Neurologic Complications Following Obesity Surgery

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Course Description
Bariatric surgical procedures are increasingly common. In this review, we characterize the neurologic complications of such procedures, including their mechanisms, frequency, and prognosis. Literature review yielded 50 case reports of 96 patients with neurologic symptoms after bariatric procedures. The most common presentations were peripheral neuropathy in 60 (62%) and encephalopathy in 30 (31%). Among the 60 patients with peripheral neuropathy, 40 (67%) had a polyneuropathy and 18 (30%) had mononeuropathies, which included 17 (94%) with meralgia paresthetica and 1 with foot drop. Neurologic emergencies including Wernicke’s encephalopathy, rhabdomyolysis, and Guillain-Barré syndrome were also reported. In 18 surgical series reported between 1976 and 2004, 133 of 9996 patients (1.3%) were recognized to have neurologic complications (range: 0.08-16%). The only prospective study reported a neurologic complication rate of 4.6%, and a controlled retrospective study identified 16% of patients with peripheral neuropathy. There is evidence to suggest a role for inflammation or an immunologic mechanism in neuropathy after gastric bypass. Micronutrient deficiencies following gastric bypass were evaluated in 957 patients in 8 reports. A total of 236 (25%) had vitamin B12 deficiency and 11 (1%) had thiamine deficiency. Routine monitoring of micronutrient levels and prompt recognition of neurological complications can reduce morbidity associated with these procedures.

Intended Audience
This course is intended for Neurologists, Psychiatrists, and others who practice neuromuscular, musculoskeletal, and electrodiagnostic medicine with the intent to improve the quality of medical care to patients with muscle and nerve disorders.

Learning Objectives
Upon conclusion of this program, participants should be able to:

1. characterize the neurologic complications of bariatric procedures, including their mechanisms, frequency, and prognosis.
2. identify the evidence that suggests the role for inflammation or the immunologic mechanism in neuropathy after gastric bypass.
3. recognize that routine monitoring of micronutrient levels and prompt recognition of neurological complications can reduce morbidity associated with these procedures.

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INVITED REVIEW

ABSTRACT: Bariatric surgical procedures are increasingly common. In this review, we characterize the neurologic complications of such procedures, including their mechanisms, frequency, and prognosis. Literature review yielded 50 case reports of 96 patients with neurologic symptoms after bariatric procedures. The most common presentations were peripheral neuropathy in 60 (62%) and encephalopathy in 30 (31%). Among the 60 patients with peripheral neuropathy, 40 (67%) had a polyneuropathy and 18 (30%) had mononeuropathies, which included 17 (94%) with meralgia paresthetica and 1 with foot drop. Neurologic emergencies including Wernicke’s encephalopathy, rhabdomyolysis, and Guillain–Barré syndrome were also reported. In 18 surgical series reported between 1976 and 2004, 133 of 9996 patients (1.3%) were recognized to have neurologic complications (range: 0.08–16%). The only prospective study reported a neurologic complication rate of 4.6%, and a controlled retrospective study identified 16% of patients with peripheral neuropathy. There is evidence to suggest a role for inflammation or an immunologic mechanism in neuropathy after gastric bypass. Micronutrient deficiencies following gastric bypass were evaluated in 957 patients in 8 reports. A total of 236 (25%) had vitamin B12 deficiency and 11 (1%) had thiamine deficiency. Routine monitoring of micronutrient levels and prompt recognition of neurological complications can reduce morbidity associated with these procedures.

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NEUROLOGIC COMPLICATIONS AFTER SURGERY FOR OBESITY

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Obesity affects a significant portion of the population. Alarming, 26% of American adults and children are obese with a body mass index (BMI) >30 kg/m². An additional 35% of the adult population is overweight (BMI >25 kg/m²). Deaths attributed to obesity in the United States are estimated at 280,000–325,000 annually. Complications of obesity include hypertension, arthralgias, idiopathic intracranial hypertension, sleep apnea, and type 2 diabetes mellitus.

