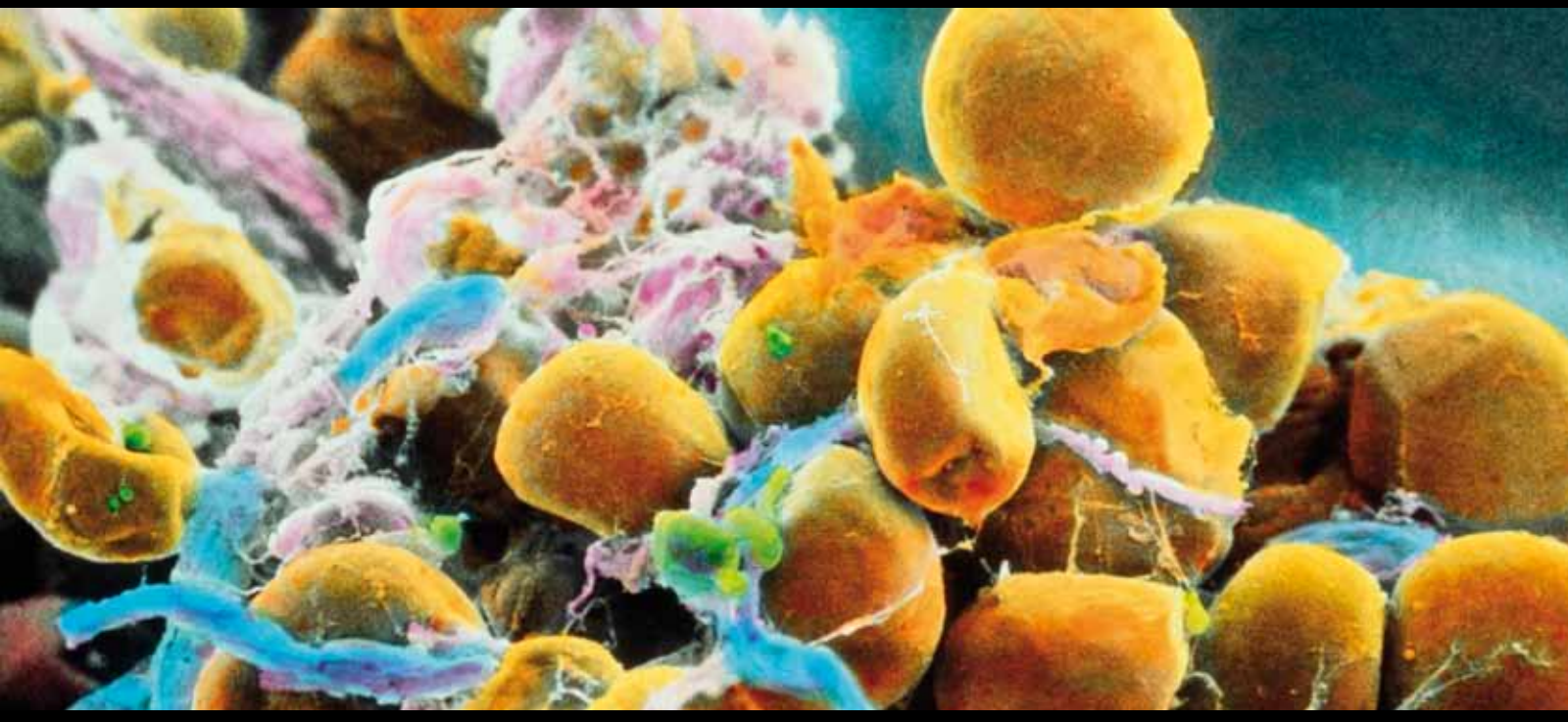
Journal of Obesity

Optimizing Outcomes in Bariatric Surgery: A Primer in Patient Selection

Guest Editors: Natan Zundel, Sayeed Ikramuddin, and Raul Rosenthal



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Editorial Board

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Editorial

Optimizing Outcomes in Bariatric Surgery: A Primer in Patient Selection

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We are very pleased to introduce a series of six individual papers addressing important areas in bariatric and metabolic surgery. Particularly, these papers highlight patient selection, preparation for surgery, and optimizing outcomes. The metabolic benefits of surgery are well established, but adequate patient selection can help realize better outcomes for our patient population. The first paper reviews the impact of inflammatory gene polymorphisms on bioelectrical parameters in obese subjects specifically looks at outcomes of single-nucleotide polymorphisms of IL-6 on body composition following the laparoscopic adjustable gastric banding. The authors have demonstrated that these polymorphisms lead to improved outcomes following bariatric surgery whereas gene-wide association and screening is not an accepted modality today; it certainly will be something that is easily and readily available for patients in the next few years and will be obtainable in a pharmaceutical store.

Y. F. Wei and colleagues evaluate the candidacy of morbidly obese patients with pulmonary dysfunction for bariatric surgery. Pulmonary dysfunction is a broad topic and classically it has been understood that the impact on sleep apnea is a dynamic and rapid improvement in many patients, but not all patients; however, other diseases such as pulmonary fibrosis pose significant clinical problems for a number of surgeons and in this context the authors provide some meaningful insight into care in this patient population.

D. K. Kadeli and colleagues address an important question that asks payers, policy makers, and surgeons alike, what is the role of preoperative weight loss and its impact on long-term weight loss at one year? Whereas the authors acknowledge that a low-calorie diet preoperatively can enhance perioperative safety by reducing the size of the liver and physiologically stabilizing the patient, this specific review addresses the notion of preoperative weight loss impacting long-term weight loss. The results are intriguing in that they suggest that initial weight, that is, weight at the time of surgery, indicates an important starting point with a weight loss proportional to that at the time of nadir suggesting that weight loss preoperatively may, in fact, result in improved outcomes postoperatively at one year.

Fourth, D. A. Becker and colleagues examined the neurologic complications of nutrition deficiency following bariatric surgery. Whereas the incidence of this appears to be low, nutritional deficiencies can result in significant potential neurologic compromise in these patients. The authors outlined the best evidence in terms of outcome and some of the more esoteric yet clinically relevant aspects of neurologic deficiency and how these can be addressed, diagnosed, and managed.

C. E. Owers and colleagues address steps to optimize perioperative care of patients undergoing bariatric surgery. Here, the authors discussed the important role of low-calorie diets in shrinking the liver, the importance of the use of a multidisciplinary team in evaluation of patients, and appropriate control of comorbid illnesses. This is an excellent review of salient topics in this area.

Finally, an important area that has not been addressed adequately in the literature to date is the impact of the sleeve gastrectomy on a super morbid obese group. J. M. Catheline and colleagues review their outcomes on weight in this population demonstrating durable and significant outcomes of the sleeve gastrectomy in the super obese population.

In this group of 30 patients, in which they had followup on 23 at 18 months, 77% of patients were defined to have sufficient weight loss, with insufficient weight loss in the remaining six patients requiring either resleeve or conversion to a gastric bypass. This suggests that for super obesity a more robust operation may be indicated as a first procedure and that certainly these patients are amenable to an operation such as the duodenal switch.

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Clinical Study

Weight Loss after Sleeve Gastrectomy in Super Superobesity

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Objective. This prospective study evaluated laparoscopic sleeve gastrectomy for its safety and efficiency in excess weight loss (%EWL) in super superobese patients (BMI > 60 Kg/m^2). *Results*. Thirty patients (33 women and 7 men) were included, with mean age of 35 years (range 18 to 59). Mean preoperative BMI was 66 Kg/m^2 (range 60 to 85). The study included one patient with complete situs inversus and 4 (14%) with previous restrictive gastric banding. The mean operative time was 120 minutes (range 80 to 220 min) and the mean hospital stay was 7.5 days (4 to 28 days). There was no postoperative mortality or need for a laparotomy conversion. Two subphrenic hematomas, one gastric fistula, and one pulmonary embolism, were the major complications. After 18 months 17 (77%) had sufficient weight loss and six had insufficient results, leading to either re-sleeve gastrectomy (3), or gastric bypass (2). Three years after the initial laparoscopic sleeve gastrectomy, the mean EWL was 51% (range 21 to 82). *Conclusion*. The laparoscopic sleeve gastrectomy is a safe and efficient operating procedure for treating super superobesity. In the case of insufficient weight loss, a second-stage operation like resleeve gastrectomy or gastric bypass can be proposed.

1. Introduction

Surgery is the only effective treatment of morbid obesity. It is accepted that surgical treatment of super superobese patients (BMI > 60 kg/m^2) and high-risk patients with comorbidities, is responsible for an increased risk of postoperative morbidity and mortality after bariatric surgery [1, 2].

Sleeve gastrectomy is a recently used surgical technique, with an acceptable rate of postoperative complications [3]. It has been described as a first step before a gastric bypass or biliopancreatic diversion with duodenal switch [3]. The restrictive technique of sleeve gastrectomy reduces the gastric capacity by approximately 80%. In his study, we report our experience with sleeve gastrectomy in super superobese patients.

2. Methods

This is a prospective study that included 30 consecutive super superobese patients and was designed to study the efficacy and safety of the sleeve gastrectomy in this group of these patients. The patients were operated between May 2004 and November 2009. For the 30 super superobese patients, we evaluated: the duration of intervention, the early (less than 30 days) and late postoperative complications, hospital stay, loss of excess weight (% EWL), and the need for a second operation in the case of insufficient weight loss.

All patients were operated by laparoscopy, and they were placed in the operating table according to the French position (the surgeon was positioned between the legs of the patient). Each intervention involved six trocars. The gastrocolic ligament was opened 4 cm from the pylorus. The greater curvature of the stomach was freed with the Ligasure (Covidien, Norwalk, CT, United States) until the angle of Hiss. The left crura of the diaphragm was systematically visualised and posterior attachments of the stomach released. A 34 French boogie was introduced into the stomach and positioned along the lesser curvature. The stomach was cut with an incision parallel to the boogie using a linear stapler (Endo GIA 45 Covidien, 4.8 mm, Norwalk, CT, United States). In each case, the resected stomach was placed in a plastic bag and was extracted via the umbilical trocar. Staple line was consistently reinforced by a nonabsorbable suture (Endostich Surgidac-2/0, Covidien, Norwalk, CT, United

Kingdom). The fascia of each port site greater than 12 mm in diameter was always closed. A methylene blue test was performed to eliminate a leak. A drain was placed along the staple line. An upper gastrointestinal contrast study was performed the third postoperative day. Cautious refeeding was permitted in the absence of fistula, and patients were discharged after removal of the drain. Iron, vitamin, and essential mineral supplements were systematically given to the patient at their discharge.

3. Results

Thirty patients underwent a laparoscopic sleeve gastrectomy, 23 women and 7 men. The average age was 35 years. All patients were super superobese with a mean BMI of 66 kg/m^2 (range from 60 to 85 kg/m^2). The average preoperative weight was 168 kg (range 140–258 kg). Comorbidities are summarized in Table 1. One patient had a complete situs inversus and 4 others (14%) had previous gastric banding.

Mean operative time was 120 minutes (range 80 to 220 min). There was no conversion to laparotomy and no postoperative mortality. The average length of hospital stay was 7.5 days (range 4–28 days). Immediate postoperative complications occurred in 4 patients (14%): two presented subphrenic hematomas, one developed a gastric fistula, and one had pulmonary embolism. All three surgical complications required the creation of a laparoscopic drainage with no need for further surgical treatment.

The mean followup was 24 months. Of the 23 patients that had a followup greater than 18 months, weight loss was satisfactory in 17 patients (77%). Six patients had insufficient weight loss defined by a BMI between 35 to 40 kg/m^2, progressive weight regain or persistence of comorbidities supposed to improve with further weight loss. If the patient gave his consent for a second operation, then a gastrointestinal contrast study was performed, in the presence of a dilated gastric pouch due either to incomplete gastric resection or to the persistence of hyperphagia responsible for a mechanical dilation a resleeve was proposed, otherwise, the choice of a gastric bypass was made (Figure 1). The choice of resleeve as a revisional surgery was made for 2 reasons firstly it is reasonable to reoperate a stomach when there is still a secondary gastric pouch a known cause of weight loss failure and secondly, resleeve according to our previous experience, although we do not have a long term followup, has been shown to have better results associated to less morbidity and mortality rates for superobese patients [4]. Three out of six patients were reoperated with a resleeve gastrectomy, and two with a gastric bypass surgery 18 to 23 months after the initial procedure. The last patient refused a second operation. Three years after the original sleeve gastrectomy, the average loss of BMI was 20 kg/m^2 (range 10 to 39 kg/m^2, Figure 2). The average percentage of excess weight loss at 3 years was 51% (range 21–82%, Figure 3), while the average weight loss was 56 kg (range 28–144 kg) (Figure 4). During the followup, a port site hernia requiring surgical treatment was observed in 2 patients (7%). There were no other complications or iron and vitamin nutritional deficiencies during the followup.

Table 1: Co-morbidities of the 30 super superobese patients.

	Nb patients	%
Sleep apnea syndrome	17	58%
Hypertension	15	50%
Arthritis	15	50%
Diabetes	13	42%
Dyslipidemia	13	42%
Asthma	6	21%
Stress incontinence	1	3%

4. Discussion

Perioperative risks (morbidity and mortality) are known to be high for patients with super superobesity. The multidisciplinary team preoperatively should carefully evaluate the benefit/risk ratio of bariatric surgery in any given patient. Gastric banding presents less risk but is also less effective in super superobese patients [5]. Gastric bypass and biliopancreatic diversion although associated to a higher morbidity ratio demonstrate excellent efficiency in regard to weight loss [6]. The Magenstrasse technique uses a longitudinal section of the stomach without gastric resection has been proposed in super superobesity because of its lower morbidity and mortality [7]. This procedure that divides the stomach into two compartments should be distinguished from sleeve gastrectomy, the technique reported in this paper. Preliminary results showed that the sleeve gastrectomy, after a 24-month period postroperatively was equally effective as gastric bypass in terms of weight loss in the super superobese patients while presenting lower risk for complications (3,6% to 9% resp.). The frequency of complications after gastric bypass in the super superobese can reach up to 23% [8] and up to 38% for duodenal switch [6]. In the super superobese patients, the death rate was assessed up to 2.7% after gastric bypass [8] and 6.25% after duodenal switch [6]. Among our 30 patients, we had 3 immediate postoperative complications like hematoma or fistula that were successfully treated with laparoscopic drainage. Current studies on the sleeve gastrectomy have published an average followup of less than 3 years [7, 9, 10] while two separate studies [6, 9] using a stapler line reinforcement, that is, the same technique with our team, reported also no postoperative morbidity and mortality.

