Nutritional Implications of Obesity: Before and After Bariatric Surgery

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Introduction

OBESITY IS DEFINED as the accumulation of excess body fat to the extent that it may have an adverse effect on health. Generally, the body mass index (BMI) is utilized to characterize further the degree of obesity, and it is calculated based on height and weight in kg/m². According to the definition established by the World Health Organization, individuals are classed as overweight if their BMI is ≥ 25 , whereas obese individuals are those with a BMI ≥ 30 . Based on the degree, obesity is further categorized into class I (BMI 30–34.9), class II (BMI 35–39.9), and class III (BMI ≥ 40). There is a linear correlation between incidence of chronic diseases and increased BMI.

Obesity is now recognized as a worldwide epidemic, and its incidence is increasing exponentially. According to the World Health Organization's projections from 2005, approximately 1.7 billion people are considered overweight, and at least 400 million adults are obese.¹ In the United States alone, nearly 33% of the population (97 million) are obese, and approximately 10 million people are morbidly obese (class III).^{1,2}

Although obesity has a multifactorial etiology, the most relevant causes can be grouped into environmental, genetics, and behavioral factors. In general, increased calorie consumption and decreased physical activity play a key role.

Contrary to common beliefs, the obese individual is not well nourished. The routine screening of obese patients prior to bariatric surgery has highlighted the multiple nutritional deficiencies of this patient population. The causes of this phenomenon are not entirely understood. It seems likely, though, that the excess caloric intake does not mean the overconsumption of fresh fruit, vegetables, and unprocessed foods, but rather the lack of consumption of these types of foods, exposing obese individuals to several micronutrient deficiencies.³

Therapeutic options for weight loss include dietary and behavioral modifications, increased physical activity, pharmacologic therapy, and, lastly, surgical intervention. Commonly, caloric restriction with behavioral modifications and physical activity lead to an average weight loss of only 5–10%.⁴ The addition of pharmacologic intervention can im-

prove the results to 15%. Unfortunately, none of these interventions leads to long-lasting results, and weight regain seems to be the norm.⁵

Surgery, on the other hand, has been proven to provide consistent and durable weight loss, as stated by the National Institute of Health Consensus Development Conference Panel.⁶ In addition, weight loss surgery is associated with resolution or improvement, to different degrees, of the comorbid conditions associated with obesity.⁷ Although highly effective in terms of weight loss and resolution of comorbidities, the different bariatric surgery procedures can contribute to nutritional derangements postoperatively. Certainly, the procedures that affect the physiologic absorption of nutrients have a higher tendency to determine deficiencies, but also the procedures that solely reduce the quantity of intake can affect individuals' long-term nutritional status. It is a prime responsibility of the bariatric surgery team to assess, educate, and follow the obese patient in order to avoid dangerous nutritional abnormalities.

Physiologic Absorption of Nutrients

Macronutrients

Macronutrients consist of three primary compounds that provide the bulk of energy in food and that are consumed in the largest quantity: proteins, lipids, and carbohydrates.

Proteins. Proteins are normally ingested in the form of complex polypeptides that, after a complex breakdown process facilitated by multiple enzymes, are eventually degraded to oligopeptides and individual amino acids. The majority of the protein absorption occurs in the duodenum and jejunum.⁸

Lipids. Lipids ingested are divided into free fatty acids, triglycerides, cholesterol, and phospholipids. Their metabolism requires the presence of bile salts in order to be emulsified, incorporated into micelles, and then transported into the enterocytes. From here, chylomicrons can then be transported into the lymphatic system. Under normal circumstances most of the absorption of lipids occurs within the jejunum, but any portion of the small intestine is capable of accomplishing this task.

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Carbohydrates. Finally, the carbohydrates are degraded in oligo- and monosaccharides, which are actively or passively transported across the enterocytes of the duodenum and proximal small intestine.

Micronutrients

Micronutrients are dietary substances that are only needed in very small quantities. Most micronutrients derive from a well-balanced diet, although some of them are produced directly by the host organism. Micronutrients comprise vitamins, minerals, and trace elements (Table 1).

Vitamins. Based on their characteristics, vitamins are either fat soluble or water soluble. Fat-soluble vitamins (A, D, E, and K) follow the absorption process of lipids, and as such, the presence of bile salts is necessary. In fact, they require the inclusion in micelles in order to diffuse across the enterocytes. Just like any other lipid, the primary location of absorption is the proximal jejunum, but the entire small intestine could take over the function if necessary.