Several series note improvement in comorbid conditions of obesity following bariatric surgery, including reduced or eliminated need for insulin and antihypertensive medications, reduction in lipid disturbances, improvement in degenerative joint disease, resolution of signs and symptoms of idiopathic intracranial hypertension, and elimination of sleep apnea. Surgical treatment of severe obesity is increasing, driven by both medical and economic forces. Approximately 10,000 procedures were done annually in the early 1980s, with predictions of 80,000 bariatric procedures for 2002, and 100,000 for 2003. Hospital strategists advocate bariatric surgery programs as a potentially lucrative market, with hospital revenues in 2001 between $850 million and $1.8 billion and increases for 2002 predicted at 60%–75%. Profit margins for hospitals may surpass 20%. Surgical candidates include those who are twice their ideal weight, demonstrate recurrent failure to lose weight through dieting, have no cardiopulmonary or psychiatric contraindications, and are usually age 50 years or younger, although surgery is car-
The first surgical treatments for weight reduction were global malabsorption procedures that employed either a jejunocolic shunt or small bowel bypass, but techniques have varied and continue to evolve. Jejunocolic shunt and, subsequently, jejunoileal bypass were both abandoned due to severe metabolic derangements. Gastric restriction (gastric partitioning, gastroplasty, vertical banded gastroplasty, gastric stapling) separates the stomach into a restricted upper pouch that empties into the rest of the stomach through a narrow-caliber channel (approximately 11 mm). Weight loss following gastric restriction is not sustained and has been deemed unsatisfactory.

Mason and Ito instead advocated the use of gastric bypass, which was later modified with Roux-en-Y reconstitution and found favorable to jejunoileal bypass. Gastric bypass restricts the volume ingested and induces a dumping syndrome if a high-carbohydrate meal is ingested, yielding sustained weight loss. Roux-en-Y gastric bypass combines gastric restriction and dumping physiology, is the first-line procedure for many surgeons, and is increasingly performed laparoscopically. For persons with “super” obesity (BMI >50 kg/m²), procedures producing selective malabsorption and malabsorption with partial gastric restriction have been advocated, including partial biliopancreatic bypass or modifications such as distal gastric bypass, very, very long-limb gastric bypass, and biliopancreatic bypass with duodenal switch modification.

The goals for most bariatric procedures are: (1) limited food intake; (2) satiety; and (3) normal absorption and digestion, allowing for loss of 50–60% of excess body weight and reducing medical complications of obesity. The first two objectives are attained by forming a small gastric pouch; the limited amount of food ingested flows through a small caliber outflow and provides prolonged satiety. Leaving the small bowel relatively unaltered allows normal absorption and digestion, but even gastric bypass surgery may be complicated by malabsorption or aversion for certain foods with potential loss of essential nutrients.

**MECHANISMS OF NEUROLOGIC INJURY**

Following bariatric surgery, neurologic complications may include compression mononeuropathies as weight is lost, and dysfunction or neurologic damage at multiple levels of the neuraxis due to malabsorption. The neurologic complications of malabsorption syndromes and micronutrient (vitamin) deficiencies were reviewed in detail by Chaudhry et al. We will focus here on nutrient deficiencies specifically associated with weight-reduction surgeries.

In 8 studies evaluating micronutrient levels following bariatric surgery in 957 patients, 236 (25%; range: 2–64%) were identified with vitamin B12 deficiency, 195 (20%; range 0–35%) with serum folate deficiency, and 11 (1%) with thiamine deficiency. Micronutrient analysis was neither uniform nor consistent, and patients were not characterized clinically. The neurologic consequences of such deficiencies are predictable, and related to their biochemical functions.

**Cyanocobalamin (Vitamin B12).** Gastric bypass leaves the stomach essentially intact, yet vitamin B12 deficiency may occur. Gastric bypass reduced plasma vitamin B12 levels 1 year later in approximately 30% of 20 patients despite a theoretically adequate oral intake and supplementation. Surgical series identified low or deficient serum vitamin
B₁₂ levels in 24–70% of patients 1–9 years after surgery.\(^7\)\(^,\)\(^3\)\(^4\)\(^,\)\(^5\)\(^6\)\(^,\)\(^7\)\(^7\)

Vitamin B₁₂ deficiency following gastric bypass has been attributed to inadequate intake,\(^3\)\(^4\)\(^,\)\(^5\)\(^6\) impaired hydrolysis of vitamin B₁₂ from dietary protein,\(^3\)\(^5\)\(^4\)\(^,\)\(^5\)\(^6\) and a defect in either the amount of intrinsic factor available or the interaction between intrinsic factor and vitamin B₁₂.\(^3\)\(^4\)\(^,\)\(^1\)\(^0\) Animals are unable to synthesize vitamin B₁₂. Vitamin B₁₂ in animal products is derived primarily from bacterial synthesis. The daily adult vitamin B₁₂ requirement is 2 µg, and the body typically stores 3000–5000 µg.\(^1\)\(^0\)\(^3\)\(^,\)\(^1\)\(^3\)

Intrinsic factor, produced by gastric parietal cells, binds vitamin B₁₂ in the stomach and mediates intestinal absorption at receptors in the ileum. It is transferred across the intestinal mucosa to transcobalamin II, a plasma transport protein that mediates its distribution.\(^1\)\(^3\)\(^3\) Vitamin B₁₂ also diffuses passively across the intestinal mucosa at pharmacologic doses (ingestion of ≥30 µg).\(^6\)\(^9\) With enterohepatic circulation,\(^1\)\(^3\)\(^3\) the half-life of vitamin B₁₂ is approximately 400 days;\(^1\)\(^1\)\(^0\) symptoms of deficiency may not present until months to years after surgery.