The initial rapid weight loss, reported by previous studies [4, 9, 11], reached a plateau at 18 months after surgery [11]. We found the presence of insufficient weight loss in only 23% of patients at 18 months. In our group of 30 patients, 23 had a followup more than 18 months, 5 had a second operation 3 of them had a resleeve gastrectomy and 2 a gastric bypass. It is known that the sleeve gastrectomy in the super superobese can be a definitive treatment for an average loss of excess weight by 50% at one year [3, 10]. We have shown that the sleeve gastrectomy for the super superobese can allow an average loss of excess weight by 53% at 18 months. If weight loss was insufficient, the sleeve gastrectomy could then be followed by a second operating procedure, like gastric bypass [3] or biliopancreatic diversion [9]. The second operation

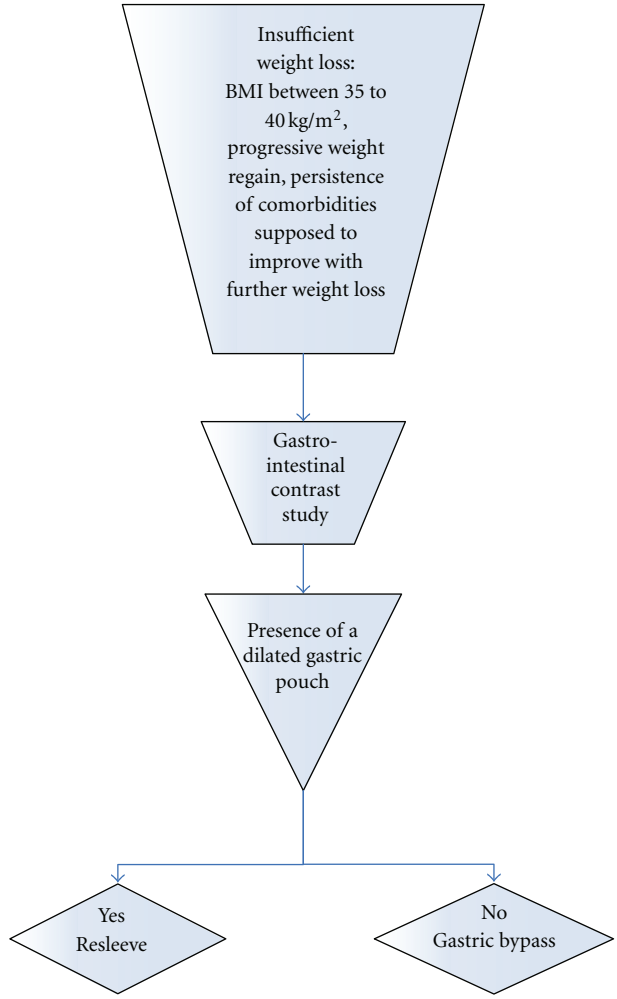

Figure 1: Decisional algorithm for the choice of revisional operation in the case of insufficient weight loss.

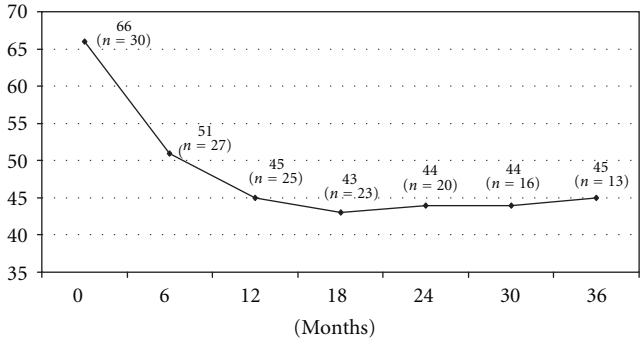

Figure 2: BMI evolution (Kg/m^2).

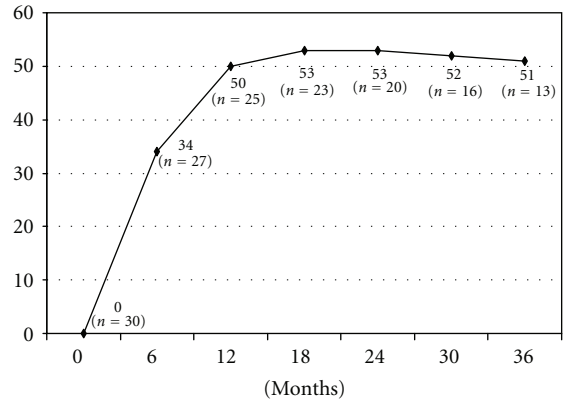

Figure 3: Variation in percentage of excess weight lost (% EWL).

presented less technical difficulties thanks to the weight loss already achieved since the first sleeve gastrectomy. Five patients were operated for a second time, three of them had a resleeve gastrectomy, and two a gastric bypass as a second-step procedure. Although we present a small group in this study, there were no postoperative complications associated to the excellent weight loss and these results demonstrate the efficacy as well as the safety of the second intervention.

It is known that bariatric surgery provokes weight loss through dietary restriction or through the malabsorption it imposes. The mechanisms responsible for decreased appetite are poorly understood. To make things more complicated some of the excellent early results like the decrease in blood sugar and insulin resistance seem to be independent from

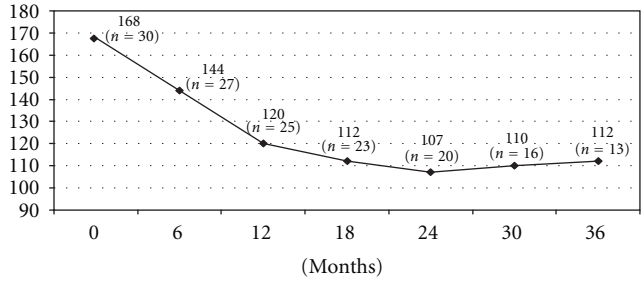

Figure 4: Weight evolution (Kg).

the weight loss [12]. A great interest has been reported for the role of ghrelin [13], a hormone that is secreted by the gastric fundus a part of the stomach that is largely resected in a sleeve gastrectomy. Ghrelin is secreted under the influence of cholinergic stimulation and has probably a major role in controlling appetite since its receptors are present in the pituitary and hypothalamus. In humans, the serum concentration of ghrelin is increased in anorexia nervosa, Prader Willi syndrome, and in patients with a reduced caloric diet [13]. Ghrelin's concentrations are decreased by food intake and after gastrectomy or gastric bypass [13, 14]. The absence of contact between food and the lining of the stomach producing ghrelin inhibits its secretion [14]. In the case of sleeve gastrectomy, the removal of the ghrelin-producing area could eventually explain the weight loss. This effect was reversed experimentally by the exogenous administration of ghrelin [15]. Two separate studies reached the same conclusions with our team and have provided evidence for both an early and late ghrelin decrease after the sleeve gastrectomy [16, 17]. These specific hormonal mechanisms leading to weight loss need to be further elucidated [18].

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Review Article

Perioperative Optimization of Patients Undergoing Bariatric Surgery

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Bariatric surgery is fast becoming an efficient and safe method of weight reduction, especially for patients in whom conservative measures have failed. As the obese population of the world increases, so will the number of patients requesting or requiring surgical weight loss methods. Bariatric patients however have numerous co-morbidities that make their operative course more difficult, and therefore is important to have a good understanding of the important issues surrounding their pre, peri and post operative management. This article aims to educate the reader about optimal management of the bariatric surgical patient.

1. Introduction

As the number of bariatric patients increases and surgical procedures become safer and more efficient, the number of patients considering bariatric surgery is likely to continue to climb. The latest UK survey conducted by the Department of Health in 2009 showed that 61.3% of adults (aged 16 or over), and 28.3% of children (aged 2–10) in England were overweight or obese [1]. A further report, known as "The foresight report" issued in 2007 predicts that if no action was taken, 60% of men, 50% of women, and 25% of children would be obese by 2050. Current UK guidelines recommend bariatric surgery be offered to patients who have a BMI (body mass index) of >40 kg/m^2, or >35 kg/m^2 with a significant obesity-related comorbidity such as diabetes or hypertension, although delivery of this varies significantly.

Conservative approaches to managing obesity such as dieting, exercise, and cognitive behavioural therapy produce significant durable weight loss in only a minority of highly motivated patients. Drugs such as orlistat lead only to modest weight loss of approximately 4–8 kg [2, 3] and can have unpleasant side effects such as steatorrhoea and diarrhoea, making compliance with medication as an issue. In patients where these lifestyle modifications have failed, surgery may be a valid option. However, bariatric surgery is not without a significant risk.

2. Preoperative Optimisation

It is important that when evaluating patients for bariatric surgery, they are managed by the multidisciplinary team because of the complexity of both their physiological state, but their psychological health too [4]. This may include a number of health professionals including diabetologists, specialist nurses, specialist dieticians, and psychologists as well as the surgeons and anaesthetists.

Bariatric operations, like many types of elective surgery, carry mortality risks, and although mortality risks are decreasing with routine postoperative high-dependent care and improving technologies, the obese population should be considered a high mortality risk. Therefore, bariatric surgery should only be performed in high-volume specialist centres. The UK's First National Bariatric Surgery Registry published data from 2009-2010—only 7 postoperative deaths were recorded from a total of 7, 045 operations. There were no deaths from gastric banding or sleeve, and roux-en-y gastric bypass showed mortality risk of 0.2%, which compares favourably with the best internationally published data.

Bariatric patients have a high number of cardiovascular and respiratory co-morbidities associated with their high BMI. Before considering surgery, it is important to assess the significance of these associated pathologies as this will

affect not only the type of surgery offered, but will have a significant impact on the anaesthetic and their recovery. Although worldwide consensus as to the best operations for minimizing comorbidities differs, many operations have been shown to contribute to significant reduction of obesity-related diseases.

Significant co-morbidities include type II diabetes, hypertension and stroke [5], hyperlipidemia [6], heart failure [7], atrial fibrillation/flutter [8, 9] venous thrombosis [10], and obstructive sleep apnoea [11–17]. In many cases, weight loss of approximately 5–10% can be associated with marked reductions in the risk of these chronic diseases [18]. A report issued by the Diabetes Prevention Program showed that a weight loss of about 5-6% among persons with a BMI of 34 kg/m^2, along with increased physical activity, resulted in a 58% reduction in the incidence of diabetes [19]. When considering the type of operation best for people with type 2 diabetes, consideration must be given to the restrictive or malabsorptive components of surgery. The biliopancreatic diversion and duodenal switch have been shown to improve glycaemic control in up to 100% of patients [20, 21], but these operations are associated with significant malnutrition. The gastric band has a more modest type 2 diabetes remission rate (50–56%) [22], gastric sleeve 50–90% [23, 24], and roux-en-y gastric bypass has been shown to have an average remission rate of 83%. Therefore when selecting an operation, clinicians should be aware of the patient's hypoglycaemic control.

All patients should be encouraged to lose weight before their surgery [25]. Small amounts of weight loss result in substantial reductions in visceral fat with a marked improvement in the ease of any subsequent bariatric procedure. Preoperative weight loss also establishes a patient's ability to comply with postoperative dietary regimens and may serve as a predictor for long-term success for the operation [26].

Morbidly obese patients are at high risk for developing DVT postoperatively following any operation—this has been shown to be as high as 2.5 times the risk as in a patient of healthy weight [27]. This can be attributed partly to the limited ambulation of obese patients, but also because of the inflammatory component of obesity [28, 29]. A rare but serious occurrence is pulmonary embolism, occurring in approximately 1% to 2% of cases [30], but which carries a 20% to 30% mortality [31]. Although no consensus exists on the practice prescribing pre- and post-operative subcutaneous anticoagulation, in many centres this is considered a routine practice. Some surgeons recommend preoperative lower extremity duplex testing for the presence of established DVT before performing bariatric operations. When found, an inferior vena cava filter can be placed to minimize the risk of postoperative pulmonary embolism [26]. The UK's National Bariatric Surgery Registry Report demonstrated that in 2009-2010, 4 patients had a documented postoperative pulmonary embolus, and there were 3 recorded DVTs.

Hypertension is one of the most common co-morbidities associated with obesity with approximately 40–70% of bariatric patients needing treatment [32, 33]. Mechanisms proposed to explain the contribution of obesity to the development of hypertension include an altered renin-angiotensin-aldosterone system, increased intra-abdominal pressure [34], increased sympathetic nervous system activity, development of insulin resistance, hyperleptinemia, leptin resistance, altered coagulation factors, as well as inflammation and endothelial dysfunction [33, 35]. Patients, in conjunction with their primary care physician, should aim to have their hypertension well controlled before undergoing any surgical procedure, especially bariatric surgery. Many patients who suffer from hypertension will have an element of cardiac failure. The combination of increased adipose cells and increased lean muscle mass in obese patients results in high cardiac output and an increased circulating volume, also contributing to hypertension. Weight loss caused by caloric restriction or surgery promotes favorable hemodynamic changes referred to as reverse remodeling. Regression of left ventricle (LV) mass and chamber size after weight loss has been shown universally. Some evidence suggests that the greatest regression of LV mass and hypertrophy may occur when weight loss is combined with beta-adrenergic blocker therapy [36]. Opinions must be sought from a specialist if the cardiac history is complex. Patients often have a poor exercise tolerance often due to arthritis and general poor mobility rather than cardiovascular disease, although any evidence of heart failure should warrant a transthoracic echo (TTE). Due to the amount of adipose tissue, poor views are most often found during this test. Transoesophageal echo (TOE) is a better investigation, but is not universally available.

Obstructive sleep apnea (OSA) has a prevalence of 77% among obese patients [37]—a neck circumference of more than 17 inches in men and 16 inches in women is a good predictor of OSA [38]. Since the majority of obese patients prior to bariatric surgery will exceed these measurements, routine polysomnography testing for all patients prior to surgery is recommended [37]. Most anaesthetists require OSA patients to use a CPAP (continuous positive airway pressure) machine for a time before the operation, although there is no consensus about the length of time in which this should be used. Patients with more complex sleep disorders such as obesity hypoventilation syndrome will need post-op BIPAP and are at a higher risk.

Optimisation of many of the known risk factors must include early implementation of an attitude of healthy lifestyle in the months prior to surgery. This encourages patients to adopt health promoting behaviours early on, which can be continued postoperatively increasing the success of the operation. Advice regarding regular physical exercise for 30 minutes a day will aid cardiac function as well as insulin control. Dietary advice regarding low fat, low salt, and high vegetable diets will decrease atherosclerosis in the long term (although unlikely to impact in the months prior to surgery), as will cessation of all smoking. In many centres, patients attend seminars preoperatively that have a strong input from a specialist bariatric dietician, who can advise on pre- and post-operative nutrition.

A higher prevalence of nutritional deficiencies was found amongst people with morbid obesity. Nutritional assessment is, therefore, a key prior to surgery to minimize postoperative complications [39]. The most prevalent deficiencies were

iron, ferritin, folic acid, and the presence of anemia, with high PTH levels reflecting low levels of vitamin D [40, 41].

Steatohepatitis frequently accompanies morbid obesity and can cause hepatomegaly; 33% of morbidly obese patients show fatty infiltration in more than 50% of hepatocytes [42]. This may result in difficulty viewing as well as risk of severe bleeding during laparoscopic surgery. The use of a 2-week VLCD (very low-calorie diet) preoperatively has been shown to cause significant weight loss if the patient complies with the liquid diet. Furthermore, an improvement in hepatomegaly associated with steatohepatitis is noted, if there is significant weight loss (>3 kg fat loss in 2 weeks) [42]. VLCDs are dietary preparations that provide all nutritional requirements together with between 1850 and 3250 KJ (450 and 800 Kcal) per day. An individual takes this meal replacement three times daily as a substitute for breakfast, lunch and dinner [43]. Obese people typically achieve a mean weight loss of 1.5–2.5 kg per week using a VLCD [44]. A 2001 meta-analysis concluded that, after using a VLCD, subjects maintained a significantly greater weight loss at compared to hypocaloric balanced diet [45, 46]. The added benefit is that these special diets may also help with several obesity-related comorbidities by reducing levels of total cholesterol, low-density lipoprotein, triglycerides and blood glucose and by reducing blood pressure [44], insulin resistance [46], and hepatic steatosis [47].

