Bariatric surgery in young massively obese diabetic patients

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Abstract

Obesity is the most important lifestyle-related risk factor for type 2 diabetes (T2DM). The prevalence of T2DM in adolescents is increasing in parallel with the increasing incidence of major obesity. In adult obese subjects, the greatest degree of T2DM prevention, improvement or recovery has been reported in patients who have undergone bariatric surgery. However, few studies are available on the benefits and risks of bariatric surgery in adolescents with T2DM. The indications for obesity surgery in this population are unusual, and should only be considered in academic settings after comprehensive interdisciplinary evaluation.

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1. Introduction

Type 2 diabetes (T2DM) is now much more frequently being observed in childhood, although its prevalence is not yet truly epidemic in proportion [1]. In the US in high-risk ethnic populations, the incidence of cases approaches 50% of all new cases of diabetes diagnosed in adolescents [2]. In Europe up to now, T2DM in children and adolescents has remained a rare disease [3, 4].

The nosology and pathogenic mechanisms of T2DM in children and adolescents are still a matter of debate, and vary depending on genetic, environmental and behavioural determinants [3–6]. However, diabetes develops mainly in young people who are obese, and particularly within groups that are prone to insulin resistance (such as African-Americans). In the very obese, diabetes is often associated with other complications of excess fat mass such as hypertension, low-grade chronic inflammation, joint disorders and non-alcoholic hepatic steatosis, and also with changes in quality of life and self-esteem. Treatment of T2DM in youths includes weight management, increases in physical activity and drug therapy (such as metformin) to reduce insulin resistance,
or insulin when oral hypoglycaemic agents fail to control glycaemia. As in adults, weight loss is the most important aspect in T2DM management, as it reduces both morbidity and mortality [6–9].

In adult obese subjects, the most successful T2DM prevention, improvement or recovery has been reported in patients who underwent bariatric surgery. However, little is known of the effects of bariatric surgery in adolescents with T2DM.

2. Risks and benefits of bariatric surgery in adults

Bariatric surgery includes restrictive procedures such as adjustable gastric banding (AGB), sleeve gastrectomy (SG) and malabsorptive techniques (biliopancreatic diversion/duodenal switch), which are less commonly used, and combination techniques such as roux-en-Y gastric bypass (GBP). In most cases, the procedures are laparoscopic [10]. AGB, the easiest procedure to perform, preserves the natural anatomy and is easily reversible, but often requires adaptation and repeat intervention. An adjustable band is wrapped around the stomach, creating a pouch that empties into the remaining stomach through a narrowed outlet. The main complications of the technique are band slippage, port problems and erosion. Excess weight loss averages 50% over 3 years, with a tendency to regain weight in the long term. GBP is a procedure that creates a small stomach pouch that is isolated from the rest of the stomach and attached to a loop of jejunum. This procedure is both restrictive (due to the gastrectomy) and malabsorptive (due to the bypass). Solely malabsorptive procedures based on major anatomical rearrangement of the intestine, albeit efficient in terms of weight loss, are associated with the higher rate of morbidity, and are not recommended for use in children and adolescents because of their high rate of complications and their impact on nutritional status.

In adults, the effects of bariatric surgery have been studied in a series of investigations including the prospective controlled Swedish Obese Subjects (SOS) study, involving 4047 subjects with an average follow-up period of 10.9 years. The average weight loss in the controls was < 2% over a 15-year follow-up. In the surgical group, the maximum weight loss was observed after 1 to 2 years, and was 32% with GBP and 20% with AGB; at 10 years, weight loss had stabilized at 25% and 14%, respectively. There were 129 deaths in the control group and 101 deaths in the surgery group. Surgery resulted in a significant decrease in cardiovascular- and cancer-related deaths. In the postoperative period (90 days), 0.25% of the surgery group and 0.1% of the control group died. The 2- and 10-year rates of recovery from diabetes, low high-density lipoprotein (HDL) cholesterol and hypertension were significantly higher in the surgery group. Indeed, the surgery group had lower rates of diabetes than did the controls [11]. In the Longitudinal Assessment of Bariatric Surgery (LABS) study, the 30-day rate of death among patients who underwent Roux-en-Y GBP or laparoscopic AGB was 0.3%, and a total of 4.3% of patients had at least one major adverse outcome [12]. In a retrospective study of 7925 GBP patients and their matched controls, Adams et al. [13] observed a 40% reduction in overall mortality in the GBP patients (decreases in cancer and cardiovascular mortality, and increases in sudden death).

The risk of death and adverse outcomes after bariatric surgery depend on the patients’ characteristics. The LABS observational study of consecutive patients undergoing bariatric surgery in the US evaluated the outcomes of patients undergoing first-time bariatric surgery, using a composite 30-day endpoint of major adverse events (death, venous thromboembolism, repeat intervention, prolonged hospitalization). The rate of deaths was 0.3% among patients who underwent either GBP or AGB, with 4.3% of patients having at least one major adverse outcome. The patient’s history of venous thrombosis or pulmonary embolism, obstructive sleep apnoea and impaired functional status was each independently associated with an increased risk of the composite endpoint. Extreme values of body mass index (BMI) were also associated with increased risk. Given that these data were obtained from highly skilled, high-volume bariatric centres, the composite endpoint occurred in 1.0% of the AGB group and in 4.8% of the GBP group [13].

3. Bariatric surgery and type 2 diabetes in adults

The most successful T2DM prevention, amelioration or recovery in adult obese subjects has been reported in patients who underwent bariatric surgery [14,15]. The conclusion of a recent meta-analysis of the impact of bariatric surgery on T2DM in adults was that 78.1% of diabetic patients had complete resolution of their disease, while it was improved or resolved in 86.6% of patients. Weight loss and diabetes resolution were greatest for patients undergoing biliopancreatic