Vitamin B₁₂ participates in two enzymatic reactions in humans:\(^5\)\(^5\) conversion of l-methylmalonyl coenzyme A into succinyl coenzyme A, and methylation of homocysteine to methionine. Succinyl coenzyme A enters the citric acid cycle and participates in the conversion of homocysteine to methionine. This pathway, linking carbohydrate and fat metabolism, plays a role in myelin synthesis.\(^1\)\(^0\)\(^3\) Methyl-B₁₂ methylates animal RNA,\(^1\)\(^4\) which slows mRNA degradation. Impaired methylation of RNA may explain the involvement of long axons in vitamin B₁₂ deficiency,\(^1\)\(^0\)\(^3\) since RNA turnover in neurons is very high, and rapid degradation of mRNA might limit production of proteins essential for axon maintenance.

Although deficiency is classically associated with subacute combined degeneration,\(^7\)\(^2\)\(^,\)\(^1\)\(^2\)\(^0\) and there are reports of myelopathy associated with vitamin B₁₂ deficiency following partial\(^1\)\(^0\)\(^5\)\(^,\)\(^1\)\(^4\) or complete gastrectomy,\(^1\) subacute combined degeneration has not been reported following gastric bypass. Common neurologic symptoms of deficiency include paresthesias (21%), ataxia (12%), and weakness (6%).\(^7\)\(^2\)

**Folate.** Folate deficiency following gastric bypass approaches 10%.\(^1\)\(^3\)\(^,\)\(^5\)\(^7\)\(^7\) MacLean et al. noted red-cell folate deficiency in 3 (18%) and serum folate deficiency in 11 of 17 (65%) patients readmitted for malnutrition or excessive weight loss following surgery.\(^7\)\(^7\) The U.S. recommended dietary allowance (RDA) for men, nonpregnant and nonlactating women, and adolescents is 3 µg/kg body weight; sources include liver, yeast, leafy vegetables, legumes, and some fruits.\(^1\)\(^3\)\(^3\)

The neurologic complications of folate deficiency are not well characterized and are even debatable. Older literature suggests that affective disorders may be associated more with folate deficiency than with vitamin B₁₂ deficiency.\(^1\)\(^2\)\(^0\) Case reports suggest that folate deficiency may be associated with peripheral neuropathy,\(^5\)\(^1\) myelopathy,\(^5\)\(^1\) or restless legs syndrome.\(^1\)\(^2\) Among 28 patients with folate deficiency, 6 (21%) had abnormal electrophysiologic findings, including abnormal sural sensory nerve action potential (SNAP), and 5 also had an abnormal median SNAP.\(^1\)\(^2\)\(^0\) Yet, there are data to suggest that folate deficiency is not responsible for neurologic deficits. Lindenbaum et al.\(^7\)\(^2\) found that 40 of 141 (28%) patients with neuropsychiatric abnormalities caused by vitamin B₁₂ deficiency did not have anemia, and, in a subsequent investigation,\(^5\)\(^9\) no correlation between the severity of neurologic deficit and serum folate was identified.

**Pyridoxine (Vitamin B₆).** Three of four patients receiving low-dose pyridoxine supplementation at 6 months after gastric bypass, and two of two patients receiving low-dose pyridoxine supplementation at 12 months were deficient, as measured by serum levels.\(^1\)\(^3\) Signs of deficiency include seizures, dermatitis, and anemia. Peripheral polyneuropathy and subacute combined degeneration attributed to pyridoxine deficiency have been reported.\(^9\)\(^2\)

Vitamin B₆ is absorbed by the intestinal mucosa. Sources include meats, eggs, soybeans, unmilled rice, grains, and nuts. The human adult RDA is 0.016 mg/g protein per day.\(^1\)\(^3\)\(^3\) Three related forms of pyridoxine (pyridoxine, pyridoxal, and pyridoxamine) are converted to pyridoxal phosphate by the liver, red blood cells, and other tissues for use as a cofactor in transamination reactions, decarboxylation and racemization of amino acids, metabolism of lipids and nucleic acids, and as a coenzyme for glycogen phosphorylase.\(^1\)\(^3\)\(^3\)

