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Origins of and Recognition of Micronutrient Deficiencies After Gastric Bypass Surgery

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Abstract Roux-en-Y gastric bypass surgery remains the major surgical option for individuals with medically complicated obesity. The importance of preoperative evaluation to permit identification of micronutrient deficiencies is being re-evaluated. The risk of complications related to pregnancy after gastric bypass supports careful follow-up. Micronutrient deficiencies are common in postoperative gastric bypass patients, despite the suggested use of routine vitamin and mineral supplements after surgery. Copper deficiency must be considered as an origin for visual disorders after gastric bypass. Vitamin D deficiency with metabolic bone disease remains common after gastric bypass and the results suggest that the present postoperative supplements of calcium and vitamin D are inadequate. Major nutritional complications of bariatric surgery are occurring more than 20 years after surgery. There is no evidence for intestinal adaptation as there remains decreased intestinal absorption of iron up to 18 months after gastric bypass surgery. This article supports ongoing examination of nutritional complications after gastric bypass surgery and supports the notion that the daily doses of micronutrient supplements, such as vitamin D, may need to be revised.

Keywords Gastric bypass surgery · Bariatric surgery · Obesity · Micronutrient · Vitamin A · Vitamin D · Iron · Thiamine · Copper · Anemia

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Introduction

A new study published this year demonstrates that the prevalence of obesity in the United States continues to rise with findings of obesity in 35.5% of adult women and 32.2% of adult men [1]. Because there is either poor weight loss or poor maintenance of weight loss resulting from dietary and activity programs, obesity surgery (or bariatric surgery) remains the major treatment option for patients with medically complicated obesity. In the United States and Canada, 220,000 bariatric surgical procedures are now performed each year [2]. Among the surgical approaches for medically complicated obesity, the "divided" or "disconnected" Roux-en-Y gastric bypass (RYGB) in the United States and Canada remains the most commonly performed bariatric surgical procedure. RYGB is still considered the "gold standard" in this surgical field in North America.

One of the most frequent medical complications of obesity is development of diabetes mellitus. A recent study of administrative claims data has shown a decline in overall health costs in patients with type 2 diabetes mellitus who have undergone bariatric surgery [3].

RYGB can be performed either laparoscopically or by an open laparotomy. As shown in Fig. 1, this procedure involves complete division of the native stomach. The resulting gastric pouch optimally provides a volume that is

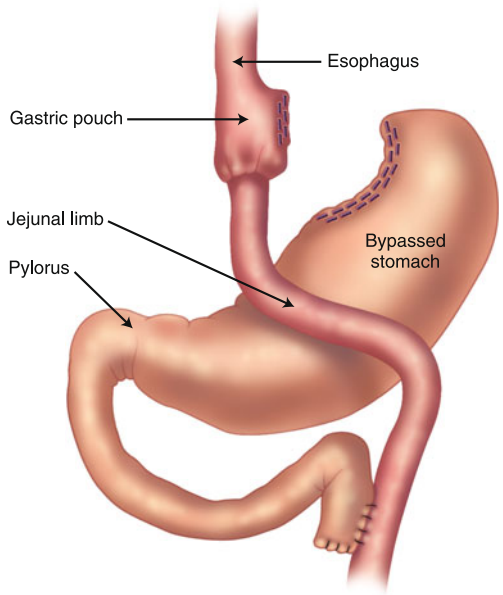

Fig. 1 Roux-en-Y gastric bypass surgery is depicted in this adapted diagram. The orientation of the gastrojejunal anastomosis may be different depending upon whether an open or laparoscopic technique is used during the surgery. The location of the jejunojejunal anastomosis varies and is dependent upon the length of the common channel, which is constructed by the surgeon. (*Adapted from* Lakhani et al. [12])

less than 1 oz, or 30 mL. The surgeon then divides the jejunum 30 to 70 cm distal to the duodenojejunal junction. The site and orientation of the gastrojejunal anastomosis is influenced by the utilization of an open versus laparoscopic surgery. The location of the jejunojejunal anastomosis determines the length of both the Roux limb as well as the length of the common channel that extends from the second anastomosis to the ileocecal valve. If the common channel is less than 120 cm in length, a more severe malabsorptive condition occurs. Therefore, an understanding of the anatomy of the RYGB is required for a clinician to ascertain the nutritional risk for each individual patient.

