



NON-SYSTEMATIC REVIEW

Peripheral Neuropathies after Bariatric Surgery: A Current Review

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Abstract

Introduction: Bariatric surgery (BS) is an effective method for sustained weight loss and better quality of life. However, it has its complications. Among those, peripheral neuropathies are important, although underdiagnosed, complications after the surgery.

Objective: The objective of this article is to describe the most prevalent peripheral neuropathies that may happen after BS, especially focusing on small fiber neuropathies, and the main nutritional deficits involved in these neuropathies.

Methods: It was made a non-systematic review on PubMed/Medline database.

Results: 32 articles were included.

Conclusion: Further studies are needed to estimate the prevalence of peripheral neuropathies after BS, especially small fiber neuropathy. This lack of epidemiological studies corroborates to the underdiagnosis. We suggest researchers to make a prospective cohort about Small fiber neuropathy after BS.

Keywords

Bariatric surgery, Peripheral neuropathy, Small fiber neuropathy

Abbreviations

BS: Bariatric Surgery; BP: Blood pressure; BMI: Body mass index; BPD/DS: Biliopancreatic diversion with duodenal switch; CSF: Cerebrospinal Fluid; DM2: Type 2 diabetes; EMG: Electromyography; GBS: Guillain-Barré Syndrome; GLP1: Glucagon-like Peptide-1; IVIG: Intravenous immunoglobulin; PN: Peripheral Neuropathy; SFN: Small fiber neuropathy

Introduction

Obesity is an important global health issue leading to severe morbidity and mortality. Over the past decades its prevalence had progressively increased, with an expected prevalence of 650 million people worldwide [1]. It has a huge impact in healthcare costs [2] and is a well-known risk factor for ischemic heart disease, stroke, dyslipidemia, hypertension and also mood disorders [3].

To avoid the aforementioned complications directly and indirectly related to obesity, and to mitigate the costs to the public health system, obesity has to be treated aggressively at different instances with multidisciplinary health workers. Tough, surgical treatment is an option required in specific situations, and it is been

more frequently used in clinical practice [3]. However, invasive procedures like bariatric surgery (BS) are not free from complications. Possible adverse events need to be carefully discussed with every patient, and they may influence the patient's decision [4].

Previous reports showed that obesity had been linked to an increased risk of peripheral neuropathy (PN) [5]. Therefore, the aim of this study is to explore the prevalence, the clinical characteristics and the possible mechanisms for the development of peripheral neuropathy in patients underwent BS.

Material and Methods

A non-systematic search was performed using PubMed. The following keywords were used to conduct the database search: "Bariatric Surgery" and "Peripheral Nervous System Diseases" or "small fiber neuropathy".

The inclusion criteria were (1) The studies were published in English; (2) Presence of peripheral neuropathy after BS; (3) There were clinical information available.

The exclusion criteria were as follows: (1) Articles that were not published in English; (2) Duplicate infor-

Table 1: Clinical findings of the neuropathies that may happen after BS.

Complications	Prevalence	Study Design	Country	Bariatric Surgery Procedure	Etiologies	References
Peripheral Neuropathies after Bariatric Surgery	2% [4]; 16% [5]; 54% [9]; 67% [15].	Cross sectional study [4]; Retrospective study [5]; Non-systematic review [9]; Non-Systematic review [15].	U.S.A [4,5,9].	Gastric bypass (GB), vertical banded gastroplasty (GP), sleeve gastrectomy [4]; GB, GP, pancreaticobiliary bypass and jejunoileal bypass [9,13].	Cobalamin, Thiamine, Folate, Vitamin E and Copper deficiencies [14,15].	[4,5,9,14,15].
Polineuropathies						
Large Fibers						
Due Vitamin B1 deficiency	1% [3], 30% [13].	Non-Systematic review [3]; Retrospective study [13].	U. S. A [3,13].	Roux-en-Y gastric bypass, Restrictive Surgery and malabsorptive surgery [3]; Roux-en-Y gastric bypass [13].	Vomiting and excessive weight loss [13]; [17]	[3]; [13]; [17].
Due Vitamin B12 deficiency	20% [3], 0,4% [4]; 70% [15].	Non-Systematic review [3]; Cross sectional study [4]; Non-Systematic review [15].	U.S.A [3,4]	Roux-en-Y gastric bypass, Restrictive Surgery and malabsorptive surgery [3]; GB, GP and sleeve gastrectomy [4]	Decrease of Intrinsic Factor and stomach acid [3]	[3]; [4]; [15].
Guillain-Barré-Syndrome	0,4% [4]	Cross sectional study [4].	U.S.A [4].	GB, GP and sleeve gastrectomy [4]	Axonal degeneration [26]	[5]; [26]
Small fibers	Unknown	Unknown	Unknown	Unknow	Copper, Thiamine, Cobalamin and Riboflavin (B2) deficiencies [3]; [8]; [16]; [20]; .	[3]; [8]; [11]; [16]; [20]; .
Focal neuropathies						
Meralgia paresthetica	Unknown	Unknown	Unknown	Unknow	Position during surgery [4].	[4].
Cubital syndrome	5% [9]	Retrospective study [9].	U.S.A [9].	GB, GP, pancreaticobiliary bypass and jejunoileal bypass [9].	Position during surgery [9].	[9].

