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Bariatric surgery as a treatment for metabolic syndrome

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Abstract

Obesity is the pandemic of the 21st century. Obesity comorbidities, including hypertension, dyslipidaemia and glucose intolerance define metabolic syndrome, which increases mortality risk and decreases the quality of life. Compared with lifestyles (diet and physical activity) and pharmacological interventions, bariatric surgery is by far the most effective treatment for obesity and its comorbidities. This minimally invasive surgical treatment is based on an increase of satiety (by hormonal regulation and decreasing stomach volume) or a decrease in nutrient retention (gastric and/or intestinal resection). Bariatric surgery has widely demonstrated a beneficial effect on excess body weight loss, cardiovascular risk, dyslipidaemia, non-alcoholic fatty liver disease or glucose homeostasis, among other obesity-related metabolic diseases. This review describes current efforts for the implementation of bariatric surgery in metabolic syndrome, which are mainly focused on the formulation of key definition criteria for targeting the most suitable population for this therapeutic approach. Patients should undergo appropriate nutritional and psychological follow up in order to achieve and maintain weight loss milestones and a healthy metabolic status.

Keywords: bariatric surgery, diabetes, dyslipidaemia, hypertension, metabolic syndrome, obesity

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Introduction

Obesity is a chronic disease characterised by a state of inflammation with elevated inflammatory markers. Physiologically, obesity is defined as an increase in body weight associated with excess adipose tissue accumulation.[1,2] Obesity has become the main health challenge in Western societies with a prevalence of 25% in the UK, and, alarmingly, a prevalence of more than 60% of overweight adults.[2] The main causes of this multifactorial disease are lifestyle (diet and physical activity) and genetic (and epigenetic) inheritance, promoting the development of associated comorbidities and in some cases, malignancies, requiring urgent targeted treatments and strict healthcare control.[3,4,5] As consequences of obesity, the prevalence of insulin resistance and type 2 diabetes, cardiovascular and cerebrovascular diseases, non-alcoholic fatty liver and non-alcoholic fatty pancreas diseases are increasing in prevalence and causing a huge economic burden.[6]

Lifestyle interventions, with or without the combination of weight loss drugs, lead to modest weight loss. However, in most cases, the results are not maintained in the long-term. Bariatrics has been shown to exceed the success of other treatment modalities that are available today against obesity and its comorbidities.[7,8,9] Compared to lifestyle interventions, glycaemic control, dyslipidaemia, cardiovascular risk and quality of life are more likely to improve after bariatric surgery. In addition, bariatric surgery is a long-term cost-effective successful intervention. Indeed, this therapeutic approach has shown a reduction in the relative risk of death by 89% in morbidly obese patients who undergo bariatric surgery, when compared with those who do not.[10]

Metabolic syndrome

Obesity is the main cause of metabolic syndrome. Although the definition criteria of metabolic syndrome can be adapted according to ethnicity or geographic area, the most common criteria in Western societies include waist circumference ≥ 94 cm (male) and ≥ 80 cm (female) plus at least two of the following parameters: hypertriglyceridemia (triglyceride levels > 1.7 mmol/L or > 150 mg/dL), low HDL cholesterol (HDL cholesterol levels < 1.4 mmol/L or < 40 mg/dL [males] and < 1.2 mmol/L or < 50 mg/dL [females]), hypertension (≥ 130 mmHg for systolic blood pressure and ≥ 85 mmHg for diastolic blood pressure) or hyperglycaemia/insulin resistance (glucose levels ≥ 5.6 mmol/L or ≥ 100 mg/dL).[11,12]

Therapeutic interventions in metabolic syndrome can be specified against each one of the associated diseases using,

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for example, anti-hypertensives, statins or hypoglycaemic drugs.[13,14] Obesity remains an elusive therapeutic target. It is widely demonstrated that weight reduction is essential for patients with metabolic syndrome and other obesity-related comorbidities.[9,15,16]

