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The incidence of iron deficiency anemia post-Roux-en-Y gastric bypass and sleeve gastrectomy: a systematic review

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Abstract

Setting The physiological and anatomical changes that occur as a consequence of bariatric surgery result in macro- and micro-nutritional deficiencies, especially iron deficiency. The reported incidence of iron deficiency and associated anemia after bariatric surgery varies widely across studies.

Objectives The aim of this systematic review is to quantify the impact of Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG) on the incidence of iron deficiency.

Methods Databases including Ovid Medline, Ovid Embase, Helthstar, Scopus, Cochrane (CDSR), LILACS, and ClinicalKey were searched for original articles with additional snowballing search. Search terms included *Obesity, nutrient deficiency, iron deficiency, iron deficiency anemia, bariatric surgery, Roux-en-Y gastric bypass, and sleeve gastrectomy*. Original articles reporting the incidence of iron deficiency and anemia pre- and post-RYGB and SG from January 2000 to January 2015 with minimum 1-year follow-up were selected. Data extraction from selected studies was based on protocol-defined criteria.

Results There were 1133 articles screened and 20 studies were included in the final analysis. The overall incidence of iron deficiency was 15.2% pre-operatively and 16.6% post-operatively. When analyzed by procedure, the incidence of iron deficiency was 12.9% pre-RYGB versus 24.5% post-RYGB and 36.6% pre-SG versus 12.4% post-SG. The incidence of iron deficiency-related anemia was 16.7% post-RYGB and 1.6% post-SG. Risk factors for iron deficiency were premenopausal females, duration of follow-up, and pre-operative iron deficiency. Prophylactic iron supplementation was reported in 16 studies and 2 studies provided therapeutic iron supplementation only for iron-deficient patients. Iron dosage varied from 7 to 80 mg daily across studies.

Conclusion Iron deficiency is frequent in people with obesity and may be exacerbated by bariatric surgery, especially RYGB. Further investigation is warranted to determine appropriate iron supplementation dosages following bariatric surgery. Careful nutritional surveillance is important, especially for premenopausal females and those with pre-existing iron deficiency.

Keywords Bariatric surgery · Iron deficiency anemia · Iron deficiency · Systematic review

Bariatric surgery is known to provide effective long-term treatment of obesity and its related comorbidities [1, 2]. The physiological and anatomical changes that occur as a consequence of these procedures result in both macro- and micro-nutritional deficiencies [3]. As the number of bariatric procedures performed annually continues to increase, it is important to quantify the risk of such long-term complications.

Patients with obesity have a higher prevalence of micronutrient deficiencies compared to normal weight individuals and this is further exacerbated by bariatric surgery [4, 5]. Iron deficiency and anemia following bariatric surgery have been reported in several studies of varying quality with a wide range of reported incidence [6–11]. The type of operation has the potential to influence the risk of iron deficiency. Sleeve gastrectomy (SG) is a restrictive procedure that results in decreased distension and early satiety. The incidence of nutritional deficiencies is expected to be less with a restrictive procedure compared to a combined

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restrictive/malabsorptive procedure, such as the Roux-en-Y gastric bypass (RYGB) [12].

While many studies have examined the post-operative nutritional status after bariatric surgery, the reported incidence of iron deficiency in these studies varies widely due to differences in patient populations, supplement protocols, and the length/completeness of follow-up [13]. A recent meta-analysis reported that the risk of iron deficiency and anemia was similar for SG and RYGB [14]. However, this meta-analysis only included studies that directly compared the two procedures.

The aim of this systematic review is to estimate the incidence of iron deficiency and related anemia following RYGB and SG, to determine risk factors for developing iron deficiency and to assess the reported effectiveness of supplementation on post-operative serum iron levels and anemia.

Methods

We performed a systematic literature search of all full-text articles published between January 1980 and June 2018 according to the Preferred Reporting Items for Systematic reviews (PRISMA) protocol [15]. An institutional review board approval was not required for this study.

Search strategy

The initial search strategy was completed by May 2015 by a health science librarian (E.L). A comprehensive search of all electronic databases was performed in MEDLINE, Embase, Helthstar, Scopus, Cochrane, LILACS, DynaMEd, Clinical Key, TRIP+, OTSeeker, Johanne Briggs Institute, and AMED. The search terms used were "Bariatric Surgery" OR "Roux-En-Y" OR "Sleeve Gastrectomy" OR "Obesity" for intervention terms AND "iron" OR "iron deficiency'" OR "iron deficiency anemia" OR "Nutritional deficiencies" with all possible variations. To increase the sensitivity of the search strategy, we combined key words with Medical Subjects Heading (MeSH) terms individually (key words AND MeSH), as well as a gray literature search. A more detailed search strategy is available on request. The search was re-run for a final retrieval (check) in June 2018.

