METABOLIC DISEASES

Nutritional status prior to bariatric surgery for severe obesity: a review

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Abstract

Obesity pandemic represents a threat to public health of paramount importance. Bariatric surgery represents the most effective and long-lasting treatment for severe obesity so far. The nutritional status of obese patients seeking bariatric surgery is impaired prior to surgery because of prevalent nutritional deficiencies. In addition, excess micronutrient levels may also occur, although this finding is not common. The onset of nutritional anomalies encountered in bariatric surgery candidates might stem from the following: obesity itself, poor quality food choices, preoperative weight loss or insufficient/excessive preoperative oral supplementation with vitamins and minerals. Nutritional management should begin preoperatively and should include a comprehensive assessment in order to identify those patients with clinical or subclinical deficiencies and hypervitaminoses. This paper provides background information on the nutritional status of bariatric surgery candidates, as well as on the prevalence and clinical significance of the most common micronutrient deficiencies and excess levels reported preoperatively among these patients.

Keywords: bariatric surgery, severe obesity, nutritional status, nutritional deficiency, hypervitaminoses

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Introduction

Obesity is a condition of major public health concern that seriously impacts the quality of life, even in allegedly healthy subjects. The obesity pandemic has nearly tripled in the last four decades and it poses greater risks to health than hunger or malnutrition [1]. Over 1.9 billion people (39% of world's adult population) were overweight or obese in 2016. Obesity has been defined by World Health Organization (WHO) as a body mass index (BMI) of 30 kg/m^2 and above [2]. Excessive weight is associated with several pathologies such as cardiovascular diseases, diabetes [1,3] and some types of cancer [4], which are responsible for >70% of premature deaths worldwide [5]. High BMI may also shorten life expectancy and was to blame for more than a half-percentage point per year decline in mortality rates improvement in US, between 1988-2011. In other words, obesity counteracts the factors that help extend human life, such as cutting down smoking or medical advances and, if its rates keep rising, a future increase in life expectancy is uncertain [6]. Since the prevalence of obesity is constantly rising, it is expected that the burden of its related comorbidities will also be increasing in the years to come [1], so much that World Obesity Federation and Canadian Medical Association, among other organizations, have pronounced obesity as a chronic, progressive disease. Hence, obesity is not only a risk factor for metabolic diseases, but also a disease itself [5].

In order to slow the progression of obesity pandemic, various prevention and treatment options have been developed that can be divided into non-surgical (lifestyle changes and pharmacotherapy) and surgical interventions (bariatric surgery, BS) [7]. Up to date, BS is considered to be the most effective treatment of clinically severe obesity (BMI ≥40 kg/m^2 or BMI ranging between 35-40 kg/m^2), leading to sustained weight loss and improvement of obesity-associated comorbidities [8,9]. Although it has proven successful in treating obesity and its complications, BS is known to predispose patients to a range of vitamin and mineral deficiencies [10]. The importance of nutritional consequences following BS correlates to the type of procedure performed and, thus, to the specific physiologic changes in digestion and absorption of food [11]. Moreover, studies have shown that patients with clinically severe obesity planning to undergo BS are often malnourished prior to surgical treatment for weight loss [12-16]. Furthermore, micronutrient deficiencies remain undiagnosed in most cases [17]. In fact, less than 25% of patients undergoing BS is subjected to a nutritional status assessment [18].

The most common micronutritional deficiencies reported in BS candidates are vitamin D, vitamin B_{12}, folate, and iron [18-22]. Baseline deficiencies are considered to be strong predictors of postoperative nutritional deficiencies. Hence, it is important to identify and correct the preoperative deficiencies as they might exacerbate after the weight loss surgery and lead to long-term complications [23]. Although micronutrient deficiencies are the most common nutritional issues encountered in BS patients prior to surgical procedures, some studies have also reported excess micronutrient levels [13,16].

The purpose of this review is to describe the determinants of the preoperative nutritional status in obese patients planning to undergo BS as well as the most widespread micronutrient anomalies in terms of deficiency or excess and their deleterious health consequences.