The vitamin A group includes retinol, β -carotene, and carotenoids, and is mostly stored in the liver. Vitamin A is essential to the eye and immune systems, but it is also involved in the cellular proliferation process and in the protection against free radicals. So its deficiency might play a role in the development of certain chronic diseases. Vitamin A can also affect iron metabolism, including its absorption, transport, release, and utilization, and, if insufficient, contribute to the development of anemia. Zinc deficiency can

also affect vitamin A absorption, transport, and metabolism, since it is essential for the synthesis of retinol-binding protein (RBP) in both the liver and the plasma and the oxidation of retinol to retinal.^{9,10} Iron deficiency also compromises the function of the intestinal mucosa, affecting the absorption of several micronutrients, including vitamin A.⁹ So iron deficiency has to be corrected, when present, in order to normalize vitamin A levels.

Vitamin A is found naturally in liver, carrots, sweet potatoes, butter, spinach, cantaloupe melon, and eggs. The first manifestation of vitamin A deficiency is night blindness, which can evolve into destruction of the cornea (keratomalacia) and total blindness. Other manifestations of vitamin A deficiency include impaired immunity, hypokeratosis, squamous metaplasia of the bladder and respiratory tract epithelium, and enamel hypoplasia. Because of its fat-soluble nature, the excretion of vitamin A is slow, and this can lead to toxic accumulations. Whereas acute toxicity occurs at doses of 25,000 IU/kg of body weight, prolonged administration of much smaller doses (4,000 IU/kg) can lead to chronic toxicity. Manifestations of toxicity include nausea, jaundice, anorexia, vomiting, and blurry vision.

Vitamin D has received particular attention lately because of its implication in multiple vital functions. Although it is best known for the skeletal effects due to its prime role in calcium homeostasis, "non-skeletal" effects have been more recently described. In particular, vitamin D has been associated with insulin resistance, hypertension, and malignancy, and its deficiency has been linked to the progression of cardiovascular disease in diabetic patients.^{11,12} Natural sources

TABLE 1. SYNOPSIS OF MICRONUTRIENTS

	<i>Daily requirements</i>	<i>Max dose</i>	<i>Normal serum values</i>	<i>Deficit</i>	<i>Treatment</i>
<i>Lipid-soluble vitamins</i>					
Vitamin A	10,000 IU	> 15,000 IU		Dry skin, night blindness, pruritus	10,000 IU PO
Vitamin D	600 IU	4,000 IU/day	> 32 ng/mL	Osteoporosis and osteomalacia	50,000 IU QW $\times$ 6 weeks Then 1,000 IU/daily
Vitamin E	15 mg (33 IU of synthetic)	1,000 mg/day		Retinopathy, neurologic symptoms	
Vitamin K	120 μ g				
<i>Water-soluble vitamins</i>					
Vitamin B1 (thiamine)	1–2 mg				
Vitamin B2 (riboflavin)	1–3 mg				
Vitamin B3 (niacin)	Women: 14 mg/day Men 16 mg/day	35 mg/day		Pellagra	500 mg TID PO
Vitamin B6	1.7 mg				
Vitamin B12	2–4 μ g	N/A		Pernicious anemia	500 μ g/day/PO 500 μ g/week/N 1000 μ g/mo/IM
Vitamin C	90 mg	2 g			
Folate	400 μ g	1 mg/day	> 3 μ g/L		1–5 mg/daily
<i>Trace elements</i>					
Zinc	Women 8 mg/day men 11 mg/day				
Selenium	55 μ g	400 μ g/day			
Chromium	35 μ g	55 μ g			
Magnesium			1.8–2.4 mEq/L		
Copper	0.9 mg/day			Anemia, myelopathy	Copper gluconate 2 mg

of vitamin D are fatty fish species such as catfish and salmon, as well as eggs and liver. Typical manifestations of vitamin D deficiency in adults include the metabolic consequences of hypocalcemia, secondary hypoparathyroidism, osteoporosis, and osteomalacia.

Vitamin E consists of tocopherols and tocotrienols. It mainly functions as a cell antioxidant, and as such, it protects cell membranes from oxidation by reacting with lipid radicals produced in the lipid peroxidation chain reaction. Vitamin E can be found in high concentrations in avocado, eggs, milk, nuts, green leafy vegetables, and wholegrain foods. Vitamin E deficiency manifests with visual symptoms (retinopathy), neurologic symptoms (muscle weakness, ataxia), and hemolytic anemia.

Vitamin K includes the 2-methyl-1,4-naphthoquinone derivatives. It plays a key role in the regulation of blood coagulation through the formation of prothrombin (factor II); factors VII, IX, and X; protein C; and protein S. Other important functions of vitamin K include regulation of bone metabolism, in particular osteocalcin, and regulation of vascular biology. Normally, vitamin K is absorbed in the jejunum and ileum in the presence of bile and pancreatic juice. Although most of the daily requirements of vitamin K derive from intestinal flora biosynthesis, vitamin K is also found in green leafy vegetables, avocado, and kiwifruit. Its deficiency manifests clinically with bleeding disorders.