Study selection

Selection criteria included original articles reporting the incidence of iron deficiency and anemia pre- and post-RYGB and SG with a minimum 12-month follow-up post-operatively. All studies were required to present data on (1) serum iron or ferritin level (2) hemoglobin level, and (3) incidence of iron deficiency anemia pre- and post-bariatric procedures in adult population.

Studies with information about iron supplements were included.

Study selection was completed through two levels of study screening. At the first level of screening, we excluded studies with the following exclusion criteria: publications of abstracts only, case reports, case series, letters, comments, and reviews; follow-up less than 1 year; non-English articles; studies with data on participants who underwent vertical banded gastroplasty, laparoscopic biliopancreatic diversion with duodenal switch, or adjustable gastric banding; and studies reporting data on participants with conditions other than obesity. Full articles were then obtained for all studies accepted at level one. For level two screening, studies reporting either the incidence of iron deficiency anemia or iron levels were included. Figure 1 illustrates the literature search and study selection.

Data extraction

Quality assessment of the included studies was done independently by two reviewers (G.E. and M.D) using the Newcastle–Ottawa Scale (NOS) assessment tool for non-randomized studies [16] and the Cochrane Collaboration's tool for randomized controlled trials. Two reviewers (G.E. and E.B.) extracted data from the included papers. This included data on study characteristics and type (author, published year, study design, and length of follow-up); patients' demographics [mean age, male to female ratio and pre- and post-operative body mass index (BMI)]; type of surgery performed; number of participants and outcomes measured (incidents of post-operative serum iron deficiency, iron deficiency anemia, and supplements intake). The incidence of iron deficiency and anemia was extracted at 0 and 12 months after surgery. Pooled data of categorical variables were reported as frequency and percentages.

Summary statistics are reported as total and percentages for categorical variables. Meta-analysis was performed using Review Manager Version 5.3 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014.). The risk of iron deficiency and unclassified anemia was compared pre-operatively to 1 year post-RYGB and SG. Pooled risk ratios were calculated using inverse variance weighting of risk ratios for each study. Random effects model was used as a significant amount of heterogeneity was observed in all analyses (i.e., $I^2 > 50\%$ or Cochran $Q < 0.05$). Publication bias was assessed visually using funnel plots for analyses with more than 10 studies but no conclusions could be made given the small number of studies. Analyses for publication bias were performed on STATA Version 14.2 (StataCorp, 405 Lakeway Drive, College Station, Texas).