All patients should undergo an appropriate nutritional evaluation, including selective micronutrient measurements [48], enabling correction of any deficiencies and optimization prior to the operation.

3. Perioperative Considerations

Most bariatric patients will have a difficult airway because of the neck circumference. However, if the patient is positioned appropriately during the anaesthetic, the incidence of difficult intubations is not higher than in the general population. Simple considerations, such as the transfer and positioning of the bariatric patient, become more complicated in the morbidly obese patient. Patient positioning is paramount. Sufficient manpower must be available to help transfer the anaesthetized patient from a bed to the operating table, and special inflation mattresses have been designed for this purpose. In a review of 155 patient safety incidents involving bariatric patients, 27 involved injury to staff as a direct result of difficulties with moving and handling [49]. Pressure points must be carefully padded, as any resulting pressure sores in patients who are at high risk of poor tissue healing can be troublesome [50].

Bariatric procedures are usually performed laparoscopically unless there is a contraindication such as previous extensive abdominal surgery. Therefore, patients are usually placed in a steep reverse Trendelenburg position, so care must be taken to ensure that patients are adequately restrained and are not likely to slip or fall off the table during surgery. Although offering a slight respiratory advantage [51, 52], this position, however, exacerbates venous pooling in the limbs, decreasing venous return and contributing to the high risk of venous thromboembolism. Using lower extremity compression devices, both during and after surgery, can decrease this risk. Often, morbidly obese patient's legs are too large for standard theatre compression stockings, so special foot pumps can be used. These devices can remain in place while the patient is in stationary during the postoperative period [53].

During the course of laparoscopic surgery, carbon dioxide must be insufflated into the abdomen. In nonobese patients, this is usually a pressure of 12 mmHg; however, this pressure is rarely sufficient to create enough space to perform bariatric surgery. Pressures of up to 15 mmHg are routine during surgery [54], occasionally up to 20 mmHg.

The high pressures required to insufflate the abdomen during laparoscopic bariatric surgery can cause significant operative concerns to both the surgeon and the anaesthetist. The anaesthetic itself severely affects respiratory function, making adequate pulmonary ventilation and oxygenation difficult by decreasing the functional residual capacity [55]. The functional residual capacity of patients has been shown to be closely related to BMI. Increased pressures within the abdomen cause splinting of the diaphragm, further exacerbating this effect. The use of continuous positive airway pressure (CPAP) preoperatively can maintain oxygenation of patient's and control apnoeic episodes as well as aiding anaesthetic management of a difficult airway.

Complications can arise during routine laparoscopic surgery, such as bowel injury during trocar insertion, and pneumothorax. Given the higher pressures used during bariatric surgery and the decreased reserves of the bariatric patient, the anaesthetist and surgeon must have a high index of suspicion for events such as extraperitoneal insufflation, gas embolism, and surgical emphysema as these may exacerbate the strain already placed on the patient [51].

3.1. Postoperatively. In the immediate postoperative setting, most patients are managed at a high dependency unit, especially if they have a history of asthma or obstructive sleep apnoea. Some institutions use the Montefiore Obesity Surgery Score (MOSS) to help decide on which patients need IUT/HDU. These criteria include patients after gastric bypass, those with a BMI of >50 kg/m^2, male sex, previous abdominal surgery, and significant comorbidity including sleep apnoea [55].

Most patients are provided with a PCA (patient-controlled analgesia) device, which allows them to stay in control of their pain. This helps with ambulation and breathing exercises, both of which are important to avoid thrombosis and respiratory problems such as atelectasis or infection. The analgesic ladder should still be adhered to, as simple measures such as paracetamol can provide a good background pain relief.

There must be a high index of suspicion of thrombotic events for any patient that complains of breathlessness, pleuritic chest pain, swelling of the limbs, or haemoptysis. Given the prothrombotic nature of obesity and the difficulty mobilizing postoperatively, the risk of thrombosis is increased. In our centre, all patients, unless contraindicated

are given thromboprophylaxis for 10 days after discharge from the hospital in order to reduce this risk. Pulmonary embolism (PE) is the most common cause of postoperative mortality, quotes around 1-2% [56, 57]. PE can be difficult to diagnose in the postoperative bariatric surgery: patients often present with profound hypoxia and hypotension, making it difficult to distinguish a PE from a postoperative leak.

Postoperative anastomotic leaks are also quoted at approximately 1-2% [56, 57]. This may be due to technical failure, or occasionally a staple line bleed causing a haematoma, which can cause the anastomosis to fail. Patients may mount signs of sepsis, although abdominal pain can be absent if analgesia is adequate. Given to poor tissue healing of bariatric patients due to inflammatory processes and poor nutritional states, these patients may be at a higher risk of anastomotic leak than nonobese patients. Again, there should be a high index of suspicion for leak. Many surgeons perform a leak test by injecting methylene blue dye down the nasogastric tube, although this may not determine which anastomoses are likely to fail postoperatively.

Bariatric surgery candidates are at risk for numerous vitamin and mineral deficiencies in the postoperative period due to altered eating patterns and malabsorptive consequences of the operation [29, 39, 58–65]. Postoperative nutritional deficiencies can depend on the type of surgery performed with fewer deficiencies with restrictive procedures (such as adjustable gastric banding and vertical banded gastroplasty, which is no longer routinely performed in the UK) as the entire gastrointestinal tract is retained [58].

In contrast, patients after gastric bypass are prone to deficiencies of the fat-soluble vitamins (A, D, E, and K) and calcium as well as an increased risk of developing anaemia secondary to deficiencies of iron, vitamin B12, and folate necessitating the indefinite supplementation of daily multivitamins [59, 60].

The partitioning of the stomach during bariatric surgery results in a dramatic decrease in the production of hydrochloric acid, affecting the absorption of calcium and iron [61]. Malabsorption of calcium and vitamin D occurs from bypassing these segments of intestine during bariatric operations. The malabsorption of vitamin D contributes further to calcium malabsorption. With a relative lack of calcium, the production of parathyroid hormone (PTH) is increased, which leads to the release of calcium from bone, potentially causing bone loss and long-term risk of osteoporosis [29]. For this reason, early bone densitometry testing, although not routine, would be sensible [61].

The duodenum is the primary site for absorption of iron and may be bypassed. Ferric iron consumed in the diet can be absorbed as ferrous by the use of ascorbic acid supplementation, which aid the acidic environment for conversion of iron [37, 63, 64]. Monthly vitamin B12 injections supplement levels of a vitamin whose absorption may be impaired due to decreased intrinsic factor, which is produced in the parietal cells of the stomach [39, 64].

Deficiencies of thiamine occur frequently in patients with good weight loss postoperatively. Thiamine stores are limited, is absorbed in the proximal small intestine and may become deficient after a combination of reduced intake, frequent vomiting, and malabsorption [29]. This may cause Wernicke's disease with irreversible neuropathy or death. Supplementation of a minimum of 10 mg thiamine during periods of rapid weight loss can prevent these serious consequences [39, 65].

Average inpatient stay in the UK according to the National Bariatric Service registry is 3 days. After that patients are discharged, but continue under the care of the bariatric services as an outpatient. Patient followup varies between units and surgeons. Currently in our unit, patients are followed up after bariatric surgery for 2 years. After this, if the patients have no complications, their followup is referred back to primary care. Patients who experience complications from their surgery often continue with followup as deemed appropriate by their surgeon.

4. Conclusion

Bariatric surgery is fraught with complexities that need careful consideration. All members of the multidisciplinary team must be involved throughout all stages of assessment, surgery, and followup. Weight loss surgery is associated with a decrease in obesity related co-morbidities, which often are not seen in lifestyle changes alone. Patients must be fully counselled on the operative and postoperative sequelae of surgery so that they understand the risks. Ensuring that patients are fully optimized before their surgery and receive the appropriate levels of care during and after their operations is paramount.

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Review Article

The Neurological Complications of Nutritional Deficiency following Bariatric Surgery

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Neurologic complications of bariatric surgery have become increasingly recognized with the rising numbers of procedures and the increasing prevalence of obesity in the US. Deficits are most commonly seen with thiamine, vitamin B_{12}, folate, vitamin D, vitamin E, and copper deficiencies. The neurological findings observed with these nutritional deficiencies are variable and include encephalopathy, optic neuropathy, myelopathy, polyradiculoneuropathy, and polyneuropathy. We review the neurological complications of bariatric surgery and emphasize that these findings may vary based on the specific type of bariatric surgery and time elapsed from the procedure.

1. Introduction

The rate of obesity continues to rise and affects more than one-third of the US adult population (over 72 million people) [1]. One of the most effective treatments for obesity and its associated comorbidities is bariatric surgery because of its dramatic and durable results. According to the American Society for Metabolic and Bariatric Surgery, the number of bariatric surgeries has increased more than 10-fold, from 16,000 in the early 1990s to approximately 220,000 in 2008 [2]. However, as the prevalence of obesity and the numbers of patients undergoing bariatric surgeries rise, the incidence and recognition of neurologic complications from bariatric surgery also continues to increase. There is a growing literature to support the effectiveness of bariatric surgery in reducing morbidity and mortality for those with BMI >40 and for patients with BMI >35 and obesity-related complications [3]. Further growth of this surgical field is supported by the recent FDA approval for the expanded use of the lap-band system to include patients with a minimum BMI of 35 kg/m^2 without comorbidities and 30 with comorbidities. Associated bariatric procedures contribute to nutritional deficiencies by restricting food intake and/or limiting intestinal absorption. The forms of surgery that are solely restrictive include gastric banding and vertical banding. The procedures that are restrictive and produce malabsorption include the Roux-en-Y gastric bypass procedure and the biliopancreatic diversion with duodenal switch. After these surgeries, patients should remain on high protein and low-fat diets with vitamin supplementation and have nutritional and metabolic blood tests performed on a frequent basis. In addition, it is important to note that nutritional recommendations and complications tend to be associated with the specific type of bariatric surgical procedure performed (Tables 1 and 2) [4–6].

Neurologic complications of bariatric surgery have an estimated incidence of up to 16% per year and need to be discussed with patients who are considering surgery [7]. Neurological deficits are most commonly associated with nutritional deficiencies that develop following surgery. The most commonly described nutritional deficiencies include

Table 1: Complications and prevalence of nutritional deficits specified according to the particular type of bariatric surgical procedure.

	Adjustable gastric band	Roux-en-Y	Duodenal switch
Complications	(i) Food intolerance or noncompliance (ii) Band slippage which can result in vomiting leading to B_1 deficiency (iii) Pouch dilatation (iv) Band erosion into the stomach	(i) Anastomotic leak (ii) Stomal stenosis can lead to vomiting (iii) Bowel obstruction (iv) Micronutrient deficiencies	(i) Malabsorption of fat soluble vitamins (A, D, E, and K), iron (ii) Protein-energy malnutrition
Vitamin A	Occurs	Occurs	Common: 50% after 1 yr, up to 70% after 4 yrs
Vitamin B_1	Rare but occurs	Rare but occurs	Rare but occurs
Vitamin B_{12}	Uncommon	Common: 12–33%	Rare but occurs
Folate	Uncommon	Uncommon	Uncommon
Iron	Uncommon	Common: 20–49%	Rare but occurs
Calcium	Uncommon	May occur: 10–25% by 2 yrs, 25–48% by 4 yrs	May occur: 10–25% by 2 yrs, 25–48% by 4 yrs
Vitamin D	Uncommon	Common: 17–52% by 2 yrs, 50–63% by 4 yrs	Common: 17–52% by 2 yrs, 50–63% by 4 yrs
Vitamin E	Uncommon	Uncommon	Uncommon
Vitamin K	Uncommon	Uncommon	Common: 50–60% after 1 year
Copper	Occurs but often unrecognized	Occurs but often unrecognized	Occurs but often unrecognized

Table 2: Postoperative vitamin supplementation recommendations differentiated by the specific type of bariatric surgical procedure.

	Adjustable gastric band	Roux-en-Y	Duodenal switch
Vitamin A	Supplementation may be required, monitor	5,000–10,000 IU/d	10,000 IU/d
Vitamin B_1	Acute: 100 mg/d × 7–14 d (IM) then 10 mg/d (oral) Prophylaxis: 50–100 mg/d	Acute:100 mg/d × 7–14 d (IM) then 10 mg/d (oral) Prophylaxis: 50–100 mg/d	Supplementation may be required, monitor
Vitamin B_{12}	Supplementation may be required, monitor	300–500 μg/d (oral) 1000 mg/q 3 months (IM)	Supplementation might be required, monitor
Folate	400 μg/d	400 μg/d	400 μg/d
Iron	Supplementation may be required, monitor	65 mg/twice daily	65 mg/twice daily
Calcium	Supplementation may be required, monitor	1,500–2,000 mg/d	1,800–2,400 mg/d
Vitamin D	Supplementation may be required, monitor	800–1,200 IU/d	2000 IU/d
Vitamin E	Supplement with standard multivitamin formulation rich in vitamin E (60 IU/d)	Supplement with standard multivitamin formulation rich in vitamin E (60 IU/d)	Supplement with standard multivitamin formulation rich in vitamin E (60 IU/d)
Vitamin K	Supplementation may be required, monitor	Supplementation may be required, monitor	300 μg/d
Copper	Oral (1 mg/d) or IV fusion, response variable	Oral (1 mg/d) or IV fusion, response variable	Oral (1 mg/d) or IV fusion, response variable

Table 3: Specific neurological complications associated with vitamin deficiencies after bariatric surgery.

Vitamin/nutrient	Incidence	Complications
Vitamin A	10%	Xerophthalmia, night blindness, and decreased immunity
Vitamin B_1	"Common" <1% symptomatic	Wernicke's encephalopathy, Korsakoff syndrome, and Beriberi (dry/wet)
Vitamin B_{12}	30–70%	Myelopathy, neuropathy, dementia, and depression
Folate	1–10%	Macrocytic anemia and fatigue may aggravate B_{12} deficiency
Vitamin D	50–60%	Myopathy
Vitamin E	Rare	Peripheral neuropathy, myopathy
Copper	Rare because undiagnosed	Myelopathy, sensory ataxia
Vitamin B_2	14%	Burning feet syndrome
Vitamin B_6	17%	Polyneuropathy

thiamine (B_1), B_{12}, folate, vitamin D, vitamin E, and copper deficiencies [3]. Risk factors for nutritional complications include vitamin noncompliance, protracted vomiting, and excessive alcohol consumption [3, 8]. The associated complications can involve many areas of the nervous system and include encephalopathy, optic neuropathy, myelopathy, polyradiculoneuropathy, and polyneuropathy (Table 3) [3, 8]. As a preventative measure, guidelines suggest that patients (regardless of the type of procedure) should take multivitamins that contain 400 μg of folate (1 to 2 tablets per day); calcium citrate (1,200–2,000 mg/d); vitamin D (400 to 800 units per day, but higher doses have been advocated in the range of 1000 to 2000 units per day); elemental iron (40–65 mg/d); vitamin B_{12} (300–500 μg/d of the oral crystalline form; dose and route are dependent upon levels). The standard recommendation for postoperative supplementation for thiamine in symptomatic patients is 100 mg/d $\times$ 7–14 d (IM) and then 10 mg/d (oral) until complete recovery of neurologic symptoms. The standard recommendation for daily oral supplementation after surgery in asymptomatic patients is 50–100 mg/d (Table 2) [4–6, 9, 10].