Water-soluble vitamins are absorbed by simple diffusion in the jejunum. The only exception is vitamin B12. In fact, after B12 has been hydrolyzed from food in the presence of acid in the stomach, the free B12 is bound to the glycoprotein R. It is after B12 is freed from the protein R that it can bind the intrinsic factor produced by the parietal cells of the stomach and then absorbed in the terminal ileum. Vitamin B complex consists of several water-soluble vitamins that play important roles in cell metabolism.

Vitamin B1 (thiamine) is a coenzyme involved in the catabolism of carbohydrates and amino acids, and thiamine-dependent enzymes are present in all cells of the body. It is present in cereal grains, legumes, and animal products (pork in particular), and absent in refined carbohydrates. Food preparation and alcohol ingestion can significantly alter the absorption of this vitamin. Certain stressors such as surgery, trauma, and pregnancy may increase thiamine requirements. Certain medications, such as diuretics, can further decrease the vitamin level by promoting its excretion. The common clinical manifestation of vitamin B1 deficiency is known as beriberi, which includes both neurologic and cardiovascular derangements. The two major forms of the adult disorder are dry beriberi and wet beriberi. The dry form is characterized by peripheral neuropathy affecting mostly the distal extremities and causing muscle tenderness. Wet beriberi is associated with signs and symptoms of congestive heart failure in addition to peripheral neuropathy.

Since the nervous system requires thiamine, its lack causes neurologic manifestations. These manifestations are typical of alcohol abuse individuals and include Wernicke's encephalopathy (WE; also known as Wernicke-Korsakoff syndrome) and Korsakoff's psychosis.

WE is the most frequent manifestation of thiamine deficiency in Western society. This is a neuropsychiatric disorder characterized by paralysis of eye movements, abnormal stance and gait, and markedly deranged mental function.

Korsakoff's psychosis is considered the late stage progression with deterioration of brain function of patients with WE. This is characterized by retrograde and anterograde amnesia and impairment of cognitive functions. Although some of the neurologic and cardiac impairments of thiamine deficiency can be reversed with vitamin supplementation, some of the more advanced manifestations of WE leave permanent damage. Since only a small percentage of thiamine is present in the blood, the diagnosis of thiamine deficiency can be confirmed by measurement of the erythrocyte transketolase activity, which is thiamine dependent.¹³

Vitamin B2 (riboflavin) is present in the coenzymes flavin adenine dinucleotide and flavin adenine mononucleotide, and is involved in many key metabolic pathways. Common sources of the vitamins are milk, cheese, green vegetables, liver, legumes, and tomatoes. Riboflavin deficiency manifests with cracked and red lips, inflammation of the lining of mouth and tongue, mouth ulcers, scaling skin, and iron-deficiency anemia.

Vitamin B3 (niacin or niacinamide, or vitamin PP) is involved in both DNA repair and the production of steroid hormones in the adrenal gland. Niacin is converted to nicotinamide and then to nicotinamide adenine dinucleotide, involved in catabolic reactions, and the corresponding phosphate form is involved in anabolic functions. It is naturally found in liver, chicken, beef, fish, cereal, peanuts, and legumes. Its deficiency causes the disease known as pellagra, which is characterized by diarrhea, dermatitis, and dementia, as well as thickening of the skin, inflammation of the mouth and tongue, malabsorption and diarrhea, delirium, and eventually death, if left untreated. Although niacin status is more accurately tested through urinary biomarkers, the diagnosis of deficiency is supported by low plasma levels.

Vitamin B9 (folic acid) is essential to numerous functions including nucleotide biosynthesis and homocysteine metabolism. Although folate is primarily absorbed in the proximal jejunum, the entire intestine is capable of performing this function. Leafy vegetables are the highest natural source of folate, but in order to decrease the potentially devastating consequences of its insufficiency, especially in pregnant women, many cereals and bread have this vitamin added. During pregnancy, the circulating levels of folate drop due to the production of red blood cells during the first trimester and the fetal demand during the latter part of pregnancy. Folate deficiency, in particular in the first few weeks of pregnancy, has been associated with congenital malformations including neural tube defects, congenital heart defects, cleft lip, limb defects, and urinary tract anomalies.¹⁴ Low levels of folate also increase the risk for cardiovascular diseases and malignancies, as well as causing anemia. In fact, folate and vitamin B12 deficiencies alter the metabolism of homocysteine, increasing its serum levels. Although there is evidence that an elevated homocysteine level is an independent risk factor for heart disease and stroke, it is controversial whether folate supplementation protects from cardiovascular accidents.¹⁵ The relationship between folate and cancer is complex. In fact, folate regulates the biosynthesis, repair, and methylation of DNA. As such, its deficit can induce and accelerate carcinogenesis, especially in the colon, rectum, breast, ovary, pancreas, brain, and lung.¹⁶

At the other extreme, an excessive intake of synthetic folic acid may accelerate the growth of precancerous lesions,

especially in the prostate, probably because of the increased availability of folate for the faster nucleotide synthesis of tumor cells.¹⁷ For now, the majority of human studies indicate that dietary folate is protective against colon cancer.¹⁶

Folate deficiency may also cause glossitis, diarrhea, depression, confusion, and megaloblastic anemia. Folate deficiency is diagnosed by a complete blood count and by measuring plasma vitamin B12 and folate levels. It is imperative to correct vitamin B12 deficiency, if present, in order to avoid worsening neurologic defects.