Bariatric surgery: summary of indications, outcomes, and most common procedures

Most international guidelines still widely used, developed according to National Institute for Health (NIH) statement released in 1991, recommend BS as suitable for subjects whose BMI is greater than 40 kg/m^2 without comorbid conditions or 35 kg/m^2 in the presence of at least one or more comorbidities – such as heart disease, type 2 diabetes (T2DM) or severe sleep apnea and who have reported unsuccessful attempts to lose weight or maintain the weight loss obtained by non-surgical means [24]. The European Association for Endoscopic Surgery clinical guidelines issued in 2020, endorsed by the International Federation Surgery of Obesity and Metabolic Disorders – European Chapter, recommend BS for patients with an even lower BMI, respectively between 30–35 kg/m^2, and poor-controled T2DM and/or arterial hypertension despite medical therapy [25].

Although anti-obesity drugs and lifestyle changes do hold a role in obesity management [26], BS has been proven effective in inducing a more significant long-term weight reduction, as well as in decreasing obesity-associated comorbidities and improving the life quality (QoL) and life expectancy of patients with severe obesity [27]. The Swedish Obese Subjects Study (SOS), a prospective, landmark controlled trial with an extended follow-up period (between 10-20 years), found that BS was related to clinically important weight loss (>15%) after 10 years that markedly improved cardiovascular risk factors in these patients; BS resulted in a lower long term all-cause mortality rate compared with usual medical treatment [adjusted hazard ratio (HR)=0.71], increased T2DM remission rate (adjusted OR=3.45; $p<0.001$), improved QoL [8] and also in a prolonged survival (adjusted median for life expectancy was 3 years longer in the surgery group compared to the control group) [28].

The clinical benefits of BS explain the rapid growth of bariatric procedures performed worldwide with an estimated number of over 600,000 operations in 2016 [29]. The mechanisms underpinning weight loss and health outcomes associated with BS are not fully elucidated and include restriction and malabsorption, neuro-hormonal and metabolic factors as well as postsurgical eating behavior modification. Currently, the most common procedures performed worldwide are sleeve gastrectomy (45.9%) and Roux-en-Y gastric bypass (39.6%) [30].

Preoperative evaluation of BS candidates

Regardless of the type of planned surgery, all BS candidates should be submitted to a comprehensive nutritional, medical and health-related behavior assessment prior to surgery, followed by suitable counseling and intervention. Patients planning to undergo BS must be also provided with appropriate knowledge about the surgical treatment for weight loss [31,32]. Preoperative screening of baseline nutritional deficiencies should be performed (Table I) [33] and adequate nutritional supplementation, based on micronutrient laboratory tests results, should be recommended [16].

Preoperative nutritional status of BS candidates

Determinants of micronutrient deficiencies in BS candidates

Although it seems unlikely, obese patients present various micronutrient deficiencies before undergoing BS [23,34]. These disturbances generally occur due to obesity *per se*, poor diet quality, preoperative weight loss, and altered nutrient metabolism and increased nutrients requirements [35].

Table I. Preoperative nutrient screening prior to BS.

Screening	Recommended	Optional
Iron studies	√	
B_{12}	√	
Folic acid	√	
Vitamin D	√	
Red blood cell folate		√
Homocysteine		√
Metylmalonic acid		√
Vitamin A		√
Vitamin E		√
Routine laboratory tests: fasting blood glucose, lipid panel, kidney function, liver profile, lipid profile, urine analysis, prothrombine time/INR, blood type, complete blood count	√	

INR: international normalized ratio

A major contributor to an altered nutritional status in BS candidates is obesity itself [36]. Obesity is a chronic disease that causes a state of low-grade inflammation [37] Inflammation may alter nutrient metabolism, synthesis of nutrient transporters and induce oxidative stress, leading to an increased antioxidant utilization [35]. For example, iron homeostasis may be dysregulated by adipose tissue inflammation and by the increased level of hepcidin, the master iron regulatory hormone [38]. Another mechanism underpinning the obesity-impaired nutritional status is attributed to the volume of distribution, which is greater in obese patients due to elevated adipose tissue and total body water. Extracellular fluid is increased compared to the intracellular fluid, possibly leading to the dilution of the extracellular micronutrient concentration [39]. Lastly, adipose tissue might be storage depot for lipophilic compounds, such as vitamin D, which provides an explanation for low plasma levels of 25(OH)D documented in most obese patients [38].