**Thiamine.** Thiamine is found in both plants (fortified grains, cereals, legumes, seeds, nuts, brewer’s yeast) and animals (organ meats, pork).\(^1\)\(^3\)\(^3\) The adult RDA for thiamine is 1 mg.\(^1\)\(^3\)\(^3\) Thiamine can be depleted from a healthy body in 18 days.\(^1\)\(^5\)\(^6\) Thiamine is likely absorbed in the proximal small intestine by a carrier-mediated process when luminal concentrations are low, and also by passive diffusion with pharmacologic doses.\(^1\)\(^0\)\(^1\)\(^3\)\(^3\)
Thiamine pyrophosphate is a cofactor in oxidative decarboxylation of carbohydrates by providing the prosthetic group for three important enzymes. Pyruvate dehydrogenase and α-ketoglutarate dehydrogenase catalyze the conversion of pyruvate to acetyl coenzyme A and α-ketoglutarate to succinyl coenzyme A, respectively. Transketolase transfers activated aldehydes in the hexose monophosphate shunt (pentose phosphate pathway) in the generation of the reduced form of nicotinamide adenine dinucleotide phosphate (NADPH) for reductive biosyntheses. Thiamine deficiency causes lactic acidosis, reduced oxygen uptake, and depression of transketolase activity predominantly in the brainstem, which correlates with the clinical presentation of Wernicke’s encephalopathy.

Thiamine deficiency results in both acute and chronic encephalopathies (Wernicke’s encephalopathy and Korsakoff’s syndrome). The clinical triad of Wernicke’s encephalopathy (encephalopathy, nystagmus or ophthalmoplegia, and ataxia) can be precipitated by malnutrition, administration of carbohydrates, and intake of thiaminase present in teas and fish.

Wernicke’s encephalopathy is associated with nutritional polyneuropathy (dry beriberi). It is unclear whether nutritional polyneuropathy is due to isolated thiamine deficiency or multiple vitamin deficiencies.

**Vitamin D.** Sources of vitamin D include fortified foods and conversion of inactive to active vitamin D by skin exposure to ultraviolet radiation or sunlight. The human adult RDA of vitamin D is 5 μg (200 IU). Classic manifestations of vitamin D deficiency include rickets in children and hypocalcemia and osteopenia in adults. An associated syndrome of osteomalacic myopathy has also been described, with features of myopathy and diffuse pain. Vitamin D deficiency is a common finding among persons with chronic nonspecific musculoskeletal pain. Myopathy attributed to vitamin D deficiency was identified in 3 of 106 patients following a gastrectomy procedure; nerve conduction studies were normal in each case, and all three demonstrated “myopathic” motor units on electromyography. All improved with treatment.

**Vitamin E.** Among 21 patients followed prospectively after gastric bypass, 6 of 20 had marginal tocopherol levels at 6 months, and 2 of 21 had marginal tocopherol levels at 12 months. Tocopherol, a fat-soluble vitamin, is secreted into the lymph and taken up by chylomicra, transported to the liver, and then into the blood in very low-density lipoproteins (VLDLs). During VLDL metabolism, tocopherol is transferred to low- or high-density lipoproteins. It functions as an antioxidant. Sources include vegetable oils, vegetable oil products (margarine, shortening), leafy vegetables, nuts, and wheat germ. The adult RDA is 10 mg for males and 8 mg for females.

Human vitamin E deficiency has been associated with both myopathy and neuropathy. Myopathy has been associated with reduced serum concentration of vitamin E and prolongation of the QT interval on electrocardiogram. Vitamin E–deficient rats and monkeys consistently develop a reversible necrotizing myopathy.

Neuropathic changes are also significant. Severe vitamin E deficiency in humans can produce a progressive (primarily) sensory axonopathy, especially involving large fibers in the posterior columns, sensory roots, and peripheral nerves. Vitamin E neuropathy and myopathy are important to consider since they are potentially treatable.

**Other Micronutrients.** Minerals (calcium, phosphorus, and magnesium) and trace elements (zinc, iodine, copper, manganese, fluoride, chromium, molybdenum, selenium, and iron) have seldom been studied in patients following gastric bypass. Calcium is the best-characterized mineral following bariatric surgery. Calcium intake was reduced to <70% of RDA in 31 of 41 (75%) patients; serum calcium was low in 1 patient. New or worsening aches or pains >1 year following gastric bypass occurred in 26 of 41 (65%) patients, usually within 5 years after surgery. This pain has been called “bypass bone disease” and is thought due to bone demineralization from impaired calcium absorption. Byrne recommended a calcium supplement of 1200 mg daily.

Phosphorus intake was reduced to <70% of RDA in 26% of patients undergoing gastric bypass for obesity. Sugerman identified patients with magnesium deficiency following bariatric procedures and recommended monitoring.