Vitamin B12 (cobalamin) plays a key role in DNA synthesis and regulation, and as such, it is involved in the metabolism of every cell of the body, particularly the nervous system, and hematopoiesis. It is also involved in fatty acid synthesis and energy production. Vitamin B12 is naturally found in fish, meat, poultry, eggs, and milk. The typical manifestation of vitamin B12 deficiency is known as Biermer's disease (pernicious anemia), and it is characterized by a triad of symptoms: megaloblastic anemia, gastrointestinal symptoms, and neurologic symptoms. The latter ones constitute the neurologic complex known as myelosis funicularis (impaired deep perception, persistent paresthesias, dorsal ataxia, decreased deep muscle-tendon reflexes, and pathologic reflexes). Since the enzymes methylmalonyl coenzyme A mutase and methionine synthase are vitamin B12 dependent, lack of the vitamin produces an increased serum level of their respective substrates methylmalonic acid and homocysteine. The increased serum level of methylmalonic acid and homocysteine are confirmatory tests of vitamin B12 deficiency.¹⁸

Vitamin C is an antioxidant and also a cofactor in several enzymatic reactions, including collagen synthesis. It has a positive effect on the immune system, and there is some evidence that it reduces the symptoms of, but does not protect from, the common cold. Since the human body cannot store vitamin C, its constant supply is necessary. The highest concentration of vitamin C is found in fruits and vegetables, but it is also present in some meats, especially liver. Its absorption is by active sodium-dependent transport and simple diffusion. Vitamin C deficiency leads to scurvy, which is characterized by brown skin lesions, spongy gums, and bleeding from all mucous membranes. If left untreated, it can evolve into open wounds, infections, and eventually death.

Minerals and trace elements. Minerals and trace elements are absorbed throughout the small intestine. A prime example is zinc. Zinc mostly functions as an antioxidant by producing the free radical scavengers metallothioneins. Zinc is also necessary for DNA synthesis and regulation; sexual maturation; wound healing; preservation of visual, olfactory, and taste acuity; and immunitary functions. Zinc has gained interest in the scientific community for its role in lipid metabolism and glucose uptake. In fact, it seems to regulate leptin secretion and promote free fatty acid release and glucose uptake.¹⁹ The latter function, in addition to the synthesis of insulin, may play a positive role in diabetes and in the management of metabolic syndrome.²⁰ Most of the dietary intake comes from meat and poultry. Its deficiency causes malabsorption, dermatitis enteropathica, chronic liver and renal disease, sickle cell disease, diabetes, anorexia, hair loss, and malignancy.

Selenium functions as an antioxidant by activating the glutathione peroxidase. Like any other antioxidants, selenium may play a role in the prevention of chronic disease and malignancies. Selenium is found in meat and bread, and its concentration in common foods depends on the content in the soil where the animals are fed. Its deficiency leads to cardiomyopathy and propensity to develop malignancies.²¹ The effects of selenium deficiency are more pronounced in the presence of vitamin E deficiency because of the increased oxidant stress. Selenium toxicity has been well described. It affects the immune system and produces neurologic derangements and gastrointestinal symptoms.

Iron-containing enzymes and proteins are involved in many biological oxidative reactions and in molecular transport. Dietary sources of iron include red meat, beans, poultry, fish, leafy vegetables, and fortified bread and cereals. Under normal circumstances, iron is released from food and reduced to the ferrous form by the low gastric pH. This process facilitates its absorption in the duodenum and proximal jejunum. Iron deficiency manifests with anemia, although a normal hemoglobin level does not rule out the presence of iron deficiency. Ferritin levels better assess the status of the body's iron reserves.

