*[72]	Fe < 10 µmol/l	♂: Hb < 130 mmol/l ♀: Hb < 120 mmol/l	NR
Dalcanale *et al.*[59]	NR	♂: Hb < 13·5 g/dl ♀: Hb < 12 g/dl	NR	Gillon *et al.*[73]	NR	Hb < 11·5 g/dl	NR
Dogan *et al.*[60]	Fer < 20 µg/l	♂: Hb < 8·4 mmol/l ♀: Hb < 7·4 mmol/l	NR	Van Rutte *et al.*[74]	NR	♂: Hb < 8·5 mmol/l and ♂: HC < 0·40 l/l, ♀: Hb < 7·5 mmol/l and ♀: HC < 0·35 l/l	NR
Skroubis *et al.*[61]	Fe < 50 mg %	♂: Hb < 13·5 g/dl ♀: Hb < 12·5 g/dl	NR	Ben-Porat *et al.*[75]	Fe < 60 µg/dl or Fer < 12 ng/dl	♂: Hb < 14 g/dl ♀: Hb < 12 g/dl	NR
Gesquiere *et al.*[30]	Fer < 30 µg/l and/or TSAT < 20 %	♂: Hb < 14 g/dl ♀: Hb < 12 g/dl	NR	Ben-Porat *et al.*[76]	Fe < 60 µg/dl	♂: Hb < 14 g/dl ♀: Hb < 12 g/dl	NR
Aron-Wisnewsky *et al.*[31]	Fer < 30 µg/l	NR	NR	Damms-Machado *et al.*[77]	Fe < 60 µg/dl	NR	NR
Coupaye *et al.*[62]	TSAT < 20 %	Hb < 11·5 g/dl	NR	Cepeda-Lopez *et al.*[78]	sTfR > 28·1 nmol/l or Fer < 30 µg/l	Hb < 12 g/dl	NR
Blume *et al.*[63]	♂: Fe < 49µg/dl ♀: Fe < 37µg/dl	♂: Hb < 13 g/dl ♀: Hb < 12 g/dl	NR	Aarts *et al.*[79]	Fe < 9 µmol/l	♂: Hb < 8·5 mmol/l ♀: Hb < 7·5 mmol/l	NR

Fer, ferritin; CRP, C-reactive protein; TSAT, transferrin saturation; NR, not reported; MCV, mean corpuscular volume; MCHC, mean corpuscular Hb concentration; Fe, iron; ZPP, zinc protoporphyrin; sTfR, soluble transferrin receptor.

Table 4. Nutritional guidelines after bariatric surgery

Ref.	Year	Nutritional screening for deficiencies	Preventive postoperative vitamin and mineral supplementation	Postoperative supplementation for the treatment of iron deficiency
Mechanick *et al.*[92]	2009	Preoperatively, nutritional screening is recommended before any procedure (grade A, BEL1). Postoperatively, iron status should be monitored in all patients (grade D)	It is recommended to take two chewable supplements daily after AGB, RYGB and BPD-DS (grade B, Bel 2). In patients with malabsorptive surgery, 320 mg oral ferrous sulphate, fumarate or gluconate may be needed to prevent iron deficiency (grade A, Bel 1)	Intravenous iron infusion with iron dextran (INFeD), ferric gluconate (Ferrlecit), or ferric sucrose may be needed if oral iron supplementation is ineffective (grade D)
Mechanick *et al.*[6]	2013, update	Preoperatively, nutritional screening is recommended before any procedure (grade A, BEL1). Postoperatively, iron status should be monitored in all patients (grade D)	It is recommended to take one chewable supplement daily after AGB and two chewable supplements daily after SG, RYGB and BPD-DS (grade B, Bel 2). Total iron provided should be 45–60 mg (grade B, Bel 2)	Recommended for patients at risk or with iron deficiency to be treated with the respective nutrient (grade A, BEL2). Treatment regimens include ferrous sulphate, fumarate or gluconate providing 150–200 mg elemental iron daily (grade A, Bel 1). Intravenous iron may be needed for patients intolerant to oral iron or with severe malabsorption (grade D)
Fried *et al.*[91]	2007	Preoperatively, assessment of nutritional status is recommended. Postoperatively, it is recommended after AGB, RYGB and BPD (evidence level: not specified)	It is recommended after AGB, RYGB, BPD (evidence level: not specified)	In case of deficiency, parenteral administration should be given (evidence level: not specified)
Fried *et al.*[5]	2013, update	Preoperatively, assessment of nutritional status is recommended. Postoperatively, it is recommended after AGB, RYGB and BPD (evidence level: not specified)	It is recommended after AGB, RYGB, BPD (evidence level: not specified)	In case of deficiency, oral or parenteral administration should be given after RYGB and BPD (evidence level: not specified)

AGB, adjustable gastric banding; RYGB, Roux-en-Y gastric bypass; BPD, bilio-pancreatic diversion; BPD-DS, BPD with duodenal switch; SG, sleeve gastrectomy.

proposed new guidelines. For instance, Parrott *et al.* updated the recommendations of the ASMBS by providing additional guidelines to prevent iron deficiency for patients at low risk, menstruating females and patients after RYGB, SG or biliopancreatic diversion with duodenal switch and by providing treatment guidelines for patients suffering from iron deficiency after bariatric surgery. Furthermore, the authors made recommendations for the dosing of supplements and recommendation on how to avoid potential interactions with other nutrients or medication[94]. Additionally, Dagan *et al.* proposed nutritional guidelines for vegetarian and vegan patients undergoing bariatric surgery based on their clinical experience and the current knowledge in the field of nutrition in bariatric, vegetarian and vegan patients[95]. All these different guidelines highlight the heterogeneity in the reporting of bariatric research. Therefore, the ASMBS published outcome reporting standards in 2015. In addition to improving the quality of reporting, these standards are proposed to lower the heterogeneity in outcome reporting within the field of metabolic and bariatric surgery literature. These reporting standards provide consistency and uniformity for authors on how to report the following outcomes: follow-up, diabetes, hypertension, dyslipidaemia, obstructive sleep apnoea, gastroesophageal reflux disease, complications, weight loss and quality of life[96]. However, reporting standards are missing for the diagnosis and treatment of nutritional deficiencies after bariatric surgery.

Future perspectives

To improve future evidence, a standardised reporting methodology should be included for various important aspects of bariatric research. For instance, clinical outcomes of patients regarding nutritional deficiencies have been compared in review papers and meta-analyses without accounting for differences in screening and treatment approaches. This matter leads to heterogeneity in the interpretation of similar studies. Therefore, a standardised reporting methodology for nutritional deficiencies would allow a more meaningful comparison among previously published and future studies, but will definitely provide leverage for the overall field of bariatric surgery research. In the context of the present paper, we propose to standardise the definition of iron deficiency based on a combination of iron status markers. These markers should include at least ferritin concentration, which is relevant in the absence of underlying inflammation, and TSAT, which provides more reliable information in the presence of underlying information. However, future studies in bariatric patients are needed to assess the most optimal cut-off of values for ferritin concentration and TSAT to assess the prevalence of iron deficiency and to assess how to prevent and treat iron deficiency after bariatric surgery. Therefore, we advocate for more nutritional research in order to provide strong evidence-based guidelines after bariatric surgery.

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