2. Vitamin Deficiencies

2.1. Thiamine (B_1). Thiamine deficiency can occur within 8 to 15 weeks after surgery but has been reported as early as 6 weeks [11, 12]. The mechanism is related to inadequate vitamin repletion along with persistent, intractable vomiting [13]. Deficiency can occur despite oral supplementation if emesis is present because it prevents effective absorption. Vitamin B_1 deficiency can cause lactic acidosis, reduced oxygen uptake, and depression of transketolase activity [14]. It alters mitochondrial function by impairing oxidative metabolism and diminishes vitamin B_1-dependent enzymes, resulting in selective neuronal cell death [15]. Thiamine deficiency is pertinent in the development of both acute and chronic encephalopathies such as Wernicke's encephalopathy and Korsakoff's syndrome. Wernicke's encephalopathy is associated with nutritional polyneuropathy (dry beriberi), ophthalmoparesis and nystagmus, ataxia, and confusion. Permanent impairment of recent memory, known as Korsakoff's syndrome, may result [14]. Recovery typically occurs within 3 to 6 months of initiation of therapy if the symptoms are recognized early [16]. If thiamine deficiency is not discovered early, patients may be left with permanent deficits including ocular motility abnormalities, ataxia, and mental status changes.

2.2. Cobalamin (Vitamin B_{12}). Deficient vitamin B_{12} levels may not appear for several years after bariatric surgery, since liver stores are sufficient to provide for years after initial dietary insufficiency. Low vitamin B_{12} levels following gastric bypass have been associated with inadequate intake, impaired hydrolysis of dietary protein, and defects in the amount of intrinsic factor or the interaction between intrinsic factor and vitamin B_{12} [17, 18]. The absorption of vitamin B_{12} requires the intrinsic factor derived from gastric parietal cells, acidic gastric pH, and absorption in the ileum, any or all of which may be disrupted after bariatric surgery [13]. Neurologic symptoms commonly seen with B_{12} deficiency include paresthesias, weakness, decreased reflexes, spasticity, ataxia, position and vibratory sense loss, incontinence, loss of vision from optic nerve injury, dementia, psychosis, and altered mood [19, 20]. Severe autonomic symptoms may also rarely occur [21]. The initiation of vitamin B_{12} supplementation within 6 months postoperatively is recommended by most surgical groups in the absence of controlled studies. Oral crystalline vitamin B_{12} at a dose of at least 350 mg/d has been shown to maintain normal plasma vitamin B_{12} levels (78–80) [4, 5]. Optimal dosing of oral, sublingual, or intranasal forms of B_{12} supplementation has not been well studied.

2.3. Folate. Following gastric bypass, folate deficiency can be very rare, occurring in as few as 1% of patients [22]. Folate deficiency has been associated with peripheral neuropathy and myelopathy [23]. Oral folic acid supplementation (400–500 μg/day; recommended 1 mg daily) has been shown to be effective in maintaining levels within the reference range [4, 5, 24, 25]. However, folate supplementation can mask underlying B_{12} deficiency, leading to the progression of neurological damage [25].

2.4. Vitamin D. Vitamin D deficiency has been associated with secondary hypocalcemia after gastric bypass and is commonly associated with complaints of chronic nonspecific musculoskeletal pain. Marinella described a patient who developed symptoms of intermittent facial twitching and

ophthalmoplegia in the setting of hypocalcemia years after gastric bypass surgery [26]. The patient responded to calcium repletion. Myopathy has also been attributed to vitamin D deficiency and has been shown to improve with treatment (400–800 units per day) [27], but higher daily doses of vitamin D (1000–2000 units) are frequently used in practice today. Even higher doses may be needed depending upon the level of malabsorption that exists. It is also important to note that vitamin D deficiency can contribute to hypocalcemia in patients who also have direct, primary calcium malabsorption issues. Both hypocalcemia and vitamin D deficiency lead to secondary hyperparathyroidism. Thus, potential calcium and vitamin D absorption deficits need to be considered and effectively treated in these patients. Suboptimal vitamin D levels are common and should be screened for presurgery by measuring 25-hydroxyvitamin D (25-D) levels. Doses of vitamin D and calcium should be adjusted by a qualified medical professional based on serum markers and measures of bone density. Recommended doses of elemental calcium after bariatric surgery range from 1200 to 2000 mg daily, and these usually contain vitamin D as well [4, 5].

2.5. Vitamin E. Low vitamin E levels have been found 6–12 months after surgery but may not appear for 5–10 years [26]. The most common findings associated with vitamin E deficiency include loss of deep tendon reflexes, truncal and limb ataxia, diminished perception of vibration and position, ophthalmoplegia, muscle weakness, ptosis, and dysarthria [28]. Saccadic eye movements may be slow, and progressive gaze impairment may occur. Some patients may have an impairment of medial rectus function and an associated nystagmus in the affected eye. Severe vitamin E deficiency has been associated with sensory axonopathy, radiculopathies, and peripheral neuropathies. Vitamin E neuropathy and myopathy are often treatable, and the recommended daily dose of vitamin E is 400 IU daily [29–31]. The suggested supplementation in asymptomatic postsurgical patients is a standard multivitamin formulation rich in vitamin E [6].

2.6. Copper. Symptoms of copper deficiency are often indistinguishable from those occurring with vitamin B_{12} deficiency. A myelopathy with spastic ataxic gait, symmetrically brisk lower extremity reflexes, loss of vibratory perception to the ankles, and distal pinprick and light touch sensation were reported in a patient 24 years after intestinal bypass surgery [32]. She had normal B_{12} levels, and administration of intravenous copper resulted in clinical improvement in this patient. Other signs associated with copper deficiency include peripheral neuropathy, myeloneuropathy, optic neuropathy, central nervous system demyelination, myopathy, and myelo-opticoneuropathy [33–36].

3. Early/Acute Symptoms of Vitamin Deficiencies

3.1. Polyradiculoneuropathy. Polyradiculoneuropathy, often resembling Guillain-Barré syndrome (GBS) if rapidly progressive, has been associated with vitamin B_1 deficiency and has been seen as early as six weeks after surgery [12]. These patients tend to have axonal degeneration rather than demyelination and a normal CSF protein level [8]. Symptoms are often described as pain in the feet or low back with ascending paresthesias. The symptoms may then progress to leg weakness associated with ataxia, areflexia, and vibratory and proprioceptive sensory loss. Parenteral supplementation, especially with thiamine (100 mg), has also been shown to improve symptoms [8].

3.2. Encephalopathy. Encephalopathy is often an acute, early complication of bariatric surgery that may develop within a few months. Up to 40% of patients presenting with neurologic complications develop encephalopathy, many of whom are deficient in thiamine [3, 8]. While B_{12} deficiency can present years after bariatric procedures, the onset of Wernicke's encephalopathy most commonly occurs during the weeks to months following surgery [37]. Symptoms of Wernicke's encephalopathy are typically preceded by malnutrition, which results from prolonged emesis, although vitamin noncompliance or increased alcohol consumption were also noted [3, 8]. Some studies suggest a genetic predisposition to Wernicke's encephalopathy due to reduced transketolase activity, a thiamine-requiring enzyme [8, 38]. Further research should seek to identify preoperative risk factors, such as genetic testing for transketolase activity, in an attempt to identify patients at risk for development of Wernicke's or other nutritional deficiency syndromes. In addition, MRI findings in postbariatric surgery patients may provide further support for the development of Wernicke's encephalopathy. MRI patterns in these patients have been described and often include T2 prolongation in dorsomedial thalami and periaqueductal gray matter, enhancement of the mammillary bodies, and occasional diffusion restriction [39]. Hemorrhage involving the fornix and anterior thalami has also been seen on MRI imaging of a patient with Wernicke's encephalopathy [40]. Patients with Wernicke's encephalopathy have been shown to respond to intravenous thiamine administration [41]. While the standard dose of thiamine for suspected deficiency associated with neurologic disease is 100 mg intravenously (IV) or intramuscularly (IM), more aggressive replacement may be required. A dose of 500 mg IV three times a day for 2-3 days, followed by 250 mg IV daily until improvement, has been proposed [42, 43]. These doses should then be followed by an oral dose of 50–100 mg daily as long as the patient continues to have nausea, vomiting, diarrhea, and so forth [42]. Patients with a history of bariatric surgery who present with any signs of gastrointestinal distress should receive thiamine preventively [44].

4. Subacute Symptoms

Optic Neuropathy. Optic neuropathy is often associated with copper and B_{12} deficiencies and has been reported to present 1.5–3 years after surgery [3, 8, 11, 33]. Symptoms include blurred vision with central scotoma and other signs of optic neuropathy. Optic neuropathy is often associated with

malabsorption; one patient was reported to have developed optic neuropathy 5 months after stopping B_{12} injections, only to improve once injections of B_{12} were resumed [8].

5. Late Signs and Symptoms

5.1. Myelopathy. Myelopathy in the setting of nutritional deficiency is commonly seen and frequently can be one of the most debilitating problems associated with bariatric surgery. The problem usually starts insidiously and later in the post-op course, on average 9 years after surgery. It is often attributed to B_{12} deficiency but has also been associated with copper, folate, and vitamin E deficiencies [8, 11, 36]. Patients present with ataxic gait, spasticity with hyperreflexia, loss of proprioceptive and vibratory sensations, and loss of pinprick and temperature sensation. It has been shown that treatment with oral or parenteral supplementation is associated with improvement of symptoms [8, 36].

5.2. Peripheral Neuropathies. Peripheral neuropathies of various types have been documented after bariatric surgery. They usually present years later and progress insidiously and should be distinguished from the polyradiculopathies described above that may be seen early in the course following bariatric surgery. Symptoms involve distal, painful paresthesias ("burning feet syndrome") and loss of pinprick and temperature sensation. Vitamin deficiencies most commonly associated with peripheral neuropathies are vitamin B_1, vitamin B_6, vitamin B_{12}, vitamin E, and copper [3, 11]. Patterns have included sensory-predominant polyneuropathy, motor-predominant polyneuropathy, sensory motor polyneuropathy, mononeuropathy, and radiculoneuropathy [7]. The polyneuropathies typically described are length dependent with an axonal pathophysiology. Polyneuropathy secondary to thiamine deficiency classically presents as a symmetric sensory motor axonal polyneuropathy primarily affecting the legs [45]. It is unclear whether nutritional polyneuropathy is due to isolated thiamine deficiency. The neuropathies seen in postbariatric surgery patients may be due to a combination of nutritional deficiencies, as patients are usually deficient in multiple micronutrients. Nutritional supplementation may only be partially helpful in improving the symptoms of malabsorption of vitamin B_{12}, thiamine, and vitamin E [3, 8]. Physical therapy for peripheral neuropathy has also been recommended [13].

Mononeuropathy is also a very common development in patients who have undergone bariatric surgery. Carpal tunnel syndrome is the most common. Less common are ulnar neuropathy at the elbow and radial mononeuropathy. Peroneal neuropathy and lateral femoral cutaneous neuropathy have also been reported [3].

5.3. Myopathy. Myopathy is less frequently reported in the literature but has been observed in patients with decreased global protein, vitamin D deficiency, copper deficiency, or hypokalemia in the setting of bariatric or other gastric surgeries [11]. Thiamine, vitamin E, selenium, calcium, phosphate, and magnesium deficiencies have also been proposed as etiologies for nutrition-related myopathy [46].

6. Discussion

As the prevalence of obesity rises, the number of bariatric surgeries has also increased. Surgery has proved to be a favorable option for treatment because of its cosmetic and durable effects. However, there are a number of neurological complications that can result from bariatric surgery; these are often irreversible [3, 13]. The development of these associated symptoms is not uncommon, and it is therefore important to discuss the potential for these complications with patients. In addition, patients should be educated about possible symptoms that may develop in the first few months after surgery. For example, if they experience acute symptoms of confusion, memory deficits, and rapid progressive weakness, they should notify their providers immediately, and there should be a low threshold for investigation of possible vitamin deficiencies. Preventative measures, including early vitamin supplementation presurgery and continuing postsurgery as well as frequent followup, are important in the management of these patients. Typical nutritional deficiencies reported include thiamine, B_{12}, folate, vitamin D, vitamin E, and copper deficiencies [3]. If a patient presents with any of the neurologic complications discussed above, vitamin deficiencies and metabolic derangements should be investigated immediately.

As the indication for bariatric surgery becomes less stringent, these procedures will likely continue to increase in popularity. Clinicians will need to recognize and manage neurologic complications that may appear years to decades after bariatric surgery. The clinical history, physical examination, biochemical findings, nerve conduction studies, biopsy, and response to therapy will help to come to the final diagnosis and treatment of patients presenting with associated neurologic complications after bariatric surgery. Thus, the importance of vitamin supplementation and patient education and their role in reducing neurologic complications is even more crucial than ever. Prevention of neurological complications after bariatric surgery will involve close followup with routine screening in addition to nutritional supplements. Routine monitoring of selected micronutrients every 6 months after surgery may help detect deficiencies before they become symptomatic and improve overall comorbidities of bariatric surgery.

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Review Article

The Effect of Preoperative Weight Loss before Gastric Bypass: A Systematic Review

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Background. Many insurance companies require obese patients to lose weight prior to gastric bypass. From a previous study by the same authors, preoperative weight at surgery is strongly predictive of weight loss up to one year after surgery. This review aims to determine whether preoperative weight loss is also correlated with weight loss up to one year after surgery. *Methods*. Of the 186 results screened using PubMed, 12 studies were identified. A meta-analysis was performed to further classify studies (A class, B class, regression, and rejected). *Results*. Of all 12 studies, one met the criteria for A class, six were B class, four were regression, and one was rejected. Six studies supported our hypothesis, five were inconclusive, and no study refuted. *Conclusions*. Preoperative weight loss is additive to postsurgery weight loss as predicted from the weight at the time of surgery.

1. Introduction

According to the latest statistics, one out of every three adults (33.8%) in US is obese. Additionally, the rate of morbid obesity is 5.7% in adults [1]. Bariatric surgery is a very effective intervention for the morbidly obese. More than 220,000 people underwent some form of bariatric surgery in 2008 [2]. Age, gender, race, height, initial body weight, postoperative behaviors, type of operation, and surgeon have been reported to affect weight loss following surgery. However, no consideration of factors impacting weight loss outcomes would be complete without attention to the importance of preoperative weight loss. Although the California Department of Managed Care explicitly states that "there is no literature presented by any authority that mandated weight loss, once a patient has been identified as a candidate for bariatric surgery, is indicated," yet the majority of insurance payers continue to require prolonged dietary efforts as a prerequisite to surgical treatment [3]. A reduction in the size of the liver after four weeks of dieting and an increase in ease of surgical exposure are well documented [4, 5]. The impact on overall weight loss is less clear. Numerous papers dealing with the subject provide an array of experimental models that make a comparison of results difficult. Our paper evaluates the existing publications and separates them into four groups for comparison.

In a previous publication, we showed that weight loss in the first year after gastric bypass is a percent of initial body weight [6]. The following review attempts to determine the effect of short-term preoperative weight loss on weight loss following surgery and the effect of initial body weight.

2. Methods

The study was done using PubMed search for those papers which dealt with aspects of preoperative weight loss before bariatric surgery. The search terms used were ("preoperative weight loss" or "pre-operative weight loss" or "preoperative weight" or "pre-operative weight") and ("gastric bypass" (meSH) or "bariatric surgery" (meSH) or "obesity surgery" or "weight reduction surgery" or "predicting").