Chromium is involved in the metabolism of glucose and lipids. In fact, it is a cofactor for glucose uptake and improves insulin efficacy by an unclear mechanism.¹⁹ Theories include an increase in binding capabilities between insulin and target cells and an increase in the number of insulin receptors.²² Since chromium is only needed in small amounts, its deficiency has been rarely described, except in patients undergoing prolonged intravenous hyperalimentation.²³ In this patient population, chromium supplementation has been proven to revert neuropathy and glucose intolerance.²³ The deficit of chromium has been associated with impaired glucose tolerance and, consequently, increased risk of cardiovascular diseases, although a direct relationship has been questioned.²⁴ Furthermore, the diagnosis of chromium deficiency is difficult, since the plasma levels do not reflect the overall body stores, and paradoxically its serum levels tend to be higher in poorly controlled diabetic patients.²³ Chromium supplementation in the general population is controversial because of the unclear safety of some of the available forms. In fact, the supplement form chromium picolinate is the one with the highest bioavailability, but it has been associated with chromosome damage in certain animal cells.²⁵ For these and other potential adverse interactions of the supplements, the daily chromium requirements were lowered from 50–200 μg to 35 μg for an adult male and 25 μg for an adult female.

Magnesium is essential, along with calcium, for neuromuscular activities. Magnesium also works with phosphate as an essential component to basic nucleic acid metabolism. Many enzymes require the presence of magnesium as a cofactor, including the ones involved in the synthesis of nucleotides. The absorption of magnesium is facilitated by calcium absorption in the small bowel and by protein intake, with decreased magnesium absorption in the presence of low and high protein intake. Good alimentary sources of magnesium are nuts, cereals, and vegetables. Magnesium deficiency can derive from gastrointestinal (malabsorption, vomiting, alcohol abuse, inflammatory bowel diseases) or renal losses (renal tubular acidosis, diuretics), as well as

vitamin D deficiency. The deficiency has been associated with anorexia, asthma, diabetes, and osteoporosis. In advanced deficiency states, neuromuscular, psychiatric, and cardiac symptoms (tingling, cramps, hallucination, coronary spasms) prevail. Chronic magnesium deficiencies have been correlated with diabetes, cardiovascular diseases, hypertension, and obesity.²⁶ In fact, in hypomagnesemia, there is an increased concentration of thromboxane and increased angiotensin-related aldosterone synthesis, which in turn decreases insulin activity.²⁶ Besides the association of insulin resistance and hypomagnesemia, a diet high in fructose seems to contribute to hypomagnesemia and induce a chronic inflammatory state, endothelial activation, and oxidative stress.²⁷ In the presence of normal renal function, hypomagnesemia is rare.

Copper is found in several key enzymes, including cytochrome oxidase and superoxide dismutase. It also serves as an electron transporter. Copper is commonly bound to the plasma protein ceruloplasmin and transported to the liver where it is then excreted into the bile. The absorption of zinc and copper entails a competitive mechanism. The excess of one of the trace elements can result in the deficiency of the other. Copper is also involved in the uptake of iron, so its deficiency can cause anemia. Chronic copper depletion leads to abnormalities in metabolism of lipids, nonalcoholic steatohepatitis (NASH), poor melanin and dopamine synthesis, causing depression and sunburn, as well as neurologic abnormalities (myelopathy).²⁸ Chronic copper accumulation in individuals with genetic ceruloplasmin abnormalities leads to Wilson's disease (hepatolenticular degeneration with neurologic, psychiatric symptoms and liver disease).

Nutritional Deficiencies of the Obese Patient

Contrary to common belief, obesity does not translate into overnourishment. In fact, more evidence exists to support the presence of several, mostly subclinical, nutritional deficiencies in this category of patients.²⁹ The routine screening of prebariatric surgery patients, besides the usual presurgical work-up, includes testing the following levels: vitamin B12 and folate; homocysteine; methylmalonic acid; 25-hydroxyvitamin D (25OHD; the active form of vitamin D); calcium and intact parathyroid hormone (PTH); assessment of the iron status (ferritin, transferrin, total iron binding capacity, iron); vitamins A, D, E, K, B1, B6, and C; zinc; copper; and lipid panel. This comprehensive preoperative testing has led to the identification of specific deficiencies in obese patients, and in certain series, up to 96% of patients presented either insufficiency or deficiency of one or multiple vitamins. Flancbaum *et al.* in their retrospective analysis of 379 patients undergoing Roux-en-Y gastric bypass were able to identify vitamin D deficiency in 68%, iron deficiency in 44%, and thiamin deficiency in 29% of their patients.³⁰ Contrasting evidence on the relationship between 25OHD, PTH, and BMI exist. In fact, although some authors were able to demonstrate that the hyperparathyroidism found in morbidly obese individuals is mostly secondary to vitamin D deficiency, others have suggested that excess PTH production can determine weight gain by promoting lipogenesis.^{31,32} Remarkably, even widely available vitamins, such as vitamin C, have been found to be deficient in more than 50% of tested individuals.³³