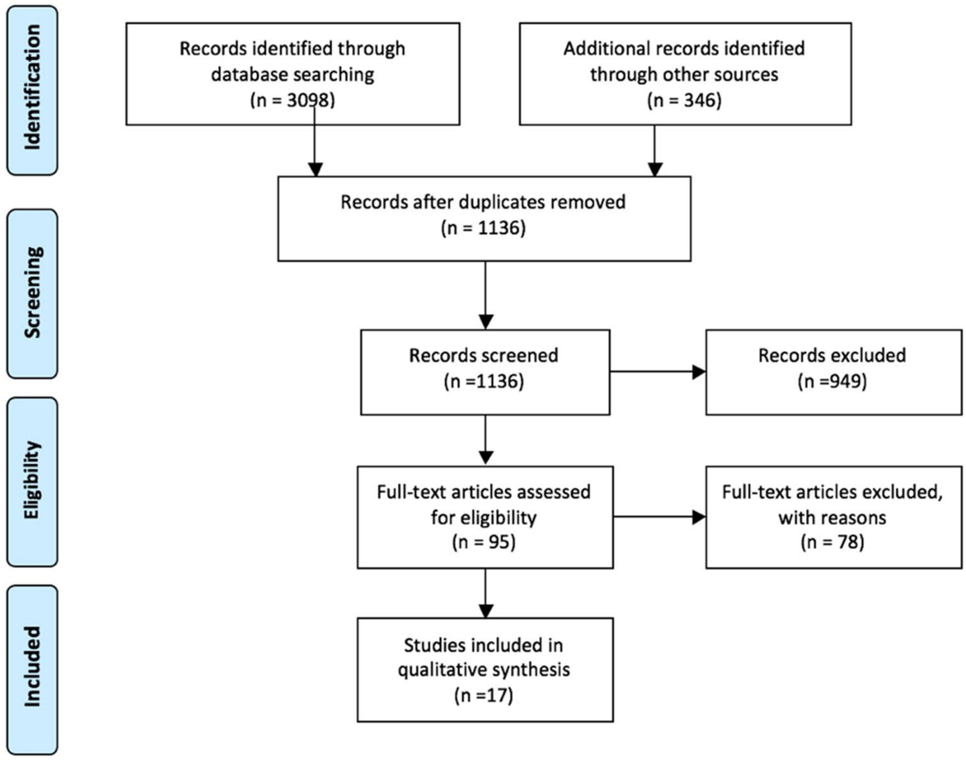

Fig. 1 Literature search and study selection

Results

Search results

There were 1133 articles identified for screening. Of those, 1041 articles were removed after level one screening of abstracts based on exclusion criteria. Full extraction and review of the remaining 95 articles in level two screening yielded a total of 15 included studies [17–33]. Two additional studies from the snowball search method that met our inclusion criteria were included [17, 18] and three additional studies were found on our updated search [13, 34, 35] (Fig. 1). In the final analysis, there were three randomized controlled trials (RCT) [13, 19, 20], 4 controlled studies [18, 21, 22, 27], 5 prospective studies [17, 23–26], and 8 retrospective studies [28–35].

Included studies

A total of 20 studies with 4007 patients were included for this review. Of those, 1897 patients had RYGB and 2110 patients had SG. Ten studies included RYGB cohorts, four included SG cohorts, and five compared SG to RYGB (Table 1).

The average follow-up time was 27.8 months (range 12–120). Mean age of the participants was 41.9 ± 18.4 years (range 32.6–46.4). Sixty-six percent of the patients were females. Body mass index was 52.1 kg/m^2 at baseline and 30.5 kg/m^2 post-operatively. The mean excess weight loss percentage (EWL%) could not be estimated due to inconsistency of reporting across studies (Table 1).

The combined total incidence of post-operative iron deficiency in patients undergoing either RYGB or LSG was 17.2% compared to 26.2% pre-operatively [13, 14, 17–35]. Differences in iron deficiency, iron deficiency anemia, and unclassified anemia existed between patients undergoing RYGB versus SG (Table 2).

RYGB

Iron deficiency

The total incidence of iron deficiency for RYGB is shown in Table 2. An increase in the incidence of iron deficiency pre- versus post-RYGB was observed in 12 studies [13, 18, 20, 21, 23–25, 27, 30–32, 35] (Table 3). Three studies [19, 22, 29] showed no increase in iron deficiency 1 year post-operatively, but one of these studies showed worsening iron deficiency at 36 months post-RYGB [29]. One study that provided 18 mg of daily iron supplementation did not prevent iron deficiency after RYGB [33].

The pooled analysis of 6 studies that assessed the number or percentage of patients who developed iron deficiency found a higher risk 1-year after RYGB OR 1.67 (95% CI 1.41–1.98). However, there was a significant