Each abstract was analyzed to include only those studies which satisfied all set criteria. Criteria for abstract review

were as follows. All studies reviewed were from a peer-reviewed source and published either in English or Spanish. Studies were required to have one of the following designs: randomized control trials, case control studies, or series/cohort studies. Additionally, the majority of study participants had to be greater than 18 years old. Accepted abstracts included both open and laparoscopic cases.

Articles were obtained for the remaining abstracts and were further analyzed. Each article was expected to have more than ten patients in each group of study (preoperative weight loss versus weight gain) or >20 patients in a regression analysis. Information on pre/post-operation weight loss had to be available for article selection. Papers were also excluded that did not stratify the data such that gastric bypass weight loss results were separated from alternate weight loss procedures such as gastric banding or sleeve gastrectomy (Figure 1). The selected studies were further searched for their references to identify more papers pertaining to our study.

The selected studies were divided into different classes: class A, class B, and regression studies. The classification was based on the patient's weight at initial consultation and the weight at surgery. Both class A and class B studies grouped patients into two follow-up cohorts, one that lost weight and the other that did not.

In class A studies, the weight loss and weight gain groups both had the same mean weight at initial consultation but different at the time they went for surgery. This is demonstrated in Figure 2 by using two groups with five hypothetical patients in each group. Both groups initially begin with similar mean weights and differ directly prior to surgery with different average weights (confidence interval 95%).

2.1. Class A Study Supporting/Refuting Criteria. Studies were deemed to support our hypothesis if both groups of patients had a persistent statistical difference in the average weight within the first 12 months, and the mean weight values did not crossover in this time frame. Refuting studies would have crossing over of the means (e.g., the weight loss group having a higher mean weight after surgery at six months than the weight gain group). Inconclusive studies lacked 50% followup during the first year or proper notation to elicit a definitive conclusion.

In class B studies weight loss and weight gain groups had different mean weights ($P < 0.05$) at initial consultation but similar means at the time of surgery. This is demonstrated in Figure 3 by using two groups with five hypothetical patients in each who begin with different weights at initial consultation but eventually enter the surgery with similar mean weights.

2.2. Class B Study Supporting/Refuting Criteria. Studies were deemed to support our hypothesis if both groups of patients did not have any statistical difference in their mean weight for the first 12 months. Refuting studies would have a statistically different differences between the weight loss and weight gain group. Inconclusive studies lacked 50% followup during the first year or proper notation to elicit a definitive conclusion.

2.3. Regression Studies. Regression studies do not have to utilize groups of patients and may look at preoperative weight loss as a variable. In regression studies the patients are no longer grouped into weight loss/gain groups or dieters/nondieters groups. The focus is on individual performance of each patient. The following concept has been explained by using six hypothetical patients who undergo gastric bypass surgery (P1, P2, P3, P4, P5, and P6). Each of these hypothetical patients had different amounts of preoperative weight loss with the exception of one patient who did not lose or gain weight.

The preoperative weight loss is considered to be a continuous variable and can be plotted on the x-axis (Figure 4). The outcome is also a continuous variable percent of initial weight loss, plotted on y-axis (Figure 5) for a period of one year after surgery. For explanation and standardization, we use percent of initial weight at surgery as the outcome for y-axis.

2.4. Regression Study Supporting/Refuting Criteria. Regression studies were judged based on the variables included and the results reported by the authors. Analysis was hampered due to absence of data or modeling protocol. Inconclusive studies were defined as <50% followup or too complex for us to interpret without additional input from the author.

Classification of studies was required to define criteria needed to support and refute our hypothesis.

A flow chart used to arrive at the chosen classification is provided in Figure 5.

3. Results

3.1. Class A Studies. The study by Solomon et al. [7] and Alami et al. [19] was a randomized control trial conducted at Stanford Medical University. The study was done for a year comparing postoperative weights between two groups, one which lost weight preoperatively and other which gained weight. The statistical difference between both groups was maintained up to 3 months. At one year, the patients in both arms of the study showed no difference in excess weight loss. But when patients were divided according to those who had lost at least five percent of their excess body weight preoperatively, the one-year results for excess weight loss were much lower for the weight-loss group. This class-A study shows that weight loss is a percent of initial body weight at the time of surgery (Table 1).

3.2. Class B Studies. In the study by Martin et al. [8], the subjects were divided into dieters and nondieters. Here, also the data show that weight loss after surgery is a percent of body weight at the time of surgery. The only statistically significant difference in mean weight between the two groups was at initial presentation (Table 2). The study by Still et al. [9] was done at Geisinger Medical Center in Danville, Pennsylvania. This study was considered

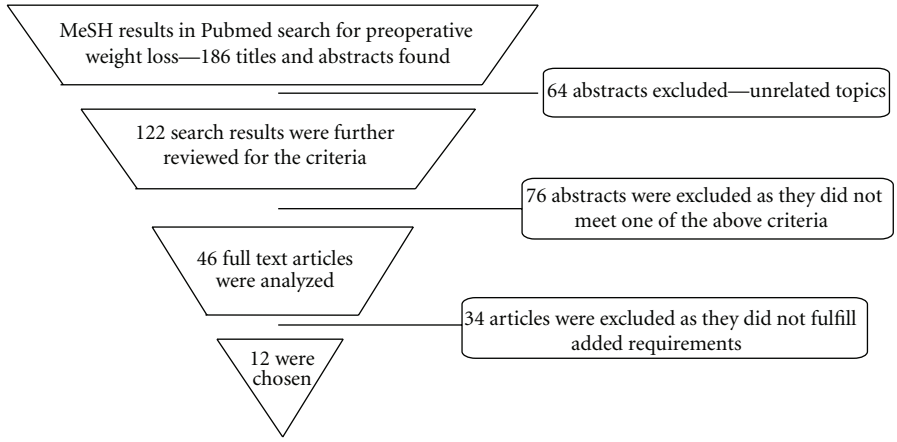

Figure 1: Diagram representing the inclusion and exclusion of PubMed search results.

Table 1: Class A studies.

Lead author	Study design	Group	Patients	Mean age (yr)	Female (%)	Results
Solomon [7]	RCT	WL	26	42.4	88.5%	Supportive
		WG	35	44.9	80.0%	

WL: weight loss; WG: weight gain; RCT: randomized controlled trial.

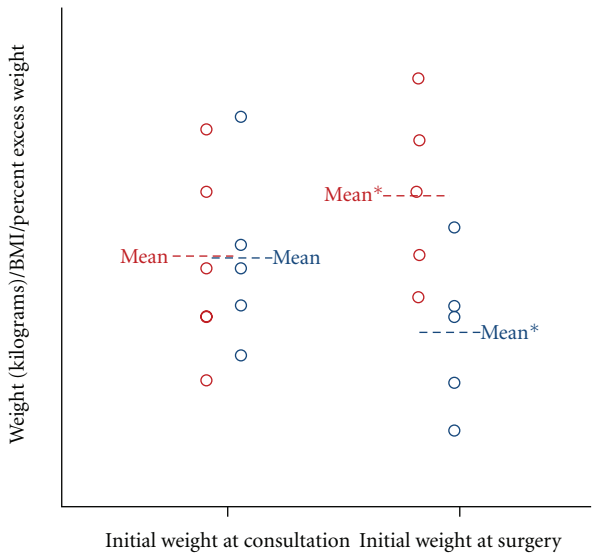

Figure 2: Example of Class A study. Graph showing ten hypothetical patients in Class A study that have been divided into weight loss (blue) and weight gain (red) groups. The weight loss group was statistically different from the weight gain group at surgery. *Confidence Interval 95%.

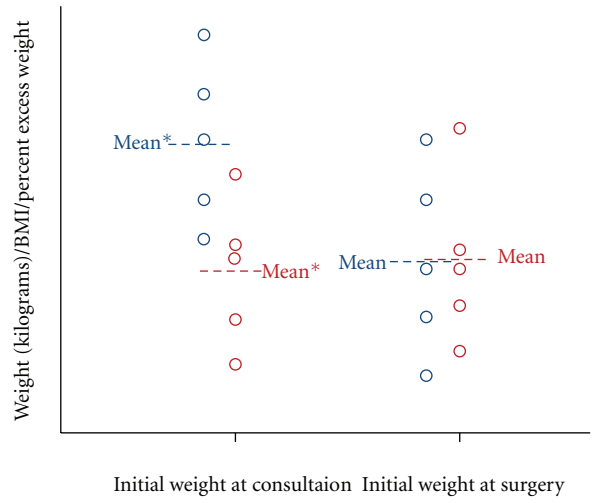

Figure 3: Example of class B study. Graph showing ten hypothetical patients in class B study who have been divided into weight loss (blue) and weight gain (red) groups. The weight loss group was statistically different from the weight gain group at initial consultation. *Confidence interval 95%.

inconclusive because its postoperative assessment was carried out in percentages of patients meeting their weight loss goal as opposed to actual weight values making analysis difficult.

Ali et al. [10] had 351 subjects who were divided into 4 groups based on the percent EWL (excess weight loss). At surgery, no significant differences were found among the 4 groups in total body weight and BMI or EBW except for a BMI difference in group 1 and 3. At 6 and 12 months, no significant difference was found in the total body weight or BMI among the 4 groups indicating again that weight loss is a function of weight at the time of surgery (Table 2).

The study by Fujioka et al. [11] divided the patients into two groups based on whether patients lost or gained weight preoperatively. Both groups had similar mean weights at surgery. When these patients were followed after surgery, no significant differences in the mean EWL were found at any follow-up point in the first 12 months thus supporting our hypothesis. Harnish's et al. [12] study also had similar structure and findings to that of Fujioka (Table 2).

Table 2: Class B studies.

Lead author	Study design	Group	Patients	Mean age	Female (%)	Results
Martin [8]	Prospective	WL (dieters)	47	40.2	74.5%	Supportive
		WG (nondiet)	53	38.8	92.5%	
Still [9]	Prospective	5–10% EBWL	67	43	77.6%	Inconclusive
		5% EBWL	86	43	74.4%	
		0–5% EBWG	137	43	78.8%	
		>5% EBWG	169	45	79.9%	
Ali [10]	Retrospective	WL > 10% TBW	23	42.7	73.9%	Supportive
		WL 5–10% TBW	102	43	87.3%	
		WL 0–5% TBW	135	42.8	95.5%	
		WG % TBW	91	42.1	96.7%	
Fujioka [11]	Retrospective	WL (>0 lbs)	55	49	80.0%	Supportive
		WG (<0 lbs)	66	48	86.4%	
Harnisch [12]	Retrospective	WL (≥10 lbs)	88	44	84.1%	Supportive
		WG (≥10 lbs)	115	41.4	85.2%	
Huerta [13]	Retrospective	WL	15	50	33.3%	Inconclusive
		WG (non-WL)	25	50	28.0%	

WL: weight loss; WG: weight gain; EBW: excess body weight; TBW: total body weight.

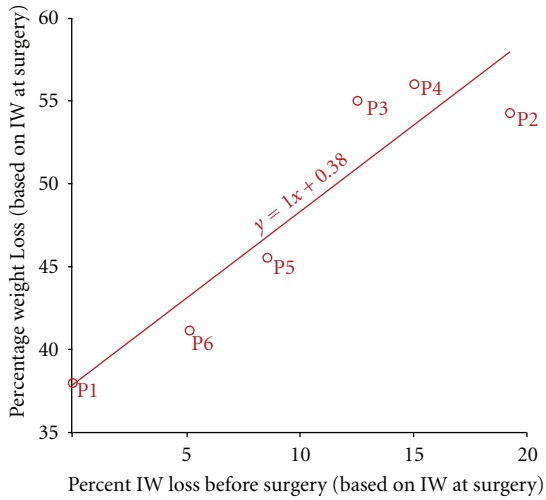

Figure 4: Example of regression. Study includes six hypothetical patients who lost weight preoperatively. The preoperative weight loss is graphed against their complete program weight loss (from initial consultation to one year after operation).

The B class study by Huerta et al. [13] was considered inconclusive as the followup was less than 50% during the first year and only had postoperative data for the second and fourth years after surgery.

3.3. Regression Studies. The study by Alger-Mayer et al. [16], which was done at Albany, NY, was analyzed using regression. Even though the year 3 and 4 results supported our hypothesis, the results were considered inconclusive because the paper lacked postoperative data in the first year after gastric bypass.

The study by Jantz et al. [14] was inconclusive because they were not looking at immediate preoperative weight loss.

Carlin et al. [17] published a paper that changed weight loss requirements based on the initial BMI. Those individuals that had BMI greater than 60 had to lose more than those that were less than 50 kg/m^2. Thus, the study was considered inconclusive due to difficulty interpreting the methodology.

The study by Alvarado et al. [15] identified a 1.8% increase in the % EWL one year after gastric bypass with each 1% total body weight lost preoperatively. This retrospective study was considered supportive due to the positive effect preoperative weight loss would have on postoperative weight loss in the absence of controlling for initial weight at surgery. Results are summarized in Table 3.

3.4. Rejected Studies. The study by Riess et al. [18] was rejected as a study because the weight loss group and the weight gain group had statistically significant difference in mean weight at both initial consultation and the time before surgery. The difference was preserved postoperatively (see Table 4).

4. Discussion

Our study found that weight at the time of surgery, rather than the amount of weight lost preoperatively, determines the weight loss outcome postoperatively. Stated differently, weight at a given time period after surgery is the same percent of initial body weight independent of starting weight. For example, if a patient weighs 160 kg at the time of surgery, he will weigh approximately 62% of that at one year after surgery or 100 kg. If he lost 22.5 kg preoperatively

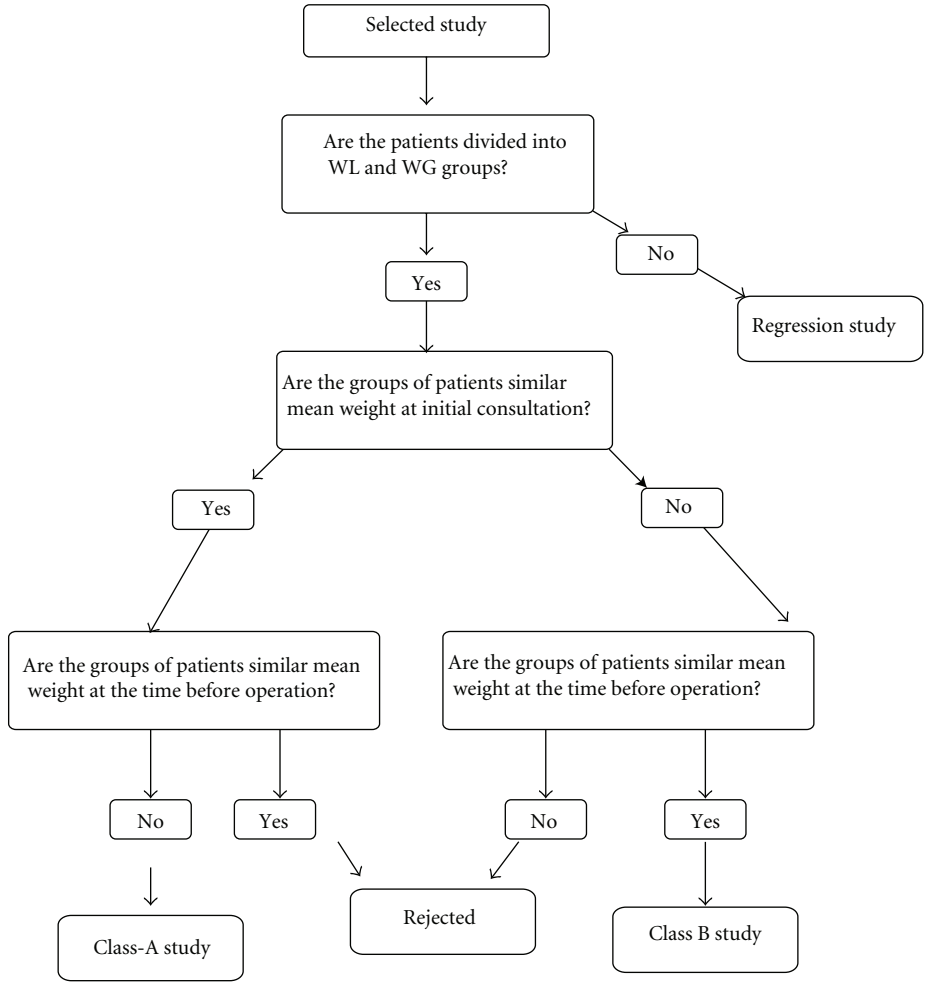

Figure 5: Flow chart depicting the classification of the selected studies into Class A, B, and regression studies. WL: weight loss; WG: weight gain.