The reason for these abnormalities, although not entirely understood, seems to be multifactorial. First, the excessive consumption of calories does not translate to consumption of healthy and nutritious foods (fruits and vegetable, lean proteins, etc.). Conversely, most overconsumption is geared toward so called "empty calories," highly processed, dense nutrients, mostly from complex sugars, which contain nearly zero nutritional value.³⁴ In fact, it is known that up to 30% of the daily caloric intake of U.S. adults derives from low-nutrient foods with a high percentage of artificially sweetened ones.³⁵ The same behavioral and cultural push toward the lack of consumption of healthier foods is translated into a preference for high-calorie drinks instead of milk and derivatives, affecting the overall intake of calcium and vitamin D.³⁶ It is known that physiologically the excess of adipose tissue affects the circulating availability of lipid soluble vitamins (such as vitamin D).³⁷ Furthermore, the lack of physical activity leads to mostly indoor activities, limiting sun exposure, depriving the individual of another important source of vitamin D.³⁸ In fact, the production of 25OHD by UVB exposure is a critical source of vitamin D in the obese population.³¹ It has been found that obese patients living at latitude higher than 40°N are at risk for vitamin D deficiency.³⁹

Anemia is also very common in obese patients, especially women. Iron deficiency either from nutritional sources or chronic loss, such as in obese patients with heavy irregular menses from hormonal imbalance, is the most common recognizable cause.

The morbidly obese patient, as previously stated, tends to have a diet rich in complex carbohydrate, which increases the need for vitamin B1 (thiamine).⁴⁰ Preoperative deficiencies of this vitamin have been reported to be as high as 29% in certain series, and it is higher in African American and Hispanic patients.³⁰

The alteration of micronutrients in obese patients, such as vitamin A, can have end-organ consequences. This is the case for nonalcoholic steatohepatitis (NASH), which can progress from steatosis to steatohepatitis, fibrosis, and cirrhosis.⁴¹ This condition is linked to insulin resistance and oxidative stress, and it is the cause of further worsening of vitamin A metabolism with decreased storage and transport of the vitamin and its metabolites. This, in turn, weakens the protection from oxygen free radicals, promoting further progression of liver damage with production of collagen, fibrosis, and progression to cirrhosis.⁴²

The incidence of folate deficiency in the obese population is relatively low (2–6%). This is probably explained by the widespread presence of added folate in commonly used grains (cereals, bread, and pasta). Actually, some authors have suggested a protective effect of folate against obesity by increasing lipolysis in adipocytes.

Zinc levels have been reported to be deficient in 28% of obese individuals.⁴³ Hypocaloric diets tend to increase circulating doses of zinc in obese individuals. Zinc concentration is inversely related to BMI.⁴⁴ Some studies have found zinc deficiencies up to 71% in individuals undergoing bariatric surgery. Similarly, selenium deficiency up to 58% has been described in obese adults prior to bariatric surgery.⁴⁵

Overview of Bariatric Procedures

Weight loss procedures are based on three different mechanisms of action: restrictive, malabsorptive, and a

combination of both. In the restrictive procedures, the volume of the stomach is drastically reduced in order to accommodate only small portions of food at any given time. Within this category, the vertical banded gastroplasty (VBG), laparoscopic adjustable gastric banding (LAGB), and sleeve gastrectomy (LSG) are the most popular. The adjustable gastric band consists of a silicone ring placed just below the gastroesophageal junction. The inner diameter of the ring can be reduced by injecting saline in the subcutaneous reservoir connected to the ring by tubing similar to the one of a chemotherapy port. The purpose is to create a mini pouch of stomach that can accommodate small amounts of food and induce early satiety. The pouch will then slowly empty in the rest of the stomach. The sleeve gastrectomy consists of removal of 70–80% of the stomach along the longitudinal axis, leaving a longitudinal “sleeve” of stomach based on the lesser curvature. Initially, this procedure was described as a first-stage operation for high-risk patients prior to more definitive malabsorptive procedures such as the biliopancreatic diversion (BPD) and duodenal switch (DS). Over time, the need for a second-stage malabsorptive procedure was found necessary only in very few cases, so the sleeve rose to the level of a primary operation. Besides the obvious mechanical advantage of a much smaller stomach (300 cc or less), the advantages of the sleeve gastrectomy may involve neurohormonal changes that decrease appetite and normalization of serum glucose. In each of the restrictive procedures, the absorption of nutrients occurs via the normal anatomy, since there is no discontinuity of the gastrointestinal tract. In the malabsorptive procedures, a variable part of the ingested food is not absorbed. The latter mechanism, although very effective for weight loss, can potentially lead to intractable diarrhea, electrolyte disturbances, nutritional and vitamin deficiencies, and long-term metabolic derangements with hepatic and renal failures. For this reason, the purely malabsorptive procedures, such as jejunoileal and jejunocolonic bypass, are no longer performed.