Changes in other trace elements following bariatric surgery have not been described, but may be important. For example, selenium deficiency can cause a cardiomyopathy (Keshan’s disease) in humans and white muscle disease in grazing cattle.
96 patients, 21 (22%) were male, 74 (77%) were female, and 1 case was unspecified; ages ranged from 20 to 65 years. The most commonly reported neurologic complication was peripheral neuropathy in 60 patients (62%) and encephalopathy in 30 (31%) (Table 1). Among the 60 patients with peripheral neuropathy, 40 (67%) had polyneuropathy, 18 (30%) had mononeuropathy, and there was 1 case each of lumbar plexopathy and radiculopathy. Mononeuropathies included 17 of 18 (94%) with meralgia paresthetica and 1 case of foot drop. Eighteen of 40 cases (45%) of polyneuropathy were attributed to thiamine deficiency. Wernicke’s encephalopathy or Wernicke–Korsakoff syndrome occurred in 27 cases (28%), and was accompanied by peripheral neuropathy in 12 (13%). Optic nerve lesions, including optic neuropathy, nyctalopia (night blindness), and central scotoma, complicated 8 cases (8%).

Outcomes were mixed, but somewhat worse for peripheral than central nervous system lesions. Overall, symptoms improved in 36, residual deficits were present in 48, outcome was not reported in 7, and death occurred in 5 (Table 1). Specifically, there was no improvement in 3 of 30 cases of encephalopathy, 2 of 2 cases of myelopathy, the 1 case of radiculopathy, 15 of 40 cases of polyneuropathy, and 4 of 17 cases of meralgia paresthetica. There are insufficient data to determine the surgical procedure with the lowest neurologic complication rate, although the majority of optic nerve lesions were associated with malabsorption procedures.

Table 1. Neurologic complications of bariatric surgeries and outcome arranged by localization.

<table>
<thead>
<tr>
<th>Brain</th>
<th>Peripheral neuropathy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Encephalopathies</td>
<td>Cranial nerve Cord</td>
</tr>
<tr>
<td>Thiamine deficiency Other</td>
<td>Radiculopathy Lumbar plexopathy Polyneuropathy</td>
</tr>
<tr>
<td>Total affected</td>
<td>Total</td>
</tr>
<tr>
<td>Improved</td>
<td>27</td>
</tr>
<tr>
<td>Not improved</td>
<td>25</td>
</tr>
<tr>
<td>Died</td>
<td>1</td>
</tr>
<tr>
<td>No data available*</td>
<td>1</td>
</tr>
</tbody>
</table>

Some patients had more than one lesion. In total, there were 96 patients from 50 case reports; reference numbers: 1, 3, 14, 15, 18, 26, 29–33, 39–41, 43, 45, 48–50, 54, 55, 58, 61, 64, 68, 70, 73, 75, 76, 80, 84, 91, 93, 98, 99, 104–106, 115, 125, 127–129, 138, 140, 141, 143, 144, 147, 148.

*There is one additional patient for whom localization details are unavailable.

96 patients who underwent gastric restriction surgery for morbid obesity: 18 (3.6%) developed neurologic complications between 3 and 14 months postoperatively.\(^{128}\) When observation was extended to 20 months,\(^{1}\) 23 patients (4.6%) developed neurologic symptoms. The incidence of neuropathy was higher in a controlled retrospective study of peripheral neuropathy following bariatric surgery.\(^{137}\) Among 435 patients, 71 (16%) developed peripheral neuropathy, including 27 with polyneuropathy, 39 with mononeuropathy, and 5 with radiculoplexopathy.\(^{137}\)

**NEUROLOGIC COMPLICATIONS BASED ON LOCALIZATION**

Complications of bariatric surgery can affect any level of the neuraxis. Except for the association of optic nerve involvement with global or selective malabsorption procedures, there was no discernible trend associating a particular neurologic lesion with one type of bariatric procedure.

**Brain.** Wernicke’s encephalopathy complicated 24 of 96 patients (25%) in case reports (Table 1), including 14 with restriction procedures and 4 with combined gastric restriction and dumping procedures. The incidence is likely low, however, as Wernicke’s encephalopathy affected 2 of 500 (0.4%) patients in the prospective series of Abarbanel et al.\(^{1}\) Additional infrequent—and possibly incidental—brain lesions included stroke in 3,\(^{3,58,79,128}\) central pontine myelinolysis in 1,\(^{61}\) and unspecified psychosis in 2.\(^{21}\)

Symptoms and signs of Wernicke’s encephalopathy following bariatric surgeries were invariably preceded by malnutrition. This usually resulted from prolonged emesis, occasionally due to mechanical obstruction,\(^{11}\) although vitamin noncompliance or
increased alcohol consumption were also noted. Weight loss in excess of 7 kg/month in the first few months may suggest intake restriction. Peltier et al.95 and Printen et al.99 recognized that prolonged emesis may precipitate Wernicke’s encephalopathy and emphasized patient education regarding the size of the gastric pouch (<50 ml) to prevent overeating that can result in vomiting and thiamine deficiency.