Therefore, to target body weight reduction, most of the treatments are based on dietary interventions, lifestyle modifications, anti-obesogenic drugs, bariatric surgery and a combination of methods.[11,13,14] By far, bariatric surgery is the most effective single therapy. For example, in a study including obese patients with uncontrolled type 2 diabetes, 12 months of intensive medical therapy plus bariatric surgery achieved glycaemic control in significantly more patients than medical therapy alone.[17] Furthermore, in a meta-analysis of randomised controlled trials comparing bariatric against non-bariatric treatment, those patients allocated to bariatric surgery had greater improvement in glucose homeostasis, body weight loss, plasma triglyceride levels and HDL cholesterol.[18] Finally, in a meta-analysis including more than 22,000 patients, type 2 diabetes was improved or resolved in 83% of cases, hypercholesterolemia improved in 96%, and hypertension resolved or improved in 87% of patients who underwent bariatric surgery.[19]

Bariatric surgery

Bariatric surgery improves metabolic syndrome by body weight reduction and, specifically, loss of visceral adipose tissue excessive depots. This improvement and remission of obesity and its comorbidities after bariatric surgery is likely to be due to a combination of body weight reduction associated with gastric volume restriction and malabsorption together with hormonal alterations related to appetite and other metabolic and physiological features. Gastric restriction results in earlier satiety, which leads to a lower food intake thus lowering the glucose load that the body has to manage. Additionally, intestinal resection leads to a malabsortive process and, therefore, a decrease of nutrient (and calorie) availability.[8,20]

There are different types of bariatric surgery interventions. Laparoscopic surgery rather than open surgery is now used in the majority of operations, minimising surgery-associated mortality rates and postoperative complications. The availability of different surgical options means that a more personalised intervention can be offered to patients. The most common procedures carried out in the NHS are laparoscopic adjustable gastric banding , laparoscopic Roux-en-Y gastric bypass and laparoscopic sleeve gastrectomy.[8,9] A study by Angrisani et al. estimated that the total number of bariatric procedures performed worldwide in 2013 was 468,609, of which 95.7% were carried out laparoscopically. The most commonly performed procedure was Roux-en-Y gastric bypass (45%); followed by sleeve gastrectomy (37%), which is the most frequently performed procedure in the USA; and adjustable gastric band (10%).[21] Depending on the specific intervention, the digestive physiology of patients is altered in a different way, with postoperative healthcare and follow up adapted to these specific changes. However, the main goal after all bariatric surgeries is the loss of body weight.

Although the main mechanism of weight loss in bariatric surgery is clearly the restriction of food intake and/or absorption, there are other molecular or metabolic mechanisms involved. There is hormonal involvement implicating gastrointestinal peptides such as glucagon-like peptide 1, peptide YY, ghrelin, gastrin, glucagon and cholecystokinin.[22] It has been shown that following Roux-en-Y gastric bypass, patients had increased postprandial plasma peptide YY and glucagon-like peptide 1 favouring enhanced satiety and insulin release. However, these changes were not observed after gastric banding intervention, which demonstrated that hormonal changes depend on the kind of bariatric intervention.[23]

Moreover, it has been shown that after bariatric surgery, there is a reduction in inflammatory markers such as alpha1-acid glycoprotein, monocyte chemoattractant protein-1, tumour necrosis factor- alpha and C-reactive protein, as well as in oxidative stress markers such as malondialdehyde, superoxide dismutase, catalase, glutathione and disulphide.[24,25] Interestingly, parallel to these physiological adaptations, microbiota profile alterations after bariatric surgery could also affect the physio-metabolic variations of the patient.[26]

Targeting metabolic syndrome by bariatric surgery

Not all patients are eligible for bariatric surgery as most procedures restructure gastrointestinal physiology therefore it may permanently affect normal metabolism. It is necessary to establish threshold criteria for bariatric surgical interventions when dietary/lifestyle and pharmacological interventions are insufficient in improving patients' wellbeing and quality of life.