Table 3: Regression studies.

Lead author	Study design	Patients	Mean age	Operation type	Female (%)	Results
Jantz [14]	Retrospective	384	43.3	LRYGB	82.5	Inconclusive
Alvarado [15]	Retrospective	90	42	LRYGB	90	Supportive
Sharon Alger [16]	Prospective	150	45.3	RYGB*	80	Inconclusive
Carlin [17]	Retrospective	295	45	LRYGB	88.8	Inconclusive

LRYGB: laparoscopic roux-en-y gastric bypass; *RYGB: Roux en Y Gastric Bypass. the roux-en-y gastric bypass was an open procedure.

and weighed 136 kg at the time of surgery, he would weigh 62% of his initial body weight or 81.5 kg. His overall weight loss would be 13.5 kg greater for having lost 22.5 kg preoperatively. Since weight loss following gastric bypass tends to be negligible after one year, this probably represents a real gain. In this paper, we have detailed two classes of studies, A and B. Combining review data with previous work by Sczepaniak et al. [6], it is possible to create visual representation of both studies. Class A and class B studies are shown in Figures 2 and 3, respectively. Both groups changed in mean weight at initial consultation, one group gaining weight and the other losing weight. Preoperative weight gain and loss were arbitrarily set for explanation purposes. In a B class study it is observed that the means of both the weight loss and weight gain groups is not different for the first year.

With regards to regression study, in the six hypothetical patients, the relationship to preoperative weight loss can now be clearly seen from Figure 6. The more preoperative percent initial body weight loss (based on initial weight at surgery), the more the percent total body weight loss (calculated from

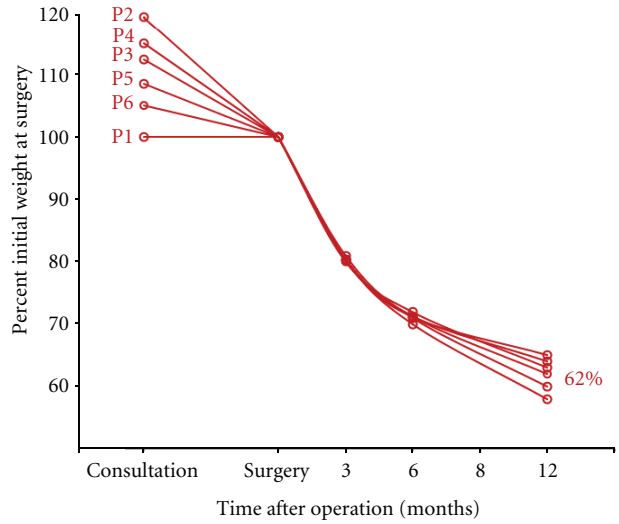

Figure 6: Hypothetical regression model. This model demonstrates the effect of preoperative weight loss in gastric bypass patients.

Table 4: Rejected Studies

Lead author	Study design	Group	Patients	Age	Female (%)
Riess et al. [18]	Retrospective	WL	74	43.4	70.3%
		WG (non-WL)	279	42.7	86.4%

WL: weight loss; WG: weight gain.

subtracting percent total body weight at initial consultation from achieved percent total body weight after surgery), see Figure 6.

From the graph on the hypothetical patients in Figure 4, it is now possible to see the benefit of losing preoperative weight on an individual level.

Our study has only dealt with studies having gastric bypass surgeries, but the preoperative weight loss might have a similar role in sleeve gastrectomy and sleeve plication (also current methods for weight reduction).

Losing weight leads to better outcomes because a patient entering surgery with a lower weight than someone entering surgery without weight loss will have more weight loss in total.

5. Conclusion

Our review of the literature supports the idea that weight loss after surgery for gastric bypass, and by extension other procedures as well, is a percent of initial body weight. Moreover, the literature is generally supportive of the idea that short-term preoperative weight loss is additive, that is, increases the total amount of weight lost.

Conflict of Interests

The authors have no commercial associations that might be a conflict of interest in relation to this paper.

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Review Article

Candidates for Bariatric Surgery: Morbidly Obese Patients with Pulmonary Dysfunction

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Obesity is a well-known major risk factor of cardiovascular disease and is associated with various comorbidities. The impact of obesity on pulmonary function remains unclear. Reductions in chest wall compliance and respiratory muscle strength due to a high percent body fat and localized fat distribution contributes to impaired pulmonary function and the occurrence of adverse respiratory symptoms. Dietary modifications and pharmaceutical agents are not effective in the long-term treatment of obesity. Treatment of morbidly obese patients using bariatric surgery has increased each year, especially after the introduction of video laparoscopic techniques. Effective weight loss after bariatric surgery may improve cardiovascular disease risk factors, including diabetes, hypertension, dyslipidemia, atherosclerosis, inflammation, chronic kidney disease, obstructive sleep apnea, and obesity hypoventilation syndrome. Bariatric surgery has also been associated with significantly improved respiratory symptoms and pulmonary function. We currently present a review of principal studies that evaluated the effects of obesity on pulmonary function and the identification of anthropometric factors of obesity that correspond to the reversal of respiratory symptoms and impaired pulmonary function after bariatric surgery.

1. Introduction

The prevalence of obesity has increased worldwide in both developing and developed countries [1]. The majority of long-term epidemiologic studies have shown that obesity is associated with increased comorbidities such as cardiovascular disease, metabolic disorders, diabetes, cancer, chronic kidney disease (CKD), and immunologic dysfunction [2–4]. Obesity has also been shown to negatively impact the respiratory system and pulmonary function; as well as, being associated with obstructive sleep apnea syndrome (OSAS), obesity hypoventilation syndrome (OHS), and obstructive airway disease [4–6]. Several studies have demonstrated that weight reduction, as a result of dietary modification or surgical intervention, can improve organ dysfunction, health-related quality of life (HRQoL), and overall mortality [3, 7–9].

Bariatric surgery, with dual mechanisms of gastric volume restriction and malabsorption, has been recommended with increasing frequency to treat patients considered morbidly obese [10, 11]. Bariatric surgery affords a rapid, sustained, and safe (operative mortality at 30 or less days was 0.1–1.1%) procedure for effective weight reduction in morbidly obese individuals [7]. Bariatric surgery may improve the overall risk and incidence of cardiovascular disease, diabetes, hyperlipidemia, hypertension, atherosclerosis, inflammation, OHS, and OSAS [7, 12–14]. Bariatric surgery has also been suggested to improve asthma control and reduce the need for pharmacologic interventions [13–16]. Furthermore, there is increasing evidence that bariatric surgery is associated with a significant improvement in respiratory symptoms and pulmonary function [17–25]. Improvements in pulmonary function may be due to a decrease in intra-abdominal pressure, which lends support to the hypothesis that individuals with abdominal obesity may be proper candidates for bariatric surgery in order to improve pulmonary function [25].

Table 1: Respiratory complications of obesity.

Respiratory physiology
↓ Chest wall and lung compliance
↑ Airway resistance
↓ Respiratory muscle strength
↑ Work of breathing
↑ Ventilation perfusion mismatch
↓ Gas exchange
Pulmonary function:
↓ FEV_1, FVC, TLC, ERV, FRC, and RV
↑ → FEV_1/FVC ratio
↓ MVV
↑↓ → DLCO

FEV_1: forced expiratory volume in the first second; FVC: forced vital capacity; TLC: total lung capacity; FRC: functional residual capacity; ERV: expiratory reserve volume; RV: residual volume; MVV: maximal voluntary ventilation; DLCO: diffusing capacity of the lung for carbon monoxide.
↑: increased; ↓: decreased; →: no change.

2. Obesity and Pulmonary Physiology

Obesity has a profound effect on the physiology of breathing, including respiratory mechanics, airway resistance, respiratory muscle function, lung volume, work of breathing (WOB), and gas exchange [5]. A summary of complications associated with obesity is presented in Table 1. Patients classified as morbidly obese typically present with increased metabolic demands due to the additional work required for activities of daily living and to overcome the increased WOB. Elevated WOB is a result of reduced chest wall compliance, commonly associated with the accumulation of fat in and around the chest wall, the diaphragm, and the abdomen [6]. Obesity may also cause a reduction in lung volume, peripheral airway diameter, and alterations in pulmonary blood volume, which may result in a reduction in lung compliance. Reduced respiratory compliance has been shown to result in an increased oxygen cost of breathing; as well as, an increased respiratory drive, both of which may increase dyspnea [21, 26]. Numerous publications have demonstrated an association between obesity and obstructive lung disease, especially asthma. An epidemiological connection between obesity and obstructive lung disease has been described—a meta-analysis has shown that obesity is associated with the incidence of asthma, independent of gender [27]. Airway inflammation, narrowing of the peripheral airways, increased respiratory resistance, and extrapulmonary trigger/aggravating factors, such as gastroesophageal reflux or sleep disordered breathing (SDB), have been proposed as explanations for the increased incidence of obstructive pulmonary disease in obese patients [6].

Body mass index (BMI) can be used to rapidly classify individuals as obese. However, there is increasing evidence that a central pattern of fat distribution (central or abdominal obesity), indicated by a larger waist circumference (WC), waist-to-hip ratio (WHR), or waist-to-height ratio (WHtR), has profoundly more negative effects on the respiratory system than other anthropometric measurements of obesity [28–33]. It has been suggested that abdominal obesity can cause an increase in abdominal and diaphragmatic pressure, altered pleural pressure, and a subsequent decrease in total lung capacity, pulmonary compliance, and pulmonary volume [34]. Sugerman et al. reported a correlation between increased abdominal pressure and WC or sagittal abdominal diameter ($r = 0.74, 0.78$), which was primarily responsible for obesity hypoventilation due to elevation of the diaphragm [35]. Lambert et al. also showed that intra-abdominal pressure correlated to the sagittal abdominal diameter, an index of the degree of central obesity, but not body weight or BMI [36].

3. Obesity and Pulmonary Function

A longitudinal study suggested that a restrictive pattern assessed with a single spirometric test was associated with increased morbidity and mortality [37]. It has been widely reported that obesity can lead to restrictive pulmonary function. This is evidenced by reductions in forced expiratory volume in the first second (FEV_1), forced vital capacity (FVC), expiratory reserve volume (ERV), residual volume (RV), and total lung capacity (TLC) [5, 6, 29, 31, 38–40]. However, the FEV_1/FVC ratio was preserved or increased in these studies. In addition, several studies have shown that excess weight or simple weight gain is associated with pulmonary dysfunction [41–44]. Chen and colleagues analyzed pulmonary function in 1202 healthy adults in a 6-year follow-up study and reported a decline in both FVC and FEV_1 after simple weight gain in both men and women. The effect of weight gain on pulmonary dysfunction has been shown to be greater in men than in women. Using a multiple regression analysis, each kilogram of weight gain was associated with reduced FVC (-26 mL) and FEV_1 (-23 mL) in men, and -14 mL and -9 mL in women, respectively [44]. The impaired pulmonary function may result from air-flow limitations, due to a reduction in the peripheral airway, and an increased abdominal load that alters chest wall mechanics [35, 43, 45]. The increased abdominal pressure may play a greater role in impaired pulmonary function and was suggested to be responsible for the elevation of the diaphragm, thereby producing a restrictive, rather than obstructive, pulmonary dysfunction [35]. An increasing number of studies have also supported the hypothesis that abdominal fat deposition is predictive of impairments in pulmonary function, more-so than BMI [29–32]. Ochs-Balcom et al. conducted a population-based study that assessed the association between pulmonary function and markers of adiposity and body fat distribution, including body weight, BMI, WC, WHR, and abdominal height. Their results suggested that abdominal adiposity (WC, abdominal height) is a better predictor of pulmonary dysfunction than weight or BMI [29]. Additional studies in different ethnic populations from Canada, the United Kingdom, and Taiwan have also demonstrated that WC is significantly associated with decreased FEV_1 and FVC [28, 40, 46].

Maximum voluntary ventilation, a reflection of respiratory muscle endurance and lung mechanics, has been

Table 2: Pulmonary function after bariatric surgery—a review of principal studies.

Authors	Year reported	Country	Case no.	Postsurgery assessment	Weight loss (kg/m^2)		FEV_1 (% predicted)		FVC (% predicted)		P value
					Before	After	Before	After	Before	After	
Weiner et al. [19]	1998	Israel	21	6-month	41.4 ± 1.3	31.77 ± 1.1	83.2 ± 4.8	86.3 ± 4.5	75.6 ± 3.2	84.6 ± 4.3	<0.05
Dávila-Cervantes et al. [20]	2004	Mexico	30	1-year	44.0 ± 4.0	32.0 ± 4.0	89 (54–117)	103 (85–131)	84 (53–116)	97.5 (84–123)	<0.01
Santana et al. [22]	2006	Brazil	39	1-year	52.5 ± 10.5	35.8 ± 9.1%**	92.5 ± 17	104.4 ± 13	93.1 ± 14.9	105.4 ± 13.1	<0.05
Martí-Valeri et al. [23]	2007	Spain	30	1-year	56.5 ± 8.4	32.1 ± 5.9	77.6 ± 14.4	104.2 ± 29.5	82.0 ± 12.7	114.6 ± 15.4	<0.01
Maniscalco et al. [16]	2008	Italy	22	1-year	45.2 ± 4.7	34.8 ± 4.2	83.0 ± 14.4	87.2 ± 14.9	87.8 ± 13.5	95.2 ± 10.7	<0.05
Nguyen et al. [24]	2009	USA	104	1-year	48 ± 6	54 ± 23%**	100 (baseline)	112 ± 16%	100 (baseline)	109 ± 16%	<0.01
Wei et al. [25]	2011	Taiwan	94	3-month	43.4 ± 7.3	35.8 ± 6.5	91.8 ± 15.3	97.7 ± 13.7	92.8 ± 15.0	97.6 ± 13.4	<0.01

* Data are presented as mean ± SD or median (range).
**Weight loss of mean ± SD% of the initial weight.
FEV_1: forced expiratory volume in the first second; FVC: forced vital capacity.

shown to decrease as BMI increases [47, 48]. The reduction in endurance may be related to increased peripheral airway resistance, reduced chest wall compliance and muscle strength, or breathing at low lung volumes [19, 48]. The effect of obesity on gas exchange, which is commonly assessed by diffusion capacity of the lung for carbon monoxide (DLCO), is heterogeneous, and the exact pathophysiological mechanism leading to changes in DLCO remains unclear. Patients classified as obese who present with no clinically apparent heart disease may have a high output state and elevated total- and central-blood volumes, which will increase capillary blood volume, and thereby cause elevations in DLCO [38]. Reduced DLCO has also been observed in obese individuals, which may be due to structural changes in the interstitium of the lung as a result of lipid deposition, alveolar enlargement, cellular hyperplasia, and/or decreased alveolar surface area [5, 49].