Table 1 Patient demographic and bariatric procedures

Publication	Study description	*N*	Surgery	Age (mean) ± SD (range)	Gender (M/F)	BMI pre-op (kg/m^2)	BMI Post-op (kg/m^2)	Follow-up
Aarts (2012) [25]	Prospective	377	RYGB	43.4	102/275	46.8	–	13.7 month
Al-Mutawa (2018) [34]	Retrospective	1560	SG	35 ± 11.2 years	463/1330	46.1 ± 8.0 kg/m2	–	36 months
Amaral (1985) [26]	Prospective	150	RYGB	35.8 (18–55)	18/132	–	–	7 year
Blume (2012) [29]	Retrospective	170	RYGB	39.5 ± 10.8	136/34	48.8	17.8	36 month
Brolin (1998) [20]	RCT	348	RYGB	36.6 ± 8.0	0/56	–	–	12-76 month
Coupaye (2009) [21]	Controlled	49	RYGB	43 ± 10.0	4/45	49 ± 8	–	12 month
Gesquiere (2014) [30]	Retrospective	164	RYGB	43 ± 10.0	41/123	117.6	28.6	60 month
Hakeem (2009) [17]	Prospective	61	SG	–	31/30	47.5	30.5	12 month
Kehagias (2011) [19]	RCT	60	SG RYGB	33.7 ± 9.9 36 ± 8.4	8/22 8/22	45.8 44.9	31.3 29.6	36 month
Kheniser (2017) [13]	RCT	50 50	SG RYGB	–	3/25 9/15	–	–	48 months
Moizé (2013) [22]	Controlled	355	SG RYGB	46.4 ± 11.6 45.2 ± 10.6	88/267	51.6_ ± 6.7 47.4 ± 6.0	–	48 month
Monaco-Ferreira (2017) [35]	Retrospective	151	RYGB	–	–	–	–	120 months
Ruz (2009) [23]	Prospective	67	RYGB	36.9 ± 9.9	0/67	45.2	29.8	18 month
Ruz (2012) [27]	Controlled	58	SG RYGB	35.9 ± 9.1	0/58	37.3 42.0	26.0 28.2	12 month
Saif (2012) [28]	Retrospective	82	SG	46.4 ± 13.9	27/55	55.7	41.2	24 month
Salgado (2014) [31]	Retrospective	102	RYGB	41.9	40/62	49.7	–	48 month
Skroubis (2002) [32]	Retrospective	79	RYGB	32.6 ± 9.4	15/64	45.6 ± 4.9	–	24 months
Toh (2009) [18]	Controlled	186	SG RYGB	46.4 ± 11.6 48 ± 10	27/37 44/77	51.0 ± 11.2 43.1 ± 5.2	–	12 months
Van Rutte (2014) [24]	Prospective	200	SG	42.7 ± 10.8	59/141	46.0	32.7	12 months
Vargas-Ruiz (2008) [33]	Retrospective	30	RYGB	41.0	5/25	44.0	–	24 months

BMI body mass index, *RYGB* Roux-en-Y gastric bypass, *SG* sleeve gastrectomy

Table 2 Iron deficiency, iron deficiency anemia, and unclassified anemia by bariatric surgery type

	RYGB %	SG %
Iron deficiency		
Pre-operative	14.7	36.6
Post-operative	22.5	12.4
Iron deficiency anemia		
Pre-operative	NR	NR
Post-operative	14.8	1.6
Unclassified anemia		
Pre-operative	11.2	19.1
Post-operative	22.9	19.6

NR not reported, *RYGB* Roux-en-Y gastric bypass, *SG* sleeve gastrectomy

heterogeneity detected for this comparison ($\chi^2 = 93.28$, $df = 13$ ($P < 0.00001$); $I^2 = 86\%$) (Fig. 2a).

Anemia

There was a significant increase in patients with unclassified anemia at 1 year post-RYGB in seven studies: 22.9% post-operatively compared to 11.2% pre-operatively [18, 19, 25, 29, 30, 32, 33] and this showed further increase by 4-year follow-up in two studies [29, 32] (Table 3). Four RYGB studies showed no significant change in the incidence of unclassified anemia at 1-year follow-up compared to baseline [19, 22, 31, 32]. However, one study showed an increased incidence of anemia at 24, 36, and 48 months of follow-up [13].

The pooled analysis of the 14 studies that reported the incidence of anemia after RYGB showed higher risk of anemia at 1-year post-surgery OR 2.49 (95% CI 2.04–3.05).