Currently, the procedures that combine restriction and a lesser degree of malabsorption are commonly utilized (i.e., gastric bypass [GBP] and BPD with or without DS [BPD ± DS]). The combined procedures tend to give better weight-loss results than the purely restrictive procedures, and are also associated with neurohormonal changes that facilitate the resolution of specific comorbid conditions, such as diabetes.⁴⁶ The most popular of the combined procedures is the GBP. This procedure consists of creating a 15–20 cc pouch from the stomach and bypassing a variable length of jejunum, creating two separate pathways: one for the biliopancreatic secretions and one for the nutrients. BPD and DS combine a similar degree of restriction with more significant malabsorption, which can intensify weight loss, but also predisposes the patient to higher nutritional deficiencies postoperatively.

Supplementation After Bariatric Surgery

One of the key elements for the success of bariatric surgery procedures is regular and long-term follow-up. Regardless of the procedure performed, the bariatric patient is instructed to follow up at least on a yearly basis with a comprehensive battery of blood work aimed at detecting micronutrient and macronutrient abnormalities.

Although there are no uniform dietary guidelines after bariatric surgery, the general consensus is to increase food consistency gradually over a period of 1 to 2 months.⁴⁷ Allowing for minor variations, the progression of food is similar for the different procedures. After a trial of clear liquids in the hospital, patients are advanced to full liquids for the next 2 weeks, then a soft diet for 3 weeks, and finally a regular diet at week 7. The purpose of this meal plan is not only to promote weight loss, but also to prevent nutritional deficiencies. In order to maintain a healthy balanced diet, the postbariatric surgery diet entails the consumption of 60–80 g of proteins per day, less than 30–40 g of fat per day with spare consumption of saturated fat, and 100–120 g of carbohydrates per day. Our typical supplementation recommendation is outlined in Table 2. These regimens can vary according to the laboratory results.

Malabsorptive procedures alter the absorption of vitamin B12 by reducing gastric acid (parietal cells) and pepsin (chief cells) production that alters the release of vitamin B12 from foods and also by the decreased availability of intrinsic factor (parietal cells), which will ultimately reduce the receptor-specific absorption. Of the restrictive procedure, the sleeve gastrectomy can alter vitamin B12 availability by reducing the parietal cell mass secondary to the removal of the greater curvature, with resulting decreased intrinsic factor, and acid content that is essential to deconjugate oral cyanocobalamin from food. As a consequence, vitamin B12 supplementation is essential after bariatric surgery. In fact, vitamin B12 deficiency has been well described after bariatric surgery.⁴⁸ The alternatives include oral supplementation with 500 µg/day, sublingual 500 µg/day, intranasal 500 µg/weekly, or intramuscular 1,000 µg/monthly.

Calcium is normally absorbed by the duodenum and proximal jejunum with the intermediation of vitamin D. After significant acid reduction secondary to the exclusion or resection of most of the stomach, the more readily absorbed form of calcium is citrate. The metabolism of calcium is affected not only by decreased solubility in the absence of acid, but also by decreased absorption due to the relative vitamin D deficiency or insufficiency commonly encountered in the postbariatric surgery population. In order to reduce the risk of osteoporosis 1,200–1,500 mg of additional calcium is necessary. It is important to remember how serum calcium levels are inaccurate to monitor the calcium–vitamin D metabolism. In fact, serum calcium levels are often kept to a normal range due to the increase in parathyroid levels with secondary hyperparathyroidism. Thus, it is important to monitor both calcemia and calciuria, which maintain calcium homeostasis, total 25OHD levels, as a marker of vitamin D

TABLE 2. TYPICAL DIETARY SUPPLEMENTS AFTER BARIATRIC SURGERY

Morning	Evening
Multivitamin × 1	Multivitamin × 1
Calcium 600 mg + Vit D × 1	Calcium 600 mg + Vit D × 1
Vitamin B12 500 µg	Vitamin D 2,000 IU
	<i>If needed based on lab values:</i>
	Ferrous sulfate 325 mg
	Vitamin C 500 mg

deficiency, and serum alkaline phosphatase, as a marker of bone reabsorption.⁴⁹ Again, due to the relative achloridia after gastric bypass, calcium citrate is more readily absorbed, and it is the preferred supplemental calcium form over carbonate in this patient population. In addition to the small amount of vitamin D already present in the calcium supplements (usually only 200 IU), additional vitamin D is mandatory. The dose of vitamin D varies according to the laboratory results (Table 3). The serum level of 25OHD increases by 1 ng/mL for every 100 IU of cholecalciferol in normal-weight individuals. In general, the maintenance dose is 2,000 IU per day of vitamin D3. Several reports have suggested the greater efficacy of cholecalciferol compared to ergocalciferol (vitamin D2). This has been indirectly confirmed by additional studies where, in order to achieve a similar reduction in PTH levels, it was found necessary to give a dose of ergocalciferol six times larger.³¹ Also, it appeared that the suppressive effect of cholecalciferol on PTH were greater than ergocalciferol.