mation; (3) No eligible for collection.

We also added review articles aiming to create a more comprehensive review.

Results

The collected information is summarized in [Table 1](#). We identified 232 articles through PubMed database according to adopted searching criteria. 32 out of the 232 articles were included in this review.

Discussion

Peripheral neuropathy is reported as the most common neurological manifestation in patients after BS, affecting up to 60% of cases [6,7]. The prevalence of peripheral neuropathy in patients who underwent BS ranged from 2% to 16% [6,8]. This huge variability is possibly explained by the criteria used to define neuropathy and the methodology used in each study. Age, sex, preexisting comorbidities, type of procedure and postoperative follow-up were not uniform among studies. In one cross-sectional study with 451 patients who underwent BS the prevalence of PN was ~2%. Authors include only patients with symptoms and abnormal nerve conduction study [6]. In another study, clinical features from 435 patients were retrospectively analyzed and the PN prevalence was ~16% [8].

Time for clinical presentation may vary considerably after BS, from months to decades [9], and could be classified as early (onset symptom occurs less than 12 months after BS), and late presentation (more than one year after the procedure) [10]. Early complication includes direct nerves trauma due patient's position during surgery, whilst late complications occurs due multiple mechanisms that will be further discussed [9,10]. Central nervous system may also be involved but is not the scope of this study.

Axonal sensory/predominant-sensory length-dependent neuropathy is the commonest presentation in up to 2/3 of patients with PN after BS [7]. Isolated focal neuropathies have been reported in ~30% of cases [7]. The most common presenting symptom is symmetrical tingling paresthesia distally in lower limbs [11]. Positive sensory phenomena are the most common presentation, but associated weakness and lack of feeling have also been previously reported [11]. The neuropathy tends to be slowly progressive. Lower extremities are usually more severely affected, and not rare the "burning feet syndrome" is observed [7,12]. Nerve conduction study reveals sensory and motor axonal neuropathy [7,10].

The mechanisms related to the development of peripheral neuropathies after BS are not fully understood, however, most authors suggest it should be linked to nutritional deficiencies [3-5,12-15], especially vitamin B12, thiamine, copper, folate, vitamin E, B3 and B6 deficiencies [10,12]. Nutritional deficiencies are found in up

to one-third of patients before surgery, and vitamin levels decrease significantly after intervention when proper replacement is not adopted [9]. Malnutrition after procedure is believed to be multifactorial including vomiting, changes in eating habits and in the microbiota [9], anatomical and physiological changes (such as removing part of the stomach and bypassing the duodenum and proximal jejunum, structures responsible for the absorption of micronutrients [13]), endocrinal changes (especially the decrease of gut hormones [14]) and reduction of intrinsic factor [12,15,16].

Additionally some risk factors as massive weight loss, prolonged gastrointestinal symptoms, inadequate nutritional management, reduced albumin and transferrin after surgery, postoperative complications requiring hospitalization and jejunioileal bypass have been consistently related to PN [10]. Most of patients with confirmed vitamin deficiency present a sensory/sensory-predominant neuropathy pattern [8] and have complete resolution of symptoms after nutritional and pharmacological interventions, a finding reported in up to 85% of symptomatic cases [16]. Diabetes mellitus is very common among this group of patients and is a well established cause of PN including different types of diabetic neuropathy as focal neuropathies, distal symmetric neuropathy (large and small fibre), autonomic and radiculoplexopathies [8].