**Cranial Nerves.** Optic nerve lesions complicated 8 reported cases (8%). These included 6 of 9 reports of neurologic complications after jejunooileal bypass, 1 of 4 reports involving bilioenteric bypass, and 1 of 56 reports of complications after gastroplasty, again suggesting increased frequency with malabsorption rather than gastric bypass procedures. Symptoms and signs included central scotoma, nystagmus, and optic neuropathy. Nutritional amblyopia and carotene deficiency following jejunooileal bypass manifested as central scotoma or nystagmus.

**Spinal Cord.** There are two reported cases of myelopathy after gastric bypass (Table 1). The cause remained uncertain, and empiric therapy was of no benefit. Possible etiologies include deficiencies of serum copper, vitamin B12, pyridoxine, and folate. Copper deficiency has been implicated in the development of a myelopathy following partial gastrectomy69,109 or intestinal bypass.69

**Peripheral Nerve.** As noted earlier, peripheral neuropathy was found in 60 of 96 patients (62%) described in case reports (Table 1). Although most presented as chronic conditions, likely related to micronutrient deficiency, Guillain–Barré syndrome was reported in 2 patients (2%), and there were several additional cases among the surgical series.

**Generalized Neuropathy.** All 27 patients with a generalized polyneuropathy were sensory-predominant in one recent series. Most had a slow onset with chronic course. Some case reports of Wernicke’s encephalopathy were associated with polyneuropathy (dry beriberi). It is unclear whether the neuropathy is due to isolated thiamine deficiency or multiple vitamin deficiencies. Nutritional polyneuropathy presents insidiously with a symmetric sensorimotor neuropathy affecting the lower extremities more than the upper extremities. Symptoms include anesthesia, tingling paresthesias, and severe pain, particularly involving the feet (“burning feet syndrome”). Examination may reveal muscle tenderness on palpation, hyporeflexia, and sensory impairment involving pain and light touch in a stocking-and-glove distribution, distal vibratory and proprioception loss, and foot drop. Potentially treatable malabsorption syndromes that may affect peripheral nerves following gastric bypass include deficiencies of vitamin B12, thiamine, and vitamin E.97 Vitamin D deficiency may affect the peripheral nerves, but this has not been confirmed.96 Although vitamin E deficiency is associated with neuropathy, no specific reports were identified as complications of bariatric surgeries. Data from sural nerve biopsies following Roux-en-Y also suggest the possibility of an immunologic mechanism in polyneuropathy (see later).

Several new terms have been proposed to identify neuropathy complicating gastric bypass surgery, including “bariatric beriberi” and “acute post-gastric reduction surgery (APGARS)” neuropathy. Unfortunately, no diagnostic criteria for this possible syndrome have been identified. Since nutritional polyneuropathies have been better characterized and are thus more informative regarding mechanism and prognosis, there is little advantage to adding a new and undefined term to the lexicon, especially when the acronym is easily confused with another firmly established medical term (the Apgar score).

**Focal Mononeuropathies.** Of 71 patients with peripheral neuropathy in the retrospective series of 435 patients by Thaisetthawatkul et al.,39 (55%) had mononeuropathies. Carpal tunnel syndrome was particularly common, as 31 (79% of mononeuropathies and 7.1% of all gastric bypass patients) presented with median mononeuropathy at the wrist. Less common syndromes included 2 patients with ulnar neuropathy at the elbow, 1 with radial mononeuropathy, 1 with superficial radial sensory neuropathy, and 1 with sciatic neuropathy. Although not especially common with bariatric surgeries, peroneal neuropathy and lateral femoral cutaneous neuropathy are of particular interest.

Thaisetthawatkul et al. reported 2 patients (0.4%) with peroneal mononeuropathy at the fibular head, and Sassaris et al. noted onset of foot drop 9 months following bariatric surgery. Foot drop has been implicated in dieting and malnutrition in literature prior to the era of bariatric surgery. Other reports identified peroneal nerve palsy following weight reduction; micronutrient deficiencies were not excluded as a contributory cause. Denny-Brown estimated that a transient foot drop developed during captivity in approximately 10% of World War II prisoners of war suffering from severe
and prolonged malnutrition; no cause was ever determined.