Table 3 Incidence of iron deficiency anemia pre- and post-bariatric surgery

Publication/year	Surgery	Indication/supplements (mg)	*N*	Iron deficiency Anemia (%)	No. % of iron deficiency pre-operative			No. % of iron deficiency post-operative		
					Anemia (%)*	Iron deficiency (%)**	Ferritin deficiency (%)**	Anemia (%)*	Iron deficiency (%)**	Ferritin deficiency (%)**
Aarts (2012) [25]	RYGB	Prophylactic/7 mg	377	–	7.1 (27)	7.8 (29)	–	18.8 (71)	20.7 (78)	–
Al-Mutawa (2018) [34]	LSG	Prophylactic/10 mg	1560	–	19.6 (305)	50 (639)	28.2 (440)	50.6 (323)	44.6 (180)	51.7 (231)
Amaral (1985) [26]	RYGB	Prophylactic/12–27 mg	150	18.0 (26)	0	19.3 (28)	–	35.5 (53)	48.6 (70)	–
Blume (2012) [29]	RYGB	Prophylactic/unknown	170	–	6.5 (11)	5.9 (10)	–	18.8 (32)	7.7 (13)	–
Brolin (1998) [20]	RYGB	Prophylactic/unknown Placebo (no prophylactic)	29 27	6.9 (2) 7.4 (2)	3.4 (1)	10.3 (3) 11.1 (3)	–	17.2 (5) 11.1 (3)	20.6 (6) 29.6 (8)	–
Coupaye (2009) [21]	RYGB	Prophylactic/60 mg	49	–	4.0 (2)	29.0 (14)	2.0 (1)	10.0 (5)	22.2 (10)	4.0 (2)
Gesquiere (2014) [30]	RYGB	None	164	–	0	0	–	1.8 (13)	37.2 (61)	–
Hakeem (2009) [17]	SG	None	61	1.6 (1)	0	0	–	4.9 (9)	4.9 (9)	–
Kehagias (2011) [19]	SG RYGB	Therapeutic/80 mg	30 30	–	20.0 (6) 13.3 (4)	20.0 (6) 20.0 (6)	3.3 (1) 3.3 (1)	20.0 (6) 13.3 (4)	16.0 (5) 20.0 (25)	16.0 (5) 10.0 (3)
Kheniser (2017) [13]	SG RYGB	None Prophylactic/18–65 mg	50 50	–	17 (8) 19 (9)	18 (22) 38 (19)	–	22 (11) 19 (9)	6 (16) 4.4 (22)	–
Moizé (2013) [22]	SG RYGB	Prophylactic/14 mg	62 294	–	10.0 (6) 22.0 (65)	30.8 (19) 26.5 (77)	8.3 (5) 18.6 (54)	11.5 (7) 19.9 (58)	10.3 (6) 15.9 (47)	6.5 (4) 19.8 (58)
Monaco-Ferreira (2017) [35]	RYGB	Prophylactic/unknown	151	11.63 (17)	3.31 (5)	23.53 (32)	2.99 (4)	28.43 (29)	22.77 (23)	32.32 (32)
Ruz (2009) [23]	RYGB	Prophylactic/18 mg	51	23.9 (12)	1.5 (1)	–	7.5 (5)	38.8 (26)	–	37.3 (15)
Ruz (2012) [27]	SG RYGB	Prophylactic/36 mg	19 23	–	19.2 (5) 9.7 (3)	–	19.5 (5) 0	15.0 (3) 39.1 (9)	– –	30.0 (6) 43.5 (10)
Saif (2012) [28]	SG	Prophylactic/unknown	82	–	20.7 (17)	6.6 (1)	–	8.8 (3)	3.0 (1)	–
Salgado (2014) [31]	RYGB	Prophylactic/60 mg	102	–	21.5 (22)	20.0 (17)	–	21.5 (25)	20.0 (25)	–
Skroubis (2002) [32]	RYGB	Prophylactic/80 mg	79	–	18.1 (14)	26.0 (21)	16.4 (13)	47.3 (37)	29.1 (23)	37.7 (30)
Toh (2009) [18]	SG RYGB	None Prophylactic/Unknown	46 121	–	8.0 (5) 6.0 (7)	18.0 (9) 12.4 (15)	0 1.6 (2)	15.0(2) 17.0(10)	11.0 (1) 21.0 (11)	0 15.0 (8)***
Van Rutte (2014) [24]	SG	Therapeutic/Unknown	200	–	5.0 (10)	38.0 (76)	7.0 (14)	6.5 (13)	18.5 (37)	8 (16)
Vargas-Ruiz (2008) [33]	RYGB	Prophylactic/18 mg	30	20.0 (6)	10.0 (3)	16.6 (5)	–	26.6 (8)	20.0 (6)	–

RYGB Roux-en-Y gastric bypass, *SG* sleeve gastrectomy

*Anemia was defined as a hemoglobin (Hb) level < 8.4 mmol/L in men and < 7.4 mmol/L in women

**Iron deficiency was defined as iron level < 9.0 mmol/L or ferritin level ≤ 20 mmol/L

***Therapeutic iron treatment was provided for those who were found to have low iron in the post-operative period with either IV iron or oral iron supplements