Origins of Micronutrient Deficiencies

Preoperative Deficiency

Reports of postoperative, catastrophic medical conditions after RYGB raise the question as to whether preoperative micronutrient deficiencies are the basis for these unfortunate postoperative disorders. Dietary supplements that are commonly used by morbidly obese individuals could be one origin for development of a micronutrient deficiency [4].

This concern has been examined by multiple investigators in the past year. In a study of preoperative obese patients from Israel, a large percentage of patients were found to have micronutrient deficiencies [5]. Common micronutrient deficiencies included iron (35%), folic acid (24%), and vitamin B_{12} (3.6%), with high levels of parathyroid hormone in 39% of patients. The high percentage of patients with low folic acid and body mass index greater than 50 kg/m^2 is evidence against the presence of small intestinal bacterial overgrowth in super-obese patients. In a similar preoperative study from Switzerland, 57% of morbidly obese individuals had a micronutrient deficiency, most commonly vitamin D deficiency [6]. The result supports the real concern that prevention of osteoporosis must begin prior to bariatric surgery. A third study from Boston demonstrated that subcutaneous and visceral adipose tissue does contain high concentrations of fat-soluble micronutrients, and in this work vitamin K was studied [7]. However, the authors noted that there was a lowered utilization of vitamin K by the liver.

In a fourth study from Rio de Janeiro, a high prevalence of vitamin A deficiency in obese, preoperative patients was described [8]. The authors found that daily, oral supplementation with 5,000 IU of retinol acetate (ester derivative of vitamin A) did not fully replete vitamin A deficiency at 6 months after RYGB surgery.

These results support the notion that a standardized preoperative evaluation should include examination of specific micronutrients that are commonly identified as origins for nutritional deficiencies after RYGB.

Pregnancy

The obstetric literature suggests that pregnancy and delivery in women who have undergone RYGB appears to be low risk for both mother and child. A recent report describes five babies with intracranial hemorrhage whose mothers had undergone bariatric surgery [9•]. The report suggests the potential for vitamin K deficiency and the authors note that careful nutritional follow-up is required in women who have undergone bariatric surgery and subsequently become pregnant. This report is of great interest because vitamin K deficiency is unusual after RYGB. This report reminds us that if a physician decides to treat a pregnant woman who has undergone RYGB with an antibiotic, careful follow-up of the patient's prothrombin time is important.

At this time, there are mainly anecdotal reports of adverse results from pregnancy in women who have undergone RYGB. We have been concerned about the potential risk of thiamine deficiency to the mother and fetus. Because the determination of specific micronutrient deficiencies is not a standardized field, further work is needed to examine the potential for adverse outcomes such as fetal loss in women who have undergone RYGB.

Roux-en-Y Gastric Bypass

Several new studies have examined micronutrient deficiencies after RYGB. In a study from Brazil, RYGB patients had deficiencies of magnesium (32.1%), iron (29.8%), zinc (40.5%), vitamin B_{12} (61.8%), vitamin D_3 (60.5%), and beta-carotene (56.8%) [10]. In a study from Australia, RYGB patients at 1-year follow-up were noted to have deficiencies of ferritin (15%), vitamin B_{12} (11%), red blood cell folate (12%), and vitamin D [11]. These studies underscore the concern that our present recommendations for postoperative nutritional supplements may not prevent development of nutritional deficiencies. This may in part be related to consumption of micronutrients by small intestinal bacterial overgrowth associated with RYGB [12].

There is a report from London suggesting that hemodialysis may increase the risk of copper deficiency in patients who have undergone RYGB [13]. The authors report a patient after RYGB who developed symptoms of cerebellar, spinal cord, and peripheral nerve disease (Table 1). This report suggests that RYGB patients undergoing hemodialysis may require more careful monitoring for the development of micronutrient deficiency.