Following gastric bypass, the incidence of lateral femoral cutaneous neuropathy is approximately 0.5%-1.4%. The etiology remains elusive. Compression by the Gomez retractor at the hip was considered a likely cause by Grace. However, MacGregor and Thoburn reported 11 cases of meralgia paresthetica, most beginning shortly after surgery (Roux-en-Y gastric bypass or silicon ring vertical gastroplasty), despite using an upper midline incision with an “upper hand” retractor above the level of the shoulders to avoid pressure at the hips (MacGregor, personal communication). MacGregor and Thoburn speculated that certain anatomic variants of the lateral femoral cutaneous nerve may predispose the nerve to compression.

Muscle. Weakness was reported in 25 of 96 patients in case reports. Thiamine deficiency accounted for some cases. Of the remaining case reports of weakness or myopathy, 7 were attributed to primary muscle disease (Table 1); among surgical series, there was one report each of a myotonic syndrome and hypokalemic paralysis. Another surgical series noted rhabdomyolysis in 1.4% of cases, and suggested that this may be an underestimate. Mogno et al. prospectively followed serum creatine kinase (CK) levels before and after operation and defined rhabdomyolysis as CK >1050 U/L; myoglobin levels were not evaluated. By this definition, the rate of rhabdomyolysis was as high as 22% of patients undergoing laparoscopic bariatric surgery, although this is likely an overestimate since serum CK may also be elevated because of surgery.

In a series of 30 patients with osteomalacia, weakness was the presenting symptom in 30%; 97% were weak on examination, and 83% had electromyographic findings of reduced motor unit action potential (MUAP) duration and amplitude without abnormal spontaneous activity, suggesting a myopathic pattern. Muscle biopsy demonstrated type 2 atrophy, enlarged interfibrillar spaces, fat infiltration, fibrosis, and glycogen granules. One report attributed myopathy following Roux-en-Y gastric bypass to global malnutrition. Myopathy may also be associated with vitamin D or E deficiencies.

EVALUATION AND MANAGEMENT

Electrodiagnosis. Electromyography and nerve conduction study have been underutilized in the diagnosis of these presentations, as only 36 (38%) of 96 patients in case reports included electrodiagnostic data, the majority in a single prospective study. Electrophysiologic findings from 25 patients in the controlled retrospective study done by Thaisethawatkul et al. demonstrated moderate to severe large-fiber neuropathy in 11, mild peripheral neuropathy in 8, and normal studies in 6 (who had clinical evidence of small-fiber neuropathy). These data provide insight into the sensitivity of electrodiagnostic evaluation, as 19 of 25 patients (76%) with clinical signs of peripheral neuropathy had abnormal studies. Normal findings are more likely when small or unmyelinated axons are involved. Among 24 of 42 partially gastrectomized patients with low serum vitamin B12, electrodiagnostic evidence of polyneuropathy was seen in only 3, which may suggest a preferential effect on unmyelinated or small fibers, or on other parts of the nervous system. The sensitivity of special testing appears higher; quantitative autonomic testing was abnormal for 2 of 7 patients, thermoregulatory sweat testing was abnormal in 4 of 4, and quantitative sensory testing (all fiber classes) was abnormal in 4 of 4 patients. However, there are insufficient published data characterizing neuropathies and myopathies after bariatric surgery for analysis of sensitivity or specificity. Electrodiagnostic testing is critical for localization and diagnosis, and to exclude potential neurologic emergencies such as Guillain–Barré syndrome.

Tissue or biopsy specimens were obtained from only 7 patients (7%) in the case reports, and several of these were at autopsy. Sural nerve biopsy findings were reported from 5 patients among the surgical series, 4 with polyneuropathy and 1 with radiculoplexopathy; findings included prominent axonal degeneration, and one biopsy had multifocal fiber degeneration. All had mononuclear inflammatory cell involvement of the epineurium and endoneurium, and small or moderate perivascular inflammatory mononuclear cells were also seen, suggesting a role for inflammation or an immunologic mechanism. Postmortem examination following gastric partitioning suggested marked fat catabolism as manifested by lipid droplet and lipofuscin deposition in anterior horn cells, in the cytoplasm of Schwann cells, and in macrophages of the brachial plexus.