Currently, bariatric surgery is recommended for patients with a BMI of 40 kg/m^2 or higher and in those with at least a BMI of 35 kg/m^2 and other obesity comorbidities.[8,9] Besides body weight reduction, surgery also results in an improvement of insulin resistance or remission of type 2 diabetes.[17] Thus, bariatric interventions are the most effective treatments for patients with obesity complicated type 2 diabetes. Comparisons between bariatric surgery interventions with intensive medical care point to weight loss as the main factor for long-term diabetes improvement.[17,27] Weight loss associated with bariatric surgery also improves blood pressure and plasma lipid profile as part of cardiovascular risk reduction.[28,29]

Cardiovascular and liver diseases may also benefit from bariatric surgery interventions. There is evidence that bariatric surgery improves non-alcoholic fatty liver disease; however, the procedure is not considered a treatment option for non-alcoholic fatty liver disease.[15] A cohort including more than 6,000 patients who had undergone bariatric surgery, matched with more than 6,000 who had not, presented a

49% lower risk of cardiovascular infarction and 59% lower cardiovascular-related death in the surgery group that in the control group. Furthermore, the risk of death in 5 years was approximately 2% for patients after surgery, compared to 6% in the control patients.[30] Weight loss after bariatric surgery also produces substantial decreases in fasting triglyceride levels, as well as an elevation of HDL cholesterol levels to normality. A cohort of hyperlipidaemic patients after bariatric surgery showed that 96% had a reduction in triglyceride levels and 83% an increase in HDL cholesterol levels.[31]

Bariatric surgery in adolescents

It is disturbing that the prevalence of severe obesity is about 4–6% in US youths.[32] Taking into account the burden of obesity comorbidities and the progressive physiological damage of this situation, although bariatric surgery incurs in a significant initial cost, it could be a cost-effective treatment for adolescents with severe obesity.[33]

A recent study that included 242 adolescents (mean age 17 years) with an average pre-operative BMI of 53 kg/m^2 showed, at 3 years after Roux-en-Y gastric bypass or sleeve gastrectomy, a decrease of 27% of the initial body weight as well as a remission of type 2 diabetes (in 95% of the patients with the condition at baseline), prediabetes (76%), hypertension (74%) and dyslipidaemia (66%).[16] Another long-term study following up adolescents aged 13–21 years, 8 years after bariatric surgery, showed a decrease in BMI from 58.5 to 41.7 kg/m^2, prevalence of hypertension from 47% to 16%, dyslipidaemia from 86% to 38% and type 2 diabetes from 16% to 2%.[34]

Follow up after bariatric surgery

Long-term follow-up is strongly advised to avoid postoperative surgical, nutritional or psychiatric complications.[35,36] In most follow ups, maximal weight reduction and obesity comorbidity improvements are usually observed during the first two years after surgery. However, longer follow up showed that the same trends are observed but the magnitude of the differences get smaller, with some bodyweight regain. Very few bariatric surgery studies report long-term results with sufficient patient follow-up to minimise bias. Gastric bypass has better outcomes than gastric band procedures for long-term weight loss, type 2 diabetes control and remission, hypertension and hyperlipidaemia.[37]

Although bariatric surgery has been the most effective treatment for immediate effect, long-term follow up studies have shown that the initial remission rate of metabolic syndrome associated diseases decreases parallel to time. The Swedish Obese Subjects study described a type 2 diabetes remission rate of 30% at 15 years compared to 72% at 2 years follow up.[38]

Most postoperative problems seem to be caused by a lack of dietary compliance by the patients. Nutritional education and follow up by a professional nutritionist should be mandatory in order to achieve long-term improvement in patients' quality of life. Although nutritional deficiencies are commonly analysed during postoperative follow up, there is a lack of nutritional diagnosis before intervention. Indeed, some of the deficiencies attributed to the procedure, such as iron and vitamin D, could be attributed to a basal malnutrition status.[35,36,39] Assessment should begin before intervention, when a blood profile nutritional assessment should be performed including iron, calcium, phosphorus, folic acid, vitamin B_{12}, alkaline phosphatase, 25-hydroxy vitamin D, parathyroid hormone, total protein and albumin concentrations. With these results, patients should be followed up by an expert nutritionist to establish the caloric, protein, fat, carbohydrate and micronutrients quality and quantity in their diets and the need to reinforce specific dietary intakes with nutritional supplements (e.g. calcium, iron, multivitamin complexes). After surgery, iron deficiencies and anaemia may occur in a higher percentage of patients, mainly as a consequence of nutrient deficiencies.[35,36,40]

