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Review

Surgery for Diabetes: Clinical and Mechanistic Aspects

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ABSTRACT

According to the most recent publication by the Canadian Public Health Agency, obesity affects 25% of adults. In addition, there is a clear association between the recent rise in obesity and the increased prevalence of type 2 diabetes. Medical therapy for obesity has shown limited long-term effectiveness, and surgical treatment is now recognized by medical authorities as part of the armamentarium for the management of type 2 diabetes in severely obese patients.

The current indications for obesity surgery and postoperative management are reviewed. The choice of surgery should balance expected benefits associated with weight loss (including remission rate of type 2 diabetes), side effects and the risks for early and long-term complications. Long-term outcomes of metabolic surgery for diabetes vary according to the type of surgery (ranging between 20% and 90% remission rates) and the underlying metabolic changes.

Several controlled trials have been published in recent years confirming the superiority of metabolic surgery over medical treatment for the management of type 2 diabetes associated with severe obesity. Some of the known underlying mechanisms of action include a combination of caloric restriction, hormonal changes, decreased nutrient absorption and changes in bile acids, microbiota and incretins. Further research is needed to clarify the mechanistic changes associated with each surgical procedure and their respective long-term outcomes.

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RÉSUMÉ

Conformément à la plus récente publication de l'Agence de la santé publique du Canada, l'obésité touche 25 % des adultes. De plus, on constate un lien évident entre la hausse récente de l'obésité et l'augmentation de la prévalence du diabète de type 2. Alors que le traitement médical de l'obésité a montré une efficacité à long terme limitée, le traitement chirurgical est maintenant reconnu par les autorités médicales comme faisant partie de l'arsenal thérapeutique pour prendre en charge le diabète de type 2 chez les patients atteints d'une obésité grave.

Nous avons passé en revue les indications actuelles de la chirurgie de l'obésité et de la prise en charge postopératoire. Le choix de l'intervention chirurgicale devrait contrebalancer les avantages escomptés associés à la perte de poids (dont le taux de rémission du diabète de type 2), les effets secondaires et les risques de complications à court et à long terme. Les résultats à long terme de la chirurgie métabolique visant le traitement du diabète varient selon le type de chirurgie (des taux de rémission allant de 20 % à 90 %) et les changements métaboliques sous-jacents.

Plusieurs essais cliniques publiés au cours des dernières années ont confirmé la supériorité de la chirurgie métabolique par rapport au traitement médical pour prendre en charge le diabète de type 2 associé à l'obésité grave. Parmi les mécanismes d'action sous-jacents connus, mentionnons la combinaison de la restriction calorique, des changements hormonaux, de la diminution de l'absorption des substances nutritives, et des changements dans les acides biliaires, le microbiote et les incrétines. D'autres recherches sont nécessaires pour élucider les changements mécanistiques associés à chacune des interventions chirurgicales et à leurs résultats respectifs à long terme.

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Introduction

Obesity rates have increased dramatically in Canada and worldwide over the past few decades. According to the most recent evaluation by the Public Health Agency of Canada (1), approximately one-quarter of Canadian adults are obese (body mass index [BMI] above 30 kg/m^2). When obesity is combined with overweight (BMI 25 to 30 kg/m^2), the prevalence in Canada in 2008 reached 62% (1). In addition, the prevalence of severe (Class II to III) obesity (BMI above 35 kg/m^2) has increased in an exponential manner, with a 225% increase in Canada between 1990 and 2003, currently affecting an estimated 5% of the Canadian population (1,2). Recent estimates, according to the National Health and Nutrition Examination Survey (NHANES) data, place the prevalence of extremely elevated (Class III) BMI (>40 kg/m^2) at 6.4% in 2012 (3). In parallel to this phenomenon, over the past 2 decades, we have witnessed a dramatic increase in the incidence of type 2 diabetes, now affecting 10% of the adult population (4). Most type 2 diabetes (80%) is due to excess weight or obesity, and type 2 diabetes has become the leading cause of chronic kidney disease, blindness and nontraumatic amputation. It is also associated with a 2- to 4-fold increase in the risk for stroke and mortality compared to the population without diabetes (5).

The first-line management of obesity should include a multidisciplinary evaluation with nutritional and medical counselling, behavioural and lifestyle modifications and increased physical activity. Unfortunately, the medium-term weight loss associated with the best medical treatments is modest (3% to 7% total weight loss), and the chance for remission of type 2 diabetes, once established, is anecdotal (under 1%) (6,7). Weight loss (bariatric) surgery has thus become an integral part of the clinical management modalities for severely obese patients who have failed medical management.