The impaired nutritional status of BS candidates is considered to be related to poor quality food choices that provide insufficient amounts of vitamins and minerals in spite of a higher total caloric intake [23]. Low fruit and vegetables consumption combined with energy-dense processed food intake have emerged main causes that lead to micronutrient deficiencies in extremely obese patients [40]. For example, excessive intake of simple sugars, milk products or fats might deplete thiamine stores [38]. Some authors hypothesized that, in turn, these deficiencies drive overconsumption in order to compensate for the scarcity of micronutrients in processed food [41]. A rapid concomitant increase in ultra-processed foods (UPFs) consumption and obesity prevalence is seen worldwide. UPFs possess unhealthy nutritional profiles, with lower vitamin and mineral content and higher fat, salt and sugar levels. The French NutriNet-Santé cohort study, which spanned 10 years and involved over 100.000 participants, showed that a higher intake of UPFs is linked with an increased weight gain and may contribute to the rise of obesity rates. It is estimated that UPFs consumption represents, in certain high income countries, up to 50-60% of the total energy intake [42].

Some studies evaluating the prevalence of micronutrient deficiencies among obese patients preparing to undergo BS have also assessed food consumption at baseline [14,15,43]. Sherf Dagan et al. conducted a cross-sectional study involving 100 BS candidates and reported a mean energy intake of 2710±1275.7 kcal/day, providing 114.2±48.5 g protein/day (respectively 1.0±0.4 g protein/kg body weight) (17%), 110.7±54.5 g fat/day (36%) of which 35.0±17.3 g saturated fatty acids/day, 321.6±176.1 g carbohydrates/day (47%) and 32.1±21.7 g fiber/day. Consumption levels of sweets and sugar-sweetened beverages, sodium, and processed meats exceeded the dietary recommendations, while intake of iron, calcium, folic acid, vitamin B_{12}, and vitamin B_1 did not meet the dietary reference intakes (DRI) requirements for 46%, 48%, 58%, 14%, and 34% of the study population. Food intake analysis showed that, regardless of calorie and macronutrient overload, most vitamin and mineral levels were below the recommended levels of consumption, suggesting a poor diet quality. However, despite the nutritional inadequacy of the diet, the authors did not report a high prevalence of nutritional deficiencies in baseline with one exception: 83% of the study population was vitamin D deficient. One possible explanation for this finding is that 59% of the study participants were taking oral supplements preoperatively. In fact, study participants using multivitamins/minerals were found to have improved levels of folic acid and vitamin B_{12}. Nevertheless, the authors did not evaluate neither adherence, nor the type or the duration of the oral supplement intake [14].

Preoperative weight loss is often recommended as a prerequisite before BS by many insurance companies in order to endorse weight loss behaviors, to achieve improved long-term outcomes, and to reduce the incidence of technical difficulties related to the bariatric procedure through decreasing visceral fat and liver size [23,44,45]. Hypocaloric diets prescribed to achieve weight loss generally provide insufficient micronutrients, including iron, zinc, calcium, potassium, magnesium, and certain B vitamins [35]. Thus, low-energy diets supplemented with micronutrients are more likely to meet the nutritional requirements of obese patients awaiting BS [31].

Other factors affecting nutritional status of patients seeking surgical weight loss treatment are related to other chronic diseases, medication (loop diuretics and metformin may deplete thiamine and mineral stores) [35] or chronic dieting [16].

Determinants of excess micronutrient levels in BS candidates

Few studies have reported hypervitaminosis in obese patients preparing to receive surgical treatment for weight loss. This might be the effect of excessive consumption of high doses of vitamin and mineral supplements due to either self-treatment with over-the-counter supplements, or to recommendations of health care professionals to optimize nutritional status in the perioperative period [13,16].