Although there is a relative achlorhydric state in the gastric pouch and exclusion of the duodenum following a gastric bypass, the need for additional iron supplementation is not routinely indicated except in the presence of iron deficiency anemia or normal hemoglobin states with low ferritin levels.⁵⁰ In general, iron sulfate preparations are better absorbed than their ferric counterparts. The standard dose should have 65 mg of elemental iron and should not be taken in conjunction with calcium supplementation, antacids, and caffeine. It is also important to note that anemia after bariatric surgery might not be corrected by supplementation of vitamin B12 or iron, and it is manifested by normocytic anemia with increased red cell distribution width. In these cases, the anemia can be due to vitamin A, E, folate, zinc, and copper deficiencies.

Additional vitamin supplements might be necessary based on laboratory values, and are indicated in Table 4.

Folic acid deficiency is less common after gastric bypass surgery because of its ubiquitous absorption along the entire small bowel and its presence in many common fortified nutrients. Nevertheless, folate deficiency has been described after weight-loss surgery, and it is indicative either of severe decreased dietary intake or an associated malabsorptive condition such as celiac sprue.⁵⁰ On the contrary, high serum levels of folate are a very specific, although not sensitive, marker of intestinal bacterial overgrowth.

Although zinc deficiency has been well described in obese individuals, as mentioned above, its incidence after bariatric surgery has not been well investigated. Some reports described asymptomatic zinc deficiencies in the postoperative period in up to 51% of patients.⁴³ Dermatologic manifestations of zinc deficiency have been reported in noncompliant patients after more malabsorptive procedures such as distal

TABLE 4. ADDITIONAL VITAMIN SUPPLEMENTATION

Supplement	Initial dose	Maintenance dose
Vitamin A	8,000 IU BID $\times$ 2 weeks	8,000 IU QD for life
Folic acid	800 μ g in AM, 400 μ g in PM for 4 months	
Thiamine (B1)	100 mg QD	
Vitamin C	500 mg BID	

QD, once a day; BID, twice a day.

gastric bypass and BPD. Furthermore, zinc deficiency can determine vitamin A deficiency by decreasing the synthesis of retinol-binding proteins, reducing the lymphatic absorption of retinol and altering the action of zinc-dependent enzymes essential in vitamin A metabolism (retinol dehydrogenase).⁹ Few but sometimes serious cases of hypovitaminosis A have been described after bariatric surgery, particularly BPD.⁹

As previously noted, copper and zinc compete for the same transport mechanism, so the excess of one might determine the deficiency of the other. Also, the liquid form of vitamins might be deficient in copper.⁵⁰ Copper deficiency has been described after RYGB, and it manifests itself with hematologic and neurologic deficit, as previously described.⁴²

Vitamin B1 (thiamin) deficiency has been reported after bariatric surgery, in particular after gastric bypass, but also after purely restrictive procedures.⁵¹ The two mechanisms involved are the decrease acidification of food and the frequent postoperative vomiting. Although most of the cases of thiamin deficiency are asymptomatic, overt WE has been well described after bariatric surgery. Lakhani *et al.* described a form of thiamine deficiency not correctable by oral supplementation in post Roux-en-Y gastric bypass patients.⁵² Bacteria overgrowth in the small intestine is responsible for the latter form of beriberi, and the diagnosis is supported by an increase of serum folate or an increase of breath hydrogen after oral glucose administration. This form of "bariatric beriberi" is corrected by intramuscular vitamin supplementation concomitantly with antibiotic therapy to counteract the bacterial overgrowth.

Although both vitamin B2 and B6 deficiencies after bariatric surgery have been described, it is unclear if the deficiency predated the surgical intervention. Vitamin B3 (niacin) deficiency is not regularly reported after bariatric surgery. Vitamin C deficiency has been reported after bariatric surgery in up to 35% of patients following GBP.⁵¹

Conclusion

Nutritional deficiencies are common in obese individuals. The abundance of highly caloric processed nutrients, along with the lack of fresh unprocessed food and outdoor exposure, contribute to this phenomenon. Additionally, certain hypovitaminosis can promote obesity. Bariatric surgery predisposes individuals to potential macro- and micronutrient deficiencies, worsening a likely preoperative deficit. Astute follow-up and monitoring is therefore essential for promptly diagnosing and treating these deficiencies. Monitoring and nutritional supplementation should be a lifelong process.

TABLE 3. VITAMIN D SUPPLEMENTATION

Definition	Serum level	Treatment
Deficiency	< 15 ng/mL	D2 50,000 IU 3 $\times$ /week for 6 weeks
Insufficiency	16–29 ng/mL	D2 50,000 IU 2 $\times$ /week for 6 weeks
Normal (goal)	> 32 ng/mL	D3 2,000 IU/daily

Levels refer to 25 OH vitamin D.

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