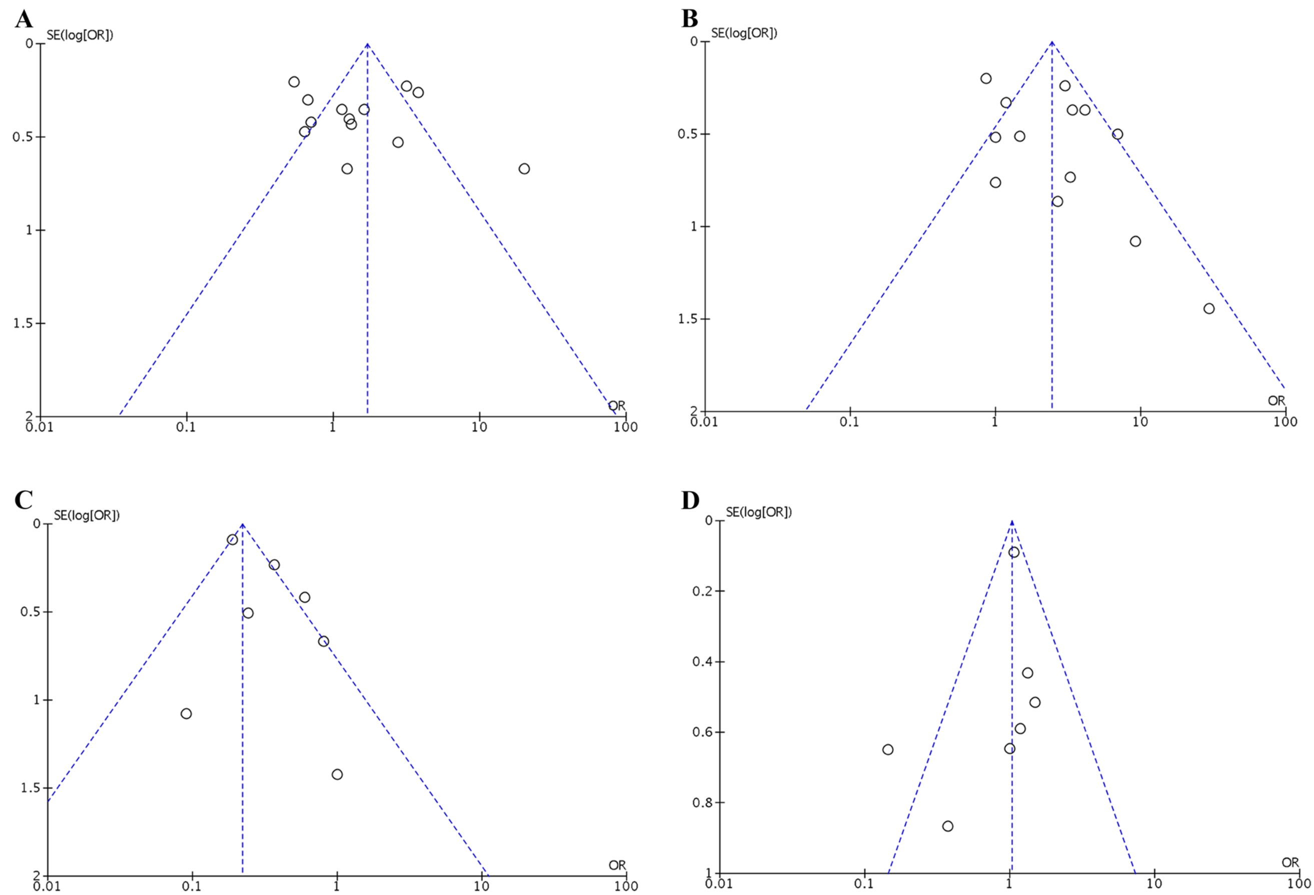

Fig. 2 **A** The incidence of iron deficiency post-Roux-en-Y Gastric bypass. **B** The incidence of unclassified anemia post-Roux-en-Y gastric bypass. **C** The incidence of iron deficiency post-sleeve gastrectomy. **D** The incidence of unclassified anemia post-sleeve gastrectomy

This comparison had significant heterogeneity ($\chi^2 = 55.89$, $df = 13$ ($P < 0.00001$); $I^2 = 77\%$) (Fig. 2b).

Iron deficiency anemia

The post-operative incidence was reported in only 5 studies (Table 3) [20, 23, 26, 33, 35]. Iron deficiency was most responsible for anemia in one study [61% of patients with anemia de novo ($P < 0.001$)] [25]. One study found a significant increase in the incidence of iron deficiency anemia at 18-month follow-up (1.5 vs. 23.9, $P < 0.05$) [23].