A number of surgical procedures have emerged over the past 40 years, including Roux-en-Y gastric bypass (RYGB) in 1971, adjustable gastric banding (AGB) in 1980, biliopancreatic diversion with duodenal switch (BPD-DS) in 1989 and sleeve gastrectomy (SG), endorsed in 2011 by the American Society for Metabolic and Bariatric Surgery (8). In this article, we review the clinical aspects of bariatric surgery and discuss the pros and cons of each procedure. We also address their expected impact on weight loss and type 2 diabetes and briefly describe current hypotheses concerning the underlying mechanisms of remission of type 2 diabetes.

Selection of Surgical Candidates and Choice of Procedure

Indications for the surgical management of morbid obesity were outlined by the National Institute of Health consensus development panel in 1991 and continue to represent generally accepted guidelines (2). Potential candidates should be between 18 and 60 years of age and able to participate in their treatment and long-term follow up.

Patients with BMIs between 35 and 40 kg/m^2 with at least 1 major obesity-related disease (i.e. type 2 diabetes, obesity-related cardiac disease, sleep apnea) or BMIs of 40 kg/m^2 or above, with or without associated diseases, are potential surgery candidates. These patients should be evaluated and carefully selected by a multidisciplinary team experienced in the field of obesity surgery. This team typically includes a bariatric nurse, nutritionist, mental health specialist and social worker, in addition to a bariatric surgeon. The team should educate patients fully regarding the risks, benefits and alternatives to weight-loss surgery. Patients should have failed conventional therapy and should also understand the need for lifelong medical surveillance to prevent and correct potential long-term nutritional deficiencies after surgery. Contraindications for weight-loss surgery include recent substance abuse (alcohol, drugs), nonstable psychiatric conditions (e.g. changes in psychiatric medications in the past 6 months), a diagnosis of cancer or an expected life expectancy fewer than 5 years.

From bariatric to metabolic surgery

The surgical procedures are illustrated in Figure 1. Historically, weight loss surgeries were classified on the basis of their fundamental mechanisms of action. AGB was considered a purely "restrictive" surgery, but a high long-term complication rate associated with weight regain has led to a loss of interest in this procedure in favour of surgeries with metabolic impacts. Malabsorptive surgeries were thought to decrease the absorption of nutrients by reorganizing or bypassing portions of the small intestine (i.e. RYGB or BPD-DS). However, mechanistic studies have described a large number of metabolic modifications associated with these surgeries (including changes in incretins, gut hormones, bile acid [BA] levels, microbiota), which have led to referring to these weight loss surgeries as metabolic operations.

The decision about the type of surgery is made in collaboration with a multidisciplinary team, based on the patients' medical conditions, including current body weights and obesity-related diseases and expected compliance with supplementation and follow up, as well as the patients' personal preferences. The goal is to find a balance between the potential complications and risks for mortality associated with obesity itself so as to improve the patients' quality of life and reduce obesity-related diseases, while aiming for acceptable short- and long-term complications and side effects related to the surgery itself. As a rule of thumb, early and long-term risks, side effects, but also maintenance of weight loss and remission of comorbidities, are proportional to the extent of the intestinal bypass (e.g. SG <RYGB <BPD-DS).

Following surgery, patients are followed every 3 to 4 months for the first year, then every 6 months for the second year and yearly thereafter. Long-term follow up is recommended after weight loss surgery, not only to detect and treat nutritional deficiencies or complications, but also to reinforce weight maintenance and to detect recurrence of associated comorbidities. Complete tests for blood count, electrolytes, urea and creatinine, calcium, parathyroid hormone, vitamin D, serum iron, total iron-binding capacity and ferritin and vitamin B_{12} are performed at the time of follow up. In addition, vitamin A is assessed following BPD-DS. Patients are discharged with vitamin and mineral supplements according to the type of surgery they have undergone. Standard supplementation after SG includes a multivitamin complex. After RYGB, patients receive, in addition, vitamin B_{12}, 1200 µg; calcium carbonate, 1000 mg with vitamin D_3 1000 U; and ferrous sulfate, 300 mg. Following BPD-DS, patients receive a multivitamin complex (Centrum Forte; Pfizer, New York, New York, United States), vitamin A, 20,000 IU; vitamin D_2, 50,000 IU; calcium carbonate, 1000 mg; and ferrous sulfate, 300 mg. Supplements are adjusted over time according to blood levels.

Clinical Outcomes in Type 2 Diabetes

Walter Pories et al (9) were among the first to look specifically at the remission of type 2 diabetes following weight loss surgery. In this historic paper, 146 of 165 patients with diabetes became euglycemic after RYGB. This remission rate could not be explained by weight loss alone and raised interest in further study of the underlying mechanisms of type 2 diabetes remission following surgery.

Subsequent studies have confirmed remission of type 2 diabetes with bariatric procedures. The Swedish Obese Subjects study is a prospective controlled trial; it has 1 of the longest follow ups in the bariatric literature and has shown impressive results with respect to long-term remission of type 2 diabetes. At 2 and 10 years, remission rates were 72% and 36%, respectively, in the pooled surgical