Prevalence and clinical significance of nutritional deficiencies

Various studies have documented the prevalence of micronutrient deficiencies among BS candidates and reported that these patients presented at least one vitamin or mineral baseline deficit [34,46]. Most common nutritional deficiencies documented in patients evaluated for BS are vitamin D, vitamin B_{12}, iron and folate (Table II). Other vitamins and minerals prevalence deficiencies are less reported.

Vitamin D

Vitamin D deficiency, measured as plasma 25(OH) D, the most prevalent nutritional deficiency encountered prior to BS, is of particular concern for bariatric patients. Up to 97.5% of BS candidates were reported to have vitamin D deficiency prior to surgery [18]. Besides poor diet and rapid preoperative weight loss, sequestration of vitamin D in adipose tissue could also explain its deficiency in patients receiving surgical treatment for obesity, as previously described [34,38,47]. However, some authors argue that rather dilution than entrapment of vitamin D in the expanded adipose tissue explains the low levels of this micronutrient in obesity [48]. Morbidly obese patients have increased body mass and therefore a higher volumetric dilution that lead to lower levels of circulating vitamin D in spite of relatively normal body stores [49]. Although its plasma levels could theoretically increase with weight loss, the amount of vitamin D released is not sufficient to compensate the preexisting deficiency. Hence, postoperative supplementation is recommended [34]. Another causes for hypovitaminosis D in obesity are the limited sun exposure due to decreased mobility and social stigma [48] and the use of sunscreen [16] given that cutaneously photoproduction of this micronutrient accounts for 90% of its replenishment [34]. Lastly, inhibition of 25(OH)D synthesis in the liver by negative feedback from elevated levels of $1,25(OH)_2D$ and parathyroid hormone might also be responsible for hypovitaminosis D in obese patients [48]. Low levels of vitamin D are related to significant clinical complications in BS candidates, such as impaired musculoskeletal health, secondary hyperparathyroidism, higher risk of infections or lesser weight loss after surgery [50].

Vitamin B_{12} (cobalamin)

Prevalence of vitamin B_{12} in morbidly obese population going to undertake BS ranges between 5.1-34.4% [17,18]. Vitamin B_{12}, ingested bound to proteins in food, is absorbed in the distal ileum after it separates from these complexes and binds itself to parietal cell secreted intrinsic factor (IF). Gastric acid plays a key role in releasing of cobalamin from protein complexes [51]. Cobalamin elaborate absorption process is affected by digestive disorders (malabsorption), medication (metformin, H_2 blockers, proton pump inhibitors etc) and changes in gastrointestinal pathways as results of BS. However, the liver stores vitamin B_{12} in a greater amount than that of any other B group vitamin. As such, cobalamin deficiency tipically takes years of insufficient intake to develop [34]. Clinical manifestations of B_{12} deficiency include megaloblastic anemia, peripheral neuropathy or neuro-psychiatric manifestations [51].

Iron

Iron and ferritin deficiency are the most common mineral deficiency among BS candidates, with studies reporting a 5.1-29.3% iron deficiency prevalence (low ferritin levels) in these subjects [19,21]. As stated before, iron status is altered in obese patients because of inflammation and increased levels of hepcidin, that impair luminal iron uptake and macrophage iron export [52]. Moreover, in obesity, hepcidin is expressed not only in the liver, but also in the adipose tissue both at protein and mRNA level. Studies showed that the expression of mRNA in the fat stores of obese patients is increased [53]. Hepcidin excess inhibits iron release into the plasma. Finally, cytokines synthetized by inflamed fat tissue (i.e. TNF-α, IL-6) stimulate hepcidin secretion which, in turn, sequestrates iron in spleen, liver or macrophages, lowering iron plasma levels. Iron deficiency anemia develops in morbidly obese patients as a result of this imbalance in iron homeostasis. Rodent studies showed that a high dietary fat intake alters iron absorption in a hepcidin-independent manner [52]. Symptoms of iron deficiency anemia may include fatigue, pallor, dry skin, brittle nails or hair, and loss of appetite [54].

Table II. Micronutrient deficiencies prevalence prior to BS.