Risk factors for iron deficiency

Risk factors for the development of iron deficiency anemia in patients undergoing RYGB included female sex, low pre-operative ferritin, and younger age. Four studies reported a significant risk of new iron deficiency anemia post-operatively in females compared to males (21.7% vs. 4.6%, female vs. male; $P = 0.005$) [20, 23, 26, 33]. Two studies found a significant drop in iron level post-operatively among menstruating women [25, 31] and two studies reported increased incidence of anemia and low iron level post-operatively [13, 29]. Another risk factor for iron deficiency anemia included greater weight loss [25, 31]. The length of Roux limb did not seem to correlate with the development of iron deficiency [25].

Iron supplementation

Eleven studies [13, 18, 21, 22, 25, 28, 29, 31–33, 35] reported the administration of empiric iron supplementation to patients post-operatively. Two studies [19, 24] provided therapeutic iron only for those with iron deficiency and 2 other studies [17, 30] did not supplement at all. The effectiveness of supplement use is difficult to quantify due to lack of consistent dosage and documented compliance of intake. Iron supplements varied across studies from 7 to 80 mg (Table 3). Studies that provided an iron supplement dose of 60 and 80 mg daily did not have worsening incidence of iron level from baseline at 1 year post-operatively [13, 19, 31] or showed decreased incidence of iron deficiency from baseline [21, 33]. One RCT found significant correlation between improvement of post-operative iron deficiency and taking prescribed iron supplementation of 320 mg per day ($P < 0.05$) [20]. Brolin's study found that adherence to multivitamin supplements was associated with improvement in 41% of iron deficiencies and 22% of anemias [20].

Iron deficiency

The SG patients had a reported incidence of iron deficiency of 12.4% post-operatively versus 36.6% pre-operatively [17–19, 22, 24, 27, 28, 34]. Four studies reported no alteration in the serum iron and ferritin levels post-operatively [17, 24, 28, 34]. One study reported the development of iron deficiency as insignificant one-year post-SG, but this finding could be explained by the fact that patients with baseline iron deficiency and anemia were excluded [17]. None of the SG studies showed a significant increase in the incidence of the unclassified anemia at one year post-operatively (Table 2) [17, 18, 28, 34]. Saif et al. [28] showed that pre-operative anemia incidence improved at 1- and 3-year follow-up but returned to pre-operative level by 5 years.

Two studies in the SG group provided prophylactic supplementation [24, 34]. One study did not provide any supplementation [17] and an additional study provided therapeutic iron supplementation for those with pre-operative or post-operative iron deficiency or anemia only [28]. Adherence to supplementation was assessed in one study where only 28.9% of patients reported taking supplements at year 1 and 42.9% at year 3 and 63.3% at year 5 follow-up [28]. However, blood serum level of micronutrient did not seem to correlate with supplement use and some supplements were inadequate to normalize low serum iron level [28].

The pooled risk of post-operative iron deficiency or unclassified anemia was not higher after LSG 0.22 (95% CI 0.19–0.26) and 1.03 (95% CI 0.87–1.21), respectively (Fig. 2C, D).

RYGB versus SG

When comparing the two procedures, one study found that patients who underwent RYGB were more susceptible to develop post-operative iron deficiency (15% post-op vs. 2% pre-op; $P < 0.01$) than the SG patients (0% post-op vs. 0% pre-op) [18]. Two other studies found no change in the incidence of iron deficiency at 1-year follow-up compared to baseline between the two procedures [19, 22].

The effect of iron supplementation on the incidence of iron deficiency was examined in few studies. Supplementation was found to be protective in 2 studies with RYGB cohorts [31, 33], while 2 studies with SG cohorts did not identify such protective effect [24, 28].

Discussion

Nutritional deficiencies after bariatric surgery are related to several factors: (1) reduced intake of nutrients, such as red meat, (2) anatomical changes in the gastrointestinal tract, (3) high rates of pre-operative nutritional deficiencies. Iron deficiency was reported among 5.9 to 42% of patients undergoing bariatric surgery [7, 17, 20, 26, 30, 33, 36]. Most of the anemia identified post-RYGB was attributed to iron deficiency with a rate of 16–26% [7, 17, 20, 23, 26, 30, 32, 33]. Patients with pre-operative iron deficiency had worsening of their iron levels following RYGB. It is important to monitor iron indices before and after weight loss surgery [20, 25, 30]. The American Society of Metabolic and Bariatric Surgery (ASMBS) guidelines recommended diagnosing iron deficiency prior to weight loss surgery, at 3 months post-operatively, then every 3–6 months for the 12-months post-operatively and annually thereafter by measuring serum iron, serum transferrin and TIBC [37]. However, there are no standard guidelines for the management of iron deficiency in those who are identified pre-operatively.