Tissue diagnosis, especially muscle biopsy, should be considered for the same reasons as electrodiagnostic studies. Many of these patients are at risk for neuropathy, myopathy, or both, and alternate causes of weakness (idiopathic inflammatory myopathy, critical illness myopathy) should be excluded. Given the low sensitivity of electrodiagnostic testing and muscle or nerve biopsy for detecting small-fiber neuropathies, skin biopsy may be particularly helpful in
patients with presumed small-fiber neuropathy or burning feet syndrome.65

**Time Course of Presentation.** Early or immediate potential complications include rhabdomyolysis and meralgia paresthetica. Rhabdomyolysis has been associated with prolonged operations and immobility; protective padding has been advocated.66 Since lateral femoral cutaneous neuropathy may not be related to surgical technique,73 there is no clear strategy for prevention, and further research is necessary to define the mechanism of injury.

Nearly half of metabolic and nutritional deficiencies occur within the first year following Roux-en-Y gastric bypass.17 Wernicke’s encephalopathy and neuropathy associated with thiamine deficiency may present more acutely, beginning days to weeks after prolonged emesis. However, nutritional polyneuropathies or myopathies may occur months or years later. Due to its long half-life and enterohepatic circulation, signs of vitamin B12 deficiency may occur years after bariatric surgery. Neurological signs of vitamin E deficiency from malabsorption may not appear for 5–10 years in adults.32,66,85,147 It may be difficult to determine whether a lesion is due to a single vitamin deficiency or multiple deficiencies.36,78 Thus, burning feet syndrome has been attributed to deficiencies of multiple vitamins78 as well as to single vitamins such as thiamine78 or folate.12

**Micronutrient Monitoring and Supplementation.** Bro- lin16 recommended monitoring complete blood count, serum iron, total iron-binding capacity, and serum vitamin B12 following Roux-en-Y gastric bypass. Checking serum CK in the immediate postoperative period is also advisable to detect rhabdomyolysis in the clinical context of pain, weakness, and skeletal muscle swelling with myoglobin-olysis in the immediate postoperative period is also advisable to detect rhabdomyolysis in the clinical context of pain, weakness, and skeletal muscle swelling with myoglobinolysis in the clinical context of pain, weakness, and skeletal muscle swelling with myoglobinolysis in the clinical context of pain, weakness, and skeletal muscle swelling with myoglobinolysis in the clinical context of pain, weakness, and skeletal muscle swelling with myoglobinolysis in the clinical context of pain, weakness, and skeletal muscle swelling with myoglobinolysis in the clinical context of pain, weakness, and skeletal muscle swelling with myoglobinolysis in the clinical context of pain, weakness, and skeletal muscle swelling with myoglobinolysis in the clinical context of pain, weakness, and skeletal muscle swelling with myoglobinolysis in the clinical context of pain, weakness, and skeletal muscle swelling with myoglobinolysis in the clinical context of pain, weakness, and skeletal muscle swelling with myoglobinolysis.85,147 Since increased serum CK levels may occur as a result of surgery, elevations in the absence of this syndrome may not be clinically relevant. Following gastric bypass, Crowle and colleagues34 advocated long-term follow-up, dietary counseling, clinical and laboratory evaluations every 6 months to include complete blood count, urinalysis, serum iron, total iron-binding capacity, serum vitamin B12, folic acid, and a chemistry profile that includes calcium, phosphorus, and alkaline phosphatase. They also recommended indefinite use of the following supplements: a multivitamin-mineral containing vitamin B12, folic acid, and iron; an additional iron tablet with vitamin C; an additional 50–100-μg vitamin B12 tablet; and a calcium supplement of 1000–1200 mg daily.23,34 Boylan et al.13 found that plasma levels of vitamins B6, B12, E, and folate correlated with vitamin supplement intake in gastric bypass patients, and also recommended use of a multivitamin-multimineral supplement providing U.S. RDA quantities daily. Although there is some disagreement about whether all patients should receive oral vitamin B12 supplementation following surgery, there is consensus about most of these recommendations.23

**CONCLUSIONS**

Thorough neurologic evaluation is essential for any patient with neurologic symptoms after bariatric surgery. We recommend obtaining levels of micronutrients (vitamins B6, B12, D, E, folate, calcium, magnesium, phosphorus, selenium, and copper), electrodiagnostic studies, biopsy, and empiric therapy (e.g., thiamine, vitamin B12, or multivitamins) after a careful search for a specific underlying cause. With the increasing popularity of bariatric surgery, clinicians will need to recognize and manage neurologic complications that may appear after an interval of years to decades.

Prevention of compression injuries and rhabdomyolysis begins in the operating room with attention to patient positioning and the duration of immobility during surgery.32,66 Routine monitoring of selected micronutrients and minerals (vitamins B6, B12, D, E, folate, iron, thiamine, and calcium) every 6 months after surgery may detect deficiencies before they become symptomatic, and vitamin/mineral supplementation at least at the U.S. RDA level are likely cost-effective in preventing neurologic complications, although further studies of this premise are needed.

**REFERENCES**