Sekhri et al. examined the influence of gender and age on pulmonary function in morbidly obese patients [39]—results showed that being male was associated with a greater negative impact on pulmonary function, and subjects aged greater than 40 years had significantly lower FVC and FEV_1/FVC than those aged less than 40 years. The differential distribution of body fat in men and women, and the direct correlation between abdominal obesity and increasing age may explain Sekhri's results [50, 51].

4. Effect of Bariatric Surgery on Pulmonary Function

The use of surgical procedures for weight-loss when treating morbidly obese individuals has increased dramatically since 1998, especially after the introduction of video laparoscopic techniques (Table 2). Bariatric surgery for individuals considered severely obese has been shown to be associated with decreased comorbidities, reversed the respiratory complications associated with obesity, and reduced all-cause mortality [9]. Several studies conducted in the 1980s reported that weight loss following gastric bypass surgery decreased abdominal pressure and sagittal abdominal diameter resulting in a reduction in pulmonary function and respiratory comorbidities, such as SDB, OHS, and OSAS [17, 52]. Increasing evidence has been become available that emphasizes improved pulmonary function after bariatric surgery [16–24]. Sugerman et al. demonstrated significantly improved lung volumes in 26 patients with OHS after gastric bypass surgery [17]. Thomas et al. reported similar results following weight loss surgery—in 29 patients, a small but significant rise in FVC (7%; $P = 0.002$) and FEV_1 (6%; $P = 0.017$) after a mean weight loss of 34.2 kg (range: 2–64 kg) [18]. Weiner et al. has reported significant increases in FVC in 21 morbidly obese patients following weight loss surgery, with no significant change in FEV_1 and FEV_1/FVC ratio [19]. Dávila-Cervantes et al. described 30 morbidly obese patients with improved FEV_1 (89% to 103%) and FVC (84% to 97.5%) one year after vertical banded gastroplasty [20]. Similarly, Martí-Valeri et al. examined 30 patients with improved FEV_1 (78% to 104%) and FVC (82% to 115%) one year after gastric bypass surgery [23]. Maniscalco et al. also reported an improvement in FEV_1 (83% to 87%) and FVC (88% to 95%) in 12 obese females with asthma one year after gastric bypass surgery [16]. In a study conducted by Santana et al., FVC and FEV_1 were significantly improved in 39 patients following weight-loss surgery. Pulmonary function was improved to a greater extent in patients considered severely morbidly obese (BMI $\geq 60\,kg/m^2$) compared with less morbidly obese patients (BMI: 40–59.9 kg/m^2) [22]. Nguyen et al. examined pulmonary function in 104 morbidly obese patients who underwent either laparoscopic gastric bypass or gastric banding. Restrictive and obstructive respiratory mechanics associated with obesity were significantly improved after surgically induced weight loss and were observed as early as three months after surgery [24]. A recent study conducted by Wei et al. showed that each kilogram of body weight lost aftersurgery was associated with an improvement of 0.28% (9.4 mL) in FEV_1 and 0.23% (9.1 mL) in FVC. In addition, reduced WC was associated with a reversal of impaired pulmonary function—with each centimeter of WC reduction FEV_1 and FVC increased by 0.44% (14.8 mL) and 0.36% (14.3 mL), respectively [25]. In a previous study reported by Zavorsky et al., DLCO was found to improve within 10 weeks of bariatric surgery and was strongly associated with changes in alveolar volume and WHR, an indicator of central obesity [53]. Lastly, a study reported by Oppenheimer et al. showed significant distal airway dysfunction, as detected by impulse oscillometry, in obese subjects despite normal spirometric findings. These abnormalities were significantly improved after bariatric surgery [54].

5. Summary

Therapeutic interventions need balance efficacy against risk. Bariatric surgery is a rapid, sustained, and safe surgical procedure for effective weight reduction in morbidly obese individuals. Overall, effective weight loss by bariatric surgery has been demonstrated to be associated with improved pulmonary function. Individuals with larger WC may be candidates for bariatric surgery in an effort to reverse impaired pulmonary function. Identification of patients who will benefit the most from bariatric surgery to improve other symptoms and clinical associations, such as dyspnea, asthma, OHS, or OSAS, is warranted and requires future investigation.

Conflict of Interests

Y.-F. Wei and H.-D. Wu have no conflict of interests or financial ties to disclose.

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Research Article

Impact of the −174 G > C IL-6 Polymorphism on Bioelectrical Parameters in Obese Subjects after Laparoscopic Adjustable Gastric Banding

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Background. Recent data demonstrated that the −174 G > C IL-6 polymorphism may account for differences in the therapeutic response to laparoscopic adjustable gastric banding (LAGB) surgery. *Objective*. We investigated the impact of −174 G > C IL-6 polymorphism on weight loss, body composition, and fluid distribution changes in obese subjects after LAGB. *Design and Outcome Measures*. Twenty obese subjects were selected and studied at baseline and 3 months after LAGB. Genetic assessment of −174 G > C IL-6 polymorphism and anthropometric and bioelectrical impedance analysis were performed. *Results*. At baseline, C(+) carriers had a lower extracellular water (ECW) and higher intra-CW, phase angle (PA), reactance X_c, and X_c/height. LAGB surgery determined significant reductions in weight and BMI. After LAGB, in C(−) carriers, significant decreases in weight, BMI, and ECW and increases in BCM, BCMI, ICW, PA, and X_c/H were highlighted. In C(+) carriers, significant reductions in weight, BMI, ICW, and PA and increases in ECW, Na/K, resistance (R), and R/height were obtained. Significant higher reductions in BMI and X_c/H were observed in C(+) with respect to C(−) carriers. *Conclusions*. Genotyping of genetic variants, for example, the −174 G > C polymorphism of IL-6, gives the opportunity to predict therapeutic response, in terms of body composition outcomes after LAGB.

1. Introduction

Assessment of body composition plays an important role in clinical evaluation and in monitoring absolute and relative changes during specific therapeutic regimens in obese subjects [1]. The weight losses induced by dietary or surgical treatment are more rapid in the first months and are associated with changes in body composition and fluid distribution [2]. Along with the increased acceptance of surgical procedures for weight loss in obesity, clinically useful baseline and follow-up measures of body composition and fluid distribution are critical to evaluate interventional outcomes.

Bioelectrical impedance analysis (BIA) is an easy-to-use, rapid, and noninvasive method to assess nutritional status and body fluid composition [3]. Whole-body BIA allows the determination of the fluid distribution when using appropriate population, age- or pathology-specific BIA equations, and established procedures [4, 5]. It makes use of formulas that estimate Total body water (TBW) on the basis

of the concept that the human body may be approximated to a cylinder of length equal to body height [6].

Previous data demonstrated that genetic factors which play an important role in the regulation of body weight may account for differences in the therapeutic response to LAGB [7]. The −174 G > C IL-6 polymorphism, which affects transcriptional regulation [8], may be sensed by the homeostatic feedback system that controls energy balance and may in turn contribute to some disturbances in weight regulation, particularly in a situation of negative energy balance, like induced weight loss [9]. We recently provided evidence that the promoter polymorphism of IL-6 (−174 G > C) gene is associated both with body composition and fluid distribution, in obese subjects, at baseline and at 6-month follow-up after LAGB, suggesting that LAGB was less effective if the subjects were carrying risk genotypes (C-carriers) for obesity [10].

The present study aims to investigate the impact of −174 G > C IL-6 polymorphism on nutritional and hydration status in obese subjects, evaluated by anthropometry and bioelectrical impedance analysis (BIA), at 3-month follow-up after LAGB surgery.

2. Methods

2.1. Patients' Recruitment. The study group consisted of 40 Italian Caucasias with obesity, that is, grade II-III obesity according to the World Health Organization criteria [11], consecutively recruited at the San Camillo-Forlanini Hospital (Rome, Italy) from November 2008 to November 2009. Patients desiring surgical intervention for the treatment of obesity were referred to the San Camillo-Forlanini Hospital experienced in the care of obese and bariatric patients to determine the patients' eligibility for surgery on the basis of the international guidelines [12]. Only patients with BMI > 40 Kg/m^2 or with BMI > 35 Kg/m^2 with comorbidities, in whom all appropriate nonsurgical measures failed to achieve or maintain adequate weight loss for at least 6 months, without any psychiatric problem and/or drug or alcohol addiction were admitted to surgery. Exclusion criteria were secondary causes of obesity, pregnancy, antipsychotic medication, eating disorder, severe altered self-body image, and nonrealistic expectations about weight reduction. Psychiatric problems were evaluated on the basis of tests such as eating disorder examination, body dysmorphic disorder examination, and other tests related to general psychopathology [13]. The binge eating scale (BES), an easily administered 16-item questionnaire with a range between 0 and 42, was used to assess symptoms of binge eating. Higher scores indicate greater degree of binge eating severity [14]. Participation in the study included a complete medical history to gather information about health status, current medications history, including supplements of vitamins and minerals, social habits, like alcohol drinking and smoking, appetite, physical activity, and family history for chronic diseases.

Patients were instructed to not modify physical activity during 3 months of follow-up after LAGB. None of the patients was receiving drug treatments at the time of the assessment. If a subject was eligible, an operation was sched-uled after an informed consent was obtained. A total of 30 subjects were eligible and admitted to the intervention and underwent LAGB surgery, an adjustable gastric band (Lap-Band, Inamed, Santa Barbara, CA, USA). A multidisciplinary team (an internist, a cardiologist, an endocrinologist, a gastroenterologist, a psychiatrist, a surgeon, a nutritionist) met each patient and provided an educational session regarding risk and benefits of bariatric surgery and a nutrition and meal-planning guidance. They gave consensus for the study assessments, completed the screening for anthropometry, body composition, and fluid distribution 3 months after surgery and were successfully genotyped for the −174 G > C IL-6 polymorphism. Twenty patients (10 females and 10 males) were selected for data analysis, to obtain homogeneous groups according to gender and IL-6 genotypes.

All patient assessments were conducted in collaboration between San Camillo-Forlanini Hospital and the University of Rome Tor Vergata, Human Nutrition Unit. The collection of DNA as well as the experiments was approved by the Ethical Commission of the University of "Tor Vergata," Rome, Italy. A statement of informed consent was signed by all participants in accordance with principles of the Declaration of Helsinki.

2.2. Dietary Intervention following LAGB. A standardized protocol for meal progression after LAGB was assigned to patients. The acute postoperative diet (first and second day) consisted of noncarbonated clear liquids with no calories, no sugar, and no caffeine. For the first month after LAGB, a semiliquid diet of 850 kcal/d was prescribed (33% proteins, 19% lipids, 48% carbohydrates). One month after LAGB, a solid diet was reintroduced, and the suggested diet was 1200 kcal/d; iron was supplemented on the basis of blood examinations performed during the second month. Diet included 48% carbohydrates (starch or bread), 33% proteins (fat-free parts of different animals and fish), and 19% lipids (olive oil); sweets, cakes, sweetened drinks, alcohol, and animal lipids were forbidden. Compliance of diet (and PA) was reviewed monthly by the multidisciplinary team.

2.3. Anthropometric Measurements. After a 12-hour overnight fast, all subjects underwent anthropometric evaluation. Anthropometric parameters of all the partici-pants were measured according to standard methods (body weight (BW) and height) [15]. Subjects were instructed to take off their clothes and shoes before performing all the measurements. BW (kg) was measured to the nearest 0.1 kg, using a balance scale (Invernizzi, Rome, Italy). Height (cm) was measured using a stadiometry to the nearest 0.1 cm (Invernizzi, Rome, Italy). BMI was calculated using the formula: BMI = BW (kg)/height (m)^2.

2.4. Bioelectrical Impedance Analysis (BIA). Resistance (R), reactance (X_c), impedance, and phase angle (PA) at 50 kHz frequency (Single Frequency, SF) were measured using

Table 1: Description of study population according to genotypes.

Parameters	C(−) ($n = 10$)	C(+) ($n = 10$)
Age[1]	40.50 ± 6.74	43.50 ± 13.37
Gender (M/F)	5/5	5/5
Obesity of II degree (%)	10	9.1
Obesity of III degree (%)	90	89.9
IL-6 (pg/mL)[1]	3.27 ± 0.41	2.85 ± 0.44
BES[1]	2.17 ± 0.98	2.60 ± 0.70

[1]Values expressed as arithmetic $\bar{x}$ ± SD. BES, Binge Eating Scale.

Table 2: Anthropometric and BIA parameters at baseline and week 12 after LAGB.[1]

Parameters	Baseline Total ($n = 20$)	Week 12 Total ($n = 20$)
Weight (Kg)	126.06 ± 23.53	114.17 ± 23.68[3]
BMI (Kg/m^2)	46.05 ± 8.81	41.32 ± 8.41[3]
BCM (Kg)	38.01 ± 8.97	37.72 ± 10.07
BCM (%)	55.71 ± 9.17	56.64 ± 4.26
BCMI	13.61 ± 3.05	13.58 ± 2.52
TBW (L)	50.35 ± 10.01	48.62 ± 10.62[2]
TBW (%)	40.98 ± 7.20	43.90 ± 7.50[3]
ECW (L)	21.27 ± 3.99	20.66 ± 3.84
ECW (%)	42.48 ± 4.30	42.90 ± 4.07
ICW (L)	29.08 ± 6.96	27.97 ± 7.28
ICW (%)	57.53 ± 4.30	57.08 ± 4.04
PA (°)	6.86 ± 1.13	6.73 ± 0.98
Na/K	0.77 ± 0.08	0.80 ± 0.09
R (ohm)	408.65 ± 53.42	422.10 ± 66.74
R/H (ohm/m)	247.75 ± 37.99	256.84 ± 50.70
X_c (ohm)	48.90 ± 8.56	49.15 ± 6.97
X_c/H (ohm/m)	29.57 ± 5.40	29.78 ± 4.73

[1]All values are arithmetic $\bar{x}$ ± SD. BMI, body mass index; BCM, body cell mass; TBW, total body water; ECW; extracellular water; ICW; intra-cellular water; PA, phase angle; R, resistance; H, height; X_c, reactance.
[2]Reflects the significance of the differences between baseline and week 12 determined with a paired t-test ($P \leq 0.05$).
[3]Reflects the significance of the differences between baseline and week 12 determined with a paired t-test ($P \leq 0.001$).

a BIA phase-sensitive system (BIA 101S, Akern/RJL Systems-Florence, Italy). Measurements were taken on left side of the body, with injection and sensor electrodes placed on the hand and foot in reference position. TBW, extracellular water (ECW), intra-cellulat water (ICW), Na/K ratio, PA, body cell mass (BCM), and body cell mass index (BCMI) were calculated from bioelectrical measurements and anthropometric data by applying the software provided by the manufacturer, which incorporated validated predictive equations [16–20].