Safety

Bariatric procedures have mortality rates similar to common laparoscopic operations. The safest is gastric band, with a 30-day peri-operative mortality rate of 0.1%; gastric bypass is 0.4%. Two years after surgery these rates are 0.0% and 0.4%, respectively.[41,42] As in most surgical interventions, in patients aged > 60 years, peri-operative risks and mortality rates are higher. Furthermore, patients with morbid obesity present a higher risk of suffering thromboembolism. In a meta-analysis including more than 160,000 patients with bariatric surgery, the mortality rate during the first 30 postoperative days was 0.08%. It was shown that re-operation and other surgical complications were higher in gastric bypass interventions compared with adjustable gastric banding and sleeve gastrectomy.[43] Other studies showed 57% of patients presenting with hypoferritinemia and 13% had undergone additional intra-abdominal procedures.[16] In adolescents, it has been shown that 8 years after bariatric surgery, a non-pathologic below normal cut off point in levels of vitamin B_{12} as well as hyperthyroidism in 45% of patients.[34]

Bariatric endoscopic surgery

A limitation of surgery is the increasing number of patients who would benefit from it.[2,44] As such the use of surgery as a first line of treatment is not a viable proposition because of the of the consequent economic burden. Not all patients want surgery or are eligible for this kind of intervention, especially given the risk of surgical-related complications and general anaesthesia. Endoscopic interventions such as endoscopic sleeve gastroplasty, intra-gastric balloon or the EndoBarrier may offer less invasive, reversible alternatives s.[45–47]

The intra-gastric balloon is a silicone device endoscopically inserted into the stomach and-filled with saline to a fixed volume. The balloon restricts the volume of the stomach without altering its functionality and accelerates satiety.[48,49] The majority of patients undergo uncomplicated insertions

and tolerate the therapy with no side effects, which can include oesophageal reflux, nausea and vomiting, and stomach cramps.[50] It is important to highlight that with this treatment it is necessary to undergo a nutritional learning process in order to change dietary habits and avoid a bodyweight rebound after device extraction. The use of intra-gastric balloon therapy has demonstrated a positive effect after 6 months in bodyweight loss parallel to improvements in glucose homeostasis, cardiovascular risk and other obesity comorbidities.[46,51] However, the effect of longer-term use of an intra-gastric balloon still requires research.

Endoscopic sleeve gastroplasty is a novel non-surgical procedure whereby the volume of the stomach is limited by creating a sleeve with a set of sutures.[45,52] In addition to sustained total bodyweight loss, endoscopic sleeve gastroplasty has been associated with a reduction in hypertension, diabetes and hypertriglyceridemia markers.[45,52]

The EndoBarrier is a duodenal bypass sleeve anchored to the duodenal bulb through a nitinol crown with barbs. The sleeve is advanced into the small bowel, allowing undigested food to reach the jejunum and creating a physical barrier between the food and the intestinal wall.[47] Besides a decrease in nutrient absorption, EndoBarrier therapy has demonstrated a positive effect on glucose metabolism and insulin sensitivity in obese and diabetic patients as a coadjutant of antihyperglycaemic agents.[53]

Due to their reversibility, the absence of surgery and general anaesthesia, and the demonstrated effectiveness of these alternative techniques in treating obesity and its associated comorbidities, these bariatric endoscopic procedures are gaining much interest among gastroenterologists and metabolic physicians.

Conclusion

Bariatric surgery widely exceeds the success of any other treatment modality available today for obesity and metabolic syndrome. Although the current usage of bariatric surgery is strictly a tool for weight loss and not directly for hypertension, dyslipidaemia or glucose homeostasis, these conditions are present in the vast majority of metabolic syndrome cases with excess bodyweight. Ongoing long-term studies have highlighted that long-term postoperative follow-up is as important as the bariatric intervention and strongly advised to avoid postoperative surgical, nutritional or psychiatric complications.

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