In addition to the development of specific medical disorders (Table 1), malabsorption of micronutrients or macronutrients after RYGB may lead to consideration of further surgery [14]. In a study from a tertiary care center in Greece, in 27% of patients undergoing revisional bariatric surgery, the major indication for reoperation was severe nutritional complication [14]. It is presently unclear whether currently suggested postoperative management programs reduce the rate of reoperation of patients after RYGB.

Medical Conditions Induced by Micronutrient Deficiencies

Visual Symptoms

As shown in Table 1, patients with complaints of visual symptoms should lead to consideration of blood testing of vitamin A, vitamin E, and whole-blood thiamine. In a recent report, a patient developed bilateral blindness due to optic neuropathy 22 years after RYGB [15•]. Copper deficiency was identified and unfortunately copper infusion therapy was not beneficial to the patient. This report confirms the importance of long-term follow-up (perhaps once yearly) of patients after RYGB. This case report also raises the potential that oral copper may not be well absorbed by the jejunum after RYGB [16]. Due to the coabsorption of zinc and copper, there is the potential that daily zinc supplementation could induce copper deficiency.

There has been a report from Chicago of a patient developing fundal white spots after RYGB [17]. The patient had both acquired night blindness and vitamin A deficiency. Visual acuity was reported to be improved after 2 months of oral vitamin A supplementation.

Metabolic Bone Disease

Due to the high frequency and serious nature of metabolic bone disease after RYGB, additional studies have been designed to add to our understanding of this area. Investigators from Detroit have reported cases of bone biopsy-proven osteomalacia with marrow fibrosis after gastric bypass surgery [18•]. In this group of five patients, symptoms had been present for 2 to 5 years. The authors reported significant improvement in the patients' clinical symptoms, functional status, biochemical indices, and bone mineral density after treatment with a combination of ergocalciferol (100,000 IU daily) and calcium carbonate (1 to 2.5 g daily). In examining this study, due to the presence of upper gut achlorhydria after RYGB, absorption of calcium carbonate is greatly decreased and so the use of an alternative calcium supplement would be preferable.

A recent study of postmenopausal women after RYGB revealed a high prevalence of bone resorption and hyperparathyroidism [19], independent of intake of calcium and vitamin D status. This work confirms clinical concerns that the present recommendations [20] for daily calcium (1,200–2,000 mg daily) and vitamin D (800–1,600 U daily) supplementation are unlikely to be protective, especially regarding female patients after RYGB. An additional study from Royal Oak, Michigan, supported the findings that postoperative hyperparathyroidism was independent of vitamin D levels in RYGB patients [21•]. An interesting finding

Table 1 Confirmation of micronutrient deficiencies after Roux-en-Y gastric bypass surgery

Medical problem	Blood tests	New blood tests
Visual symptoms	Vitamin A; vitamin E; whole-blood thiamine	Copper [13]
Neurologic disorders	Vitamin B_{12}; whole-blood thiamine; then vitamin E; copper; plasma niacin	
Anemia	Ferritin; vitamin B_{12}; folate; then vitamin A; vitamin E; zinc; copper	
Skin disorders	Vitamin A; zinc; plasma niacin	
Edema	Selenium; plasma niacin; whole-blood thiamine	

of this study was that 86% of these RYGB patients had preoperative vitamin D deficiency (or insufficiency), whereas at the 1-year postoperative follow-up, 70% of patients still had evidence for inadequate blood levels of vitamin D. This disturbing result raises the question about the difficulty in repleting vitamin D stores after RYGB. It likely supports the concern of other authors that current postoperative vitamin D supplementation is inadequate [18•].

In addition to the report above of a patient presenting with a major complication due to copper deficiency 22 years after gastric bypass [15•], there has been a report from Taiwan of a patient presenting with severe osteomalacia (initially thought to be consistent with bony metastases) 20 years after jejunoileal bypass surgery [22]. This report supports a goal of continuation of long-term nutritional evaluation and management of patients after bariatric surgery.

Iron Malabsorption

As shown in Table 1, patients with anemia should initially undergo blood testing to look for a potential deficiency of ferritin or iron, vitamin B_{12}, and/or folic acid. Especially in premenopausal women, parenteral iron infusions may be required for correction of iron deficiency anemia after RYGB.