Since nutritional deficits are mainly involved, nutritional managing and vitamin supplementation may prevent and/or treat polyneuropathies [7]. The prevalence of sensory-predominant neuropathy in group of patients who had intensive nutritional program (pre and post-operative) and avoided rapid weight loss after BS was ~1% [8], a lower prevalence when compared to a different group of patients with poor nutritional status (~7%) [8]. In a retrospective study, all patients with neurological complications after BS reported difficult in oral food intake, severe dysphagia, gastro-intestinal regurgitation and vomiting; and the percentages of excess weight loss and BMI loss in 3 months after surgery were statically different in the group who presented neurological complications [11].

The prevalence of vitamin B12 (Cyanocobalamin) deficiency after BS ranged from 0.4 to 70% of the cases [6,9,12]. Low B12 levels are associated with central and peripheral nervous system dysfunction [16]. The neuropathy is classically a length-dependent sensory ataxic neuropathy with tingling paresthesia and areflexia reflexes [9,16,17]. Changes in stomach pH associated with a significant reduction of the intrinsic factor lead to cyanocobalamin malabsorption, as they are required to its release from food and avoid its degradation by proteases [17].

Thiamine (vitamin B1) deficiency is found in up to 30% patients underwent BS [17]. It is involved in glycolysis, amino acid synthesis and myelination [10,18]. Pa-

tients may present with acute/subacute forms of motor and sensory axonal neuropathy and clinical manifestations may appear months or years after the procedure [19,20]. Dry beriberi (neuritis, peripheral neuropathy, sensorial ataxia and paraplegia) and Wernicke's encephalopathy (ataxia, eye movement disorder and mental status disturbance) are other clinical presentations [9,19]. Unfortunately, diagnosis is often delayed [11]. It is important to emphasize that vitamin B1 storage may be depleted in two or three weeks, and many patients already have thiamine deficiency before the surgery [21], measurement prior surgery and proper replacement is mandatory.

Folate (Vitamin B9) is crucial for DNA synthesis and amino acids metabolism, and its levels are decreased in 20-25% of obese people [18] and about 20% of post-BS patients [9,10]. Once more, folate's absorption is impaired due anatomical changes after BS, since its absorption happens in duodenum and proximal jejunum [18]. Clinical manifestations of Folate deficiency include peripheral neuropathy, optical neuropathy, fatigue, anemia and cognitive impairment [10,18].

Vitamin E (tocopherol) levels may also be affected, especially in biliopancreatic diversion with duodenal switch (BPD/DS), which prejudice the absorption of fat-soluble vitamins [9,14]. Tocopherol protects neural cells from oxidative damage [10], and its deficiency may manifest with hyporeflexia, ataxia, ophthalmoplegia, ptosis, dysarthria, myelopathy and decreased proprioception [9,10].

Mononeuropathies

Focal neuropathy (mononeuropathy) have been reported in up to 9% of 435 patients underwent BS [8]. Carpal tunnel syndrome was the commonest, it is believed to occur due the rapid weight loss, which turns nerves more susceptible for compression [8].

Neuropathy of the lateral cutaneous nerve of the thigh is also frequently reported, in 0.5 to 1.4% of patients [7]. It is believed to be caused by compression of the lateral cutaneous nerve during the surgical procedure, and therefore symptoms usually start right after surgery [7].

Other less frequent mononeuropathies are radial neuropathy, superficial radial sensory neuropathy, ulnar neuropathy in the elbow, occipital neuropathy, fibular head neuropathy and sciatic neuropathy [7,8].

Guillain-Barré syndrome

Guillain-Barré Syndrome (GBS) is an acute peripheral neuropathy due an autoimmune process affecting the peripheral nervous system leading to axonal degeneration [22,23]. Incidence of GBS is 1.2-3 cases per 100.000 inhabitants. BS have been linked to an increased risk to GBS development [4,6]. Two out 451 (0.4%) patients underwent BS presented an acute neuropathy that was classified as GBS [6].