2.5. DNA Genotyping. Volunteers were genotyped for the −174 G > C IL-6 gene promoter polymorphism. Genomic leukocyte DNA was extracted from peripheral blood according to the standard procedure. The genotyping of −174 G > C IL-6 polymorphism was performed by polymerase chain reaction using primers previously published [21] and was followed by the single-strand conformation polymorphism analysis. The CC and the GC genotypes were grouped and indicated as C carriers (C+), and GG genotype was named as C noncarriers (C−). Among Europeans genotype frequencies are 50% of GG, 35% of GC, and 15% of CC (http://www.SNPedia.com/).

2.6. Statistical Analysis. Data are presented as group means ± SD or percentage. Data were analyzed to check assumptions about the distribution of the measured variables. An χ^2 test was also used to evaluate the Hardy-Weinberg equilibrium of the observed genotype frequencies with respect to the general population. Three genotype groups were first considered to check differences in considered variables between groups. Because a dominant or recessive effect existed, analysis was repeated comparing carriers (C+) versus noncarriers (C−) groups. Comparisons among genotype groups were performed using analysis of variance. A paired t-test was performed to evaluate differences before and after LAGB surgery. All tests were considered significant at $P \leq 0.05$. Statistical analysis was performed using a computer software package (SPSS for Windows, version 13.0; SPSS, Chicago, IL, USA).

3. Results

Table 1 shows baseline characteristics of all the study population according to −174 G/C IL-6 genotypes. According to WHO criteria of obesity, based on BMI evaluation, most of the subjects were obese of II degree at the starting point, before LAGB intervention. According to BES questionnaire, no patients showed binge eating disorders. No association between −174 G > C IL-6 polymorphism and IL-6 plasma levels at baseline was observed. No postoperative complications occurred in selected patients. After surgery, a significant reduction in food intake was observed at the repeated dietary assessments, and the composition of the diet fits quite well with dietary prescriptions, with a good nutritional compliance (data not shown).

3.1. Effects of LAGB on Anthropometric and BIA Parameters. We evaluated the efficacy of LAGB surgery and the effects on anthropometry and body composition by BIA analysis of patients after 12 weeks follow-up (Table 2). LAGB surgery determined significant reductions in weight ($\Delta\% = -9.70 \pm 4.39$, $P < 0.001$) and BMI ($\Delta\% = -10.31 \pm 5.11$, $P < 0.01$). A significant decrease of TBW (L) and an increase of TBW (%) after intervention were observed.

3.2. Genotyping Assessment. The distribution of the IL-6 genotypes in the total screened population ($n = 30$) was compatible with the Hardy-Weinberg equilibrium. The C allele frequency was 35.0%, and the GG, GC, and CC genotype frequencies were 45%, 40%, and 15%, respectively. The study population ($n = 20$) was subgrouped in 2 groups,

Table 3: Anthropometric and BIA parameters at baseline and week 12 after LAGB, according to genotypes[1].

Parameters	Baseline		Week 12	
	C(−) ($n = 10$)	C(+) ($n = 10$)	C(−) ($n = 10$)	C(+) ($n = 10$)
Weight (Kg)	135.65 ± 20.17	117.34 ± 23.79	124.95 ± 21.11[4]	104.36 ± 22.33[4,2bis]
BMI (Kg/m^2)	48.86 ± 9.29	43.25 ± 7.74	44.97 ± 9.20[4]	37.67 ± 5.91[4,2bis]
BCM (Kg)	37.68 ± 8.29	38.27 ± 9.89	40.31 ± 8.65[2]	35.60 ± 11.03
BCM (%)	52.14 ± 5.93	58.63 ± 10.54	56.67 ± 3.29[3]	56.61 ± 5.09
BCMI	13.32 ± 2.50	13.85 ± 3.54	14.33 ± 2.18[3]	12.96 ± 2.71
TBW (L)	52.63 ± 8.26	48.47 ± 11.28	51.73 ± 9.19	46.07 ± 11.44
TBW (%)	40.17 ± 8.20	41.64 ± 6.60	43.30 ± 9.20[3]	44.38 ± 6.22[2]
ECW (L)	23.32 ± 3.37	19.50 ± 3.68[2bis]	21.84 ± 2.89[3]	19.68 ± 4.37
ECW (%)	44.69 ± 3.51	40.66 ± 4.15[2bis]	42.64 ± 3.46[2]	43.11 ± 4.67[2]
ICW (L)	29.21 ± 5.60	28.97 ± 8.18	29.89 ± 6.63	26.39 ± 7.72[3]
ICW (%)	55.31 ± 3.51	59.34 ± 4.14[2bis]	57.36 ± 3.46[2]	56.85 ± 4.61[3]
PA (°)	6.28 ± 0.80	7.34 ± 1.16[2bis]	6.77 ± 0.85[2]	6.69 ± 1.11[3]
Na/K	0.79 ± 0.10	0.75 ± 0.05	0.79 ± 0.09	0.81 ± 0.08[2]
R (ohm)	396.44 ± 54.18	418.64 ± 53.20	393.40 ± 58.96	444.64 ± 64.09[2,2bis]
R/H (ohm/m)	238.59 ± 35.58	255.24 ± 39.90	235.87 ± 41.32	272.33 ± 52.90[2,2bis]
X_c (ohm)	43.67 ± 8.34	53.18 ± 6.23[3bis]	46.90 ± 5.86	51.45 ± 7.16
X_c/H (ohm/m)	26.18 ± 4.58	32.35 ± 4.44[2bis]	27.99 ± 3.06[2]	31.39 ± 5.29[2bis]

[1] All values are arithmetic $\bar{x}$ ± SD. BMI, body mass index; BCM, body cell mass; TBW, total body water; ECW; extracellular water; ICW; intracellular water; PA, phase angle; R, resistance; H, height; X_c, reactance.
[2] Reflects the significance of the differences between baseline and week 12 determined with a paired t-test ($P \leq 0.05$).
[3] Reflects the significance of the differences between baseline and week 12 determined with a paired t-test ($P \leq 0.01$).
[4] Reflects the significance of the differences between baseline and week 12 determined with a paired t-test ($P \leq 0.001$).
[2bis] Reflects the significance of the differences between genotypes at baseline and week 12 determined with an independent t-test ($P \leq 0.05$).
[3bis] Reflects the significance of the differences between genotypes at baseline and week 12 determined with an independent t-test ($P \leq 0.05$).

that is, (C+) and (C−) carriers of the −174 G/C IL-6 gene polymorphism, as defined above.

3.3. Effects of LAGB on Anthropometric and BIA Parameters according to Genotypes. To investigate if genetic profile affects changes occurring after LAGB surgery, we compared anthropometric and body composition changes in subgroup patients according to genotypes. Table 3 shows the analysis of variance of all variables assessed in C(−) versus C(+) carriers, at baseline and at week 12. At baseline, C(+) carriers had a lower ECW (L, %) and higher ICW (%), PA, X_c, and X_c/H. At week 12, a difference in weight, BMI, R, R/H, and X_c/H between C(+) and C(−) carriers was observed.

After LAGB, in C(−) carriers, significant decreases in weight, BMI, and ECW (L, %) and increases in BCM (L, %), BCMI, TBW (%), ICW (%), PA, and X_c/H were highlighted. In C(+) carriers, significant reductions in weight, BMI, ICW (L, %), and phase angle and increases in TBW (%), ECW (%), Na/K, R, and R/H were obtained.

As reported in Figures 1 and 2, we highlighted a strong variability in relative changes of BMI, X_c/H, and R/H, after restrictive bariatric surgery, according to genotypes. Significant higher reduction in BMI ($\Delta\% = -12.63 \pm 4.11$ versus $\Delta\% = -8.00 \pm 5.13$; $P \leq 0.05$), and X_c/H ($\Delta\% = -2.79 \pm 12.51$ versus $\Delta\% = 7.62 \pm 11.63$; $P \leq 0.05$), was observed in C(+) with respect to C(−) carriers.

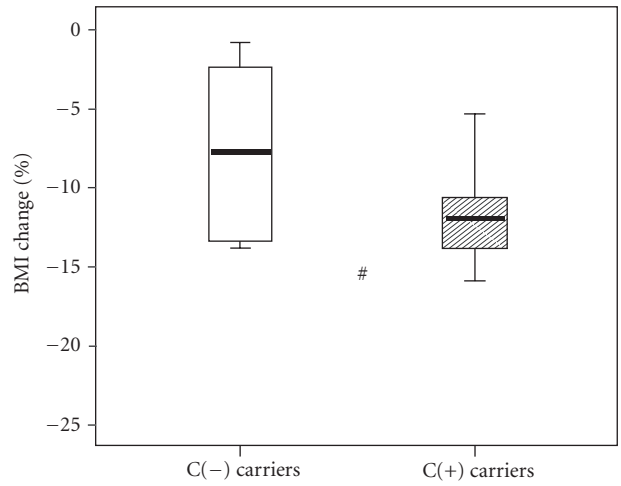

Figure 1: Relative changes of BMI 12 weeks after LAGB, according to genotypes. (Data are expressed as median, SD, and CI. SD, standard deviation; CI, confidence interval. $^{\#}P \leq 0.05$ for C(−) carriers versus C(+) carriers with independent t-sample test).

4. Discussion

Because of several, but not really exhaustive, data regarding the individual response to weight loss interventions,

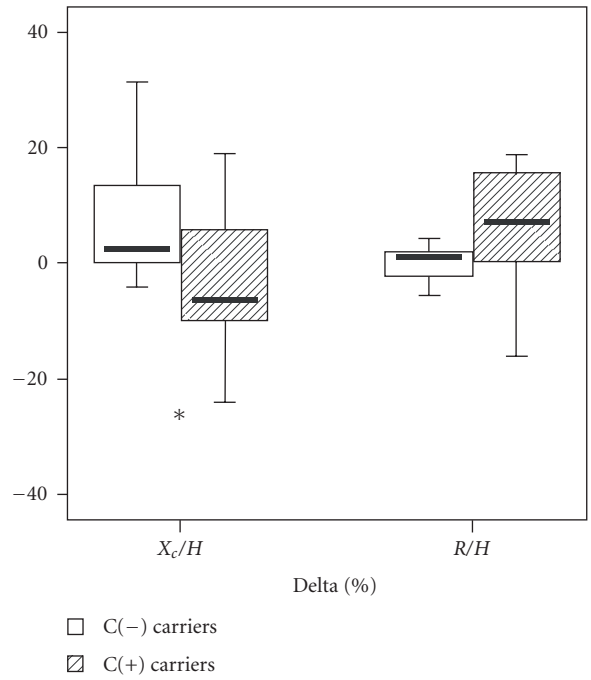

Figure 2: Relative changes of resistance over height (R/H) and reactance over height (X_c/H) 12 weeks after LAGB, according to genotypes. (Data are expressed as median, SD, and CI. SD, standard deviation; CI, confidence interval. $^*P \leq 0.05$ for C(−) carriers versus C(+) carriers with the Mann-Whitney test).

depending on genetic variants, such as the promoter −174 G > C polymorphism of IL-6, the aim of this study was to explore the relationships between body weight, body composition and fluid distribution, and the −174 G > C IL-6 polymorphism in obese subjects, before and 3 months after LAGB.

According to BMI, at baseline, only the 10% of the subjects were affected by obesity of II degree. However, for further investigation we considered the total population taking in account the body composition rather than BMI. Any differences between C(−) and C(+) carriers were observed. The results show that a significant weight reduction in all the study population, 3 months after LAGB, was observed. However, not all subjects showed decrease in weight. On average, individuals who have bariatric surgery lose about 25% of their initial body weight within the first 12 months postoperatively [22, 23]. At 3 months after LAGB, only the 60% of total subjects lost at least 10% of initial body weight. More specifically, there was a higher number of no responders (less than 10% of body weight loss) between C(−) and C(+) carriers (60% versus 20%). Moreover, despite the no significant changes in body composition and fluid distribution, evaluated by BIA, in all the study population, a difference between IL-6 genotypes, both before and after LAGB, occurred. C(−) carriers, other than losing less weight with respect to C(+) carriers (Figure 1, i.e., Δ% of BMI), incurred in significant increases in BCM (Kg, %), BCMI, TBW (%), ICW (%), PA (°), and X_c/H (Figure 2, i.e., Δ% of X_c/H). On the other hand, C(+) carriers showed a lower ECW (%), and higher levels of ICW (%), PA (°), X_c, and X_c/H, at baseline. Differently from C(−) carriers, C(+) carriers reduced ICW (%) and PA (°), without affecting BCM (Kg, %), but increased ECW (%), R and R/H. Therefore, ICW reduction could be a consequence of lean cell shrinking, due to weight loss [1, 2]. SF-BIA permits to estimate TBW, but cannot determine differences in ICW [4]. In fact, SF-BIA primarily reflects the ECW space, which represents a constant proportion of TBW in subjects without significant fluid and electrolyte abnormalities. These findings clearly demonstrate that the −174 G > C polymorphism of IL-6 has an impact on the response to weight loss induced by LAGB, in terms of body composition and fluid distribution outcomes, at 3 months after intervention.

It is important to note that previous studies have shown that during the first months after LAGB, the patients experienced the most dramatic weight loss, because they were very compliant to the administered diet. In this clinical situation, it is possible to reveal the true impact of given genetic polymorphisms or their combination on weight loss after LAGB. Thus, we aimed to explore the impact of −174 G > C IL-6 polymorphism 3 months after LAGB through anthropometry and BIA analysis.

Several mechanisms may explain the association of the −174 G > C IL-6 polymorphism and body composition at baseline and changes after LAGB. IL-6 can regulate energy expenditure centrally, as it is expressed in hypothalamus, and adipose tissue homeostasis [24–28].

To the best of our knowledge, the effect of IL-6 (−174 G > C) polymorphism on body composition, fluid distribution after 3 months of LAGB has not been studied yet. Moreover, even if data on body composition changes after weight loss are numerous, only few studies investigated fluid modifications [1, 2]. Sesti et al. reported that −174 G > C IL-6 polymorphism is associated with increased weight loss in morbidly obese subjects at 6-month follow-up after LAGB [7]. Poitou et al. in 2005 showed a relationship between −174 G > C IL-6 polymorphism and circulating product in morbidly obese subjects, during weight loss after surgery [9]. In our previous study, at 6-month follow-up after LAGB surgery, according to IL-6 genotypes, no differences in fluid distribution were highlighted [10].

Limitations of the present study, which should be considered, include the small sample size. On the other hand, our sample size of 20 subjects represented a very homogeneous group, according to gender and genotypes groups. Secondly, all subjects of the study group underwent the same bariatric intervention, that is, LAGB, associated to a well-balanced low-calorie diet.

Although larger study populations are needed to confirm this observation, this finding is comparable with our previous study [10], which has reported the relationship between the −174 G > C polymorphism of IL-6 and therapeutic response to bariatric surgery.

In conclusion, we demonstrated that genotyping of genetic variants, such as the −174 G > C polymorphism of IL-6, gives the opportunity to predict therapeutic response of obese subjects, in terms of body composition outcomes, through bioelectrical evaluation.

Conflict of Interests

The authors declared no conflict of interests.

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