A recent study of RYGB patients from Chile confirms that iron absorption is markedly reduced after surgery [23]. Of interest, repeating the iron studies at 18 months after RYGB surgery demonstrated no increase in iron absorption. In interpreting these results, this study revealed no evidence for intestinal adaptation at 18 months after RYGB surgery.

A study from New York confirmed that anemia is common after RYGB surgery (identified in 10.2% of patients) and that iron deficiency is the common origin for anemia [24]. Anemia was associated with the presence of menstruation and peptic ulcer disease. It was not clear that routine iron supplementation prevented the development of anemia. We do suggest preoperative testing for *Helicobacter pylori* and eradication therapy, if indicated, for those obese patients who live in high-risk areas for this gastric infection [25].

Additional micronutrient deficiencies are associated with the development of anemia. Further testing in RYGB patients with anemia could include determination of blood vitamin A, vitamin E, zinc, and copper (Table 1).

Thiamine Deficiency

The signs and symptoms of thiamine deficiency after RYGB are summarized in Table 2. Thiamine deficiency remains an important short-term as well as long-term complication after RYGB. Anecdotal evidence supports preoperative thiamine deficiency as a potential origin for rapid development of complications of thiamine deficiency after RYGB. Long-term complications of thiamine deficiency may be related to postoperative small intestinal bacterial overgrowth [12].

Reports of difficulty in diagnosing thiamine deficiency after RYGB persist in the literature. In a recent report from France, difficulty in the diagnosis of Wernicke's encephalopathy 10 months after RYGB was reported [26]. The authors in this report provided no insight into the reasons why progression of thiamine deficiency to Wernicke's encephalopathy is rare in patients who have undergone RYGB.

Allied reports of thiamine deficiency are important for patients who have undergone RYGB. After stabilization of postoperative weight loss, many patients consider undergoing panniculectomy for removal of excess skin, especially in the abdominal region. In a report from Los Angeles, a gastric bypass patient undergoing this surgical procedure by plastic surgery developed symptoms of Wernicke's encephalopathy [27]. This report supports the importance of excluding or treating micronutrient deficiencies in RYGB patients who are considering additional surgical procedures.

Another report of Wernicke's syndrome from Italy describes the potential risk of developing thiamine deficiency while receiving parenteral nutrition [28•]. This is one of the reasons that we advise utilization of enteral feedings (which can be delivered into the native stomach through a gastrostomy tube) if possible in those RYGB patients who require treatment of macronutrient malnutrition [25]. Of interest, a study from Greece supported improved recovery from Wernicke's syndrome by using high-dose oral thiamine (600 mg/day) and intramuscular thiamine (300 mg/day) for 2 months [29•]. This report suggests that the doses of thiamine used for treatment of acute Wernicke's syndrome may be insufficient for maximizing the likelihood of complete recovery from thiamine deficiency.

Table 2 Clinical features of thiamine deficiency

Beriberi subtypes	Symptoms and findings
Neuropsychiatric	Hallucinations; aggressive behavior; confusion; nystagmus; ataxia; ophthalmoplegia
Neurologic (Dry beriberi)	Numbness; muscle weakness and pain of lower > upper extremities; convulsions; exaggerated tendon reflexes
High output cardiac (Wet beriberi)	Tachycardia; respiratory distress; leg edema; right ventricular dilation; L-lactic acidosis
Gastroenterologic	Nausea; vomiting; slow gastric emptying; megajejunum; constipation; megacolon

Conclusions

The prevalence of obesity in the United States is 33.8% and RYGB surgery remains the major surgical option for individuals with medically complicated obesity. Micronutrient deficiencies are common in preoperative evaluation of morbidly obese individuals and remain common in postoperative gastric bypass patients, despite the suggested use of vitamin and mineral supplements after this surgery. Vitamin D deficiency with metabolic bone disease remains a major problem after gastric bypass and the results suggest that the present postoperative supplements of calcium and vitamin D are inadequate. Major nutritional complications of bariatric surgery are occurring more than 20 years after surgery. This present report supports ongoing examination of nutritional complications after gastric bypass surgery. Examination of published studies supports the notion that the daily doses of supplementation of specific micronutrients, such as vitamin D, may need to be revised.

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