Small Fiber neuropathy

Small fibre neuropathy (SFN) is caused by damage to thinly myelinated A δ -fibres and unmyelinated C-fibres. It usually presents as a distal symmetrical neuropathy with positive and/or negative sensory symptoms, and autonomic complaints [24]. The global prevalence of SFN remains unknown. The etiology of a significant number of SFN cases remain unsolved, potentially treatable causes as diabetes mellitus, HIV, hyperlipidaemia, amyloidosis, sarcoidosis and other systemic illnesses are included in most protocols. It well knows that vitamin deficiencies, diabetes mellitus and impaired glucose tolerance are frequently associated with the development of SFN. High glucose levels are among the frequent complications observed in obese patients, so it is expected that SFN should occur among this specific group of patients. A previous study reported 5 patients developed neuropathy after BS, 3 of them presented SFN [25]. It remains unknown SFN prevalence among patients underwent BS, and if it is occurring it is caused by metabolic nutritional abnormalities.

Orthostatic intolerance

Autonomic neuropathy is a serious neurological complication that have been previously reported in some patients who underwent BS [26]. Clinical presentation may include symptomatic orthostatic intolerance, sustained low blood pressure, pre-syncope symptoms or/and syncope and POTS [27].

Gastrointestinal neuropathy

Gastrointestinal tract, besides being involved in a high percentage of nutritional deficits which culminate in peripheral neuropathy [11], may also be affected. This is especially important since gut-hormones, whose concentrations are changed after BS, act both on vagal afferent endings and brainstem or hypothalamus, in a neuroendocrine circuit [28]. Interestingly, since gut peptides participate on autonomic cardiovascular disorders, the hypothesis that their modifications may interfere in autonomic features such as orthostatic intolerance has increased [27].

The most significant hormone change in gastrointestinal tract after BS is the increase of glucagon-like peptide 1 (GLP1) and Peptide YY, which increases insulin secretion and centrally controls the appetite, respectively; both exerting an orexigenic effect and contributing to the sustained weight loss [28]. The weight loss itself may reduce the sympathetic activity in SNA [29]. Nevertheless, both Leptin and Ghrelin are pointed as important regulators of cardiovascular autonomic function, and therefore they possibly contribute to low blood pressure and/or orthostatic intolerance (autonomic dysfunctions) after BS [27].

Interestingly, the nutritional deficits that occur due gastrointestinal events, besides being associated to

systemic neurological involvement, may affect the gastrointestinal tract itself as well. A case of a 44 years-old man with a history of biliopancreatic diversion who developed peripheral neuropathy (progressive paresthesia in both upper and lower limbs) and brown bowel syndrome was reported. Brown bowel syndrome consists in the deposition of lipofuscin in muscle layers of the small bowel and is usually caused by chronic vitamin E deficiency (which, among its causes, BS is an important one) [30].

Another neurological complication that must be reminded in patients who underwent BS is acute porphyria, since poor energy intake, which happens after BS (hypocaloric diets and/or malabsorption), is a substantial trigger for acute porphyria attacks [31,32]. Unexplained abdominal pain is an important initial sign. It is usually severe, diffuse and remittent and may be accompanied by nausea and vomiting [31,32]; and the association with peripheral neuropathy (sensorimotor neuropathy, muscle weakness in upper and lower limbs), confusion and/or hallucination may orient diagnosis [31,32]. In Lopes, et al. (2008) and Bronkovsky, et al. (2008) case reports, time of onset was three and four weeks after the surgery, respectively (Table 1).

Conclusion

Peripheral neuropathies are important, although underdiagnosed, complications of bariatric surgery. Unfortunately, the prevalence of the many possible presentations is still unknown. For now, it seems that nutritional deficiencies are the most important causes; but it lacks epidemiological studies, leading to much divergent data. Physicians should be aware of the development of peripheral neuropathies after BS and should be careful about the nutritional status (correctly replacing nutrients before and after the surgery) to avoid the aforementioned complications. Further studies about peripheral neuropathies after BS are needed, especially prospective cohorts about SFN in BS patients.

Acknowledgments

Declaration of conflicting interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

Ethical approval and patient consent

N/A.

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