The studies that compared iron deficiency pre- and post-SG found either no change or decreased incidence of iron deficiency after surgery [17, 24, 28]. Hakeem's study did not report iron deficiency at one-year post-SG even though the post-operative supplements did not include iron [17]. However, their study only included patients with normal iron levels pre-operatively. Therefore, iron deficiency found after SG could be partially explained by pre-operative iron deficiency state. The included studies reported higher pre-operative rate of iron deficiency in patients undergoing SG compared to RYGB (36.6% vs. 14.7%). An explanation for this vast difference could not be inferred from the included studies. However, one can assume that SG may be better offered to patients with higher risk to develop iron deficiency post-operatively than RYGB, e.g., menstruating females, those with pre-operative deficiency.

Patients with obesity are counseled to continue lifelong nutritional supplements after RYGB [38]. Recommendations for RYGB include starting the supplementation within 30 days post-operatively and continuing lifelong [39]. Commercial multivitamin supplementations contain a small amount of iron (10–20 mg) which is generally insufficient to prevent iron deficiency post-operatively. Few studies recommended adequate supplementation based on laboratory surveillance in the pre- and post-operative period for patients undergoing sleeve gastrectomy [25, 40, 41]. Eighteen milligram of elemental iron daily is recommended for average risk patients and 40–65 mg (200–400 mg of ferrous sulfate) for women in their reproductive years and patients with history of anemia [37].

However, this dose is increased in patients with anemia post-bariatric surgery to 150–200 mg (400–800 mg of ferrous sulfate) [37, 39, 42, 43]. Brolin et al. found in a randomized controlled trial that prophylactic supplementations of 320 mg of oral ferrous sulfate twice daily prevented iron deficiency anemia [20]. Parenteral iron should be administered if a patient fails to respond to oral iron supplementation post-operatively [20, 24, 32, 33].

Patients' compliance to supplementation plays an important role in developing deficiencies post-RYGB. Brolin et al. reported post-RYGB iron deficiency of 47% when only 35% of the patients were compliant with iron supplements [26]. Compliance after bariatric surgery has been reported as 29% after the first year and increasing to 63% by the fifth year, emphasizing the need for close observation, continued patient education, and treating iron deficiency beyond 1 year in the post-operative period [28]. Skroubis reported an increased incidence of anemia and iron deficiency at 4-year follow-up from baseline (anemia: 18.1% pre-op vs. 44.4% post-op and iron deficiency: 26.0% pre-op vs. 38.9% post-op) [32]. Moreover, the mean time to recognize iron deficiency after RYGB in men was almost 2 years after that in women with a mean of 29 months [20].

Iron deficiency is more common in women than men, especially premenopausal females [29, 30, 44]. This is noteworthy given that premenopausal women compromise almost 80% of bariatric surgery candidates [44]. Younger age was also found to a be risk for iron deficiency post-RYGB [7, 30, 36].

Limitations

Considerable heterogeneity was observed across studies, likely due to diversity in study participants, baseline iron deficiency, iron supplementation dose, and length of follow-up. There were few RCTs assessing the risk of iron deficiency post-bariatric surgery. The results of this analysis should be interpreted with caution due to the inevitable risk of selection bias with observational studies. Also, due to the small number of studies included in our analysis, we could not confidently assess the risk of bias in the included studies. Most of the studies could not attribute the rate of unclassified anemia to iron deficiency or other micronutrient deficiency, such as vitamin B12 or folate deficiency. Finally, most of our findings are based on observational studies and, thus, causal association cannot be established.

Conclusions

Long-term follow-up for iron deficiency is important after RYGB, especially for those patients with increased risk: premenopausal women, young populations, and those with pre-operative anemia and iron deficiency. Medical and nutritional surveillance is also important during the post-operative period, including the prescription of prophylactic iron and early parenteral replacement when indicated. The incidence of iron deficiency tends to increase with time post-operatively.

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Compliance with ethical standards

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