Authors, year	n (total)	Vitamin D	Vitamin B_{12}	Iron (ferritin)	Folate
		Deficiency (%)			
Ben-Porat et al, 2019	872	75.2	8.5	5.1	28.8
Al-Mutawa et al, 2018	1538	75.6	16.4	28.2	0
Asghari et al, 2018	2008	53.6	34.4	7.7	not assessed
Lee et al, 2018	577	92.2	9.5	29.3	31
Krzizek et al, 2017	1732	97.5	5.1	9.6	63.2
Gillon et al, 2016	336	20.4	6.4	not assessed	8.8
Wang et al, 2016	211	80	4.7	1.9	32.2

Folate

Folate deficiency may develop in up to 63.2% of BS candidates [18]. Several studies reported an inverse association between folate serum concentration and BMI. An inverse association was also observed between folic acid status and plasma homocisteine (Hcy) levels. Hyperhomocisteinemia has emerged as a strong and independent risk factor for cardiovascular disease and is associated with endothelial disfunction. Dietary intake of folate is a major contributor to Hcy levels [55]. Along with poor diet quality [56], adiposity might also be responsible for folate deficiency. Impaired folate metabolism seen in obese patients may arise either due to the dilution effect, or due to variation in cellular folate uptake. The latter may be explained by the higher red blood cell (RBC) folate concentration observed in female patients with obesity compared to their normal weight counterparts. RBC folate is an indicator of folate tissue stores and its elevated levels suggest that adiposity does not affect dietary folate absorption but rather its distribution from circulation to tissue [57]. Hence, obesity is positively associated with RBC folate, in spite of lower dietary consumption and serum concentration of this micronutrient [58]. Folate deficiency has been linked to cardiovascular disease and development of some types of cancer. Also, in association with low vitamin B_{12} serum level, folate deficiency can cause megaloblastic anemia [20].

Prevalence and clinical significance of excessive micronutrient level

A few studies investigating the micronutrient status of BS candidates also reported hypervitaminoses [13,16]. Levels above normal range were found for multiple micronutrients, but vitamin B_6 and vitamin A hypervitaminoses were the most significant.

Vitamin B_6 (pyridoxine)

Vitamin B_6 hypervitaminosis was found in 20.9 % and respectively in 24.1% of patients seeking BS [13,16]. Van Rutte et al. (2014) observed that one year after BS the number of patients with excessive levels of vitamin B_6 doubled, most probably as a result of chronic nutritional supplementation [13]. Pyridoxine, the main B_6 vitamer, is used in most nutritional supplements [59]. Vitamin B_6 is an atypical vitamin because both deficiency and excess might lead to peripheral neuropathies [60]. Toxicity of B_6 vitamin is caused by ingestion of high-dose supplements [59], but research showed that long-term intake of daily doses as low as 200 mg might also lead to nerve damage [60]. None of the patients involved in the study conducted by van Rutte et al. was found to have toxic plasma levels of vitamin B_6 and also none of them experienced neurologic symptoms [13].

Vitamin A

Excess vitamin A was reported by van Rutte et al in more than 50% of study participants. Unlike water-soluble vitamins, vitamin A, a fat-soluble compound, tends to accumulate in the body tissues leading to toxicity [61]. Hypervitaminosis A affects many organ systems, causing nausea, headaches, vomiting, mental status change, anemia, hepatotoxia, osteoporosis, alopecia or hyperlipidemia. Also, a serious adverse effect of vitamin A excess is teratogenicity [13,16]. No signs of vitamin A toxicity was reported in the study cohort [13].

Conclusions

Nutritional status is one of the most important issues in the medical management of obese patients considering BS. Preoperative deficiencies are highly prevalent among BS candidates and represent the strongest predictors of postoperative deficits. Hence, screening for micronutrient deficiencies prior to surgery plays a crucial role in order to identify, correct, and prevent further deterioration of preexisting vitamins and minerals deficiencies after BS. Also, to prevent hypervitaminoses and to optimize BS outcomes, individualized preoperative nutritional supplementation and education of BS candidates focusing on healthier food choices should represent the main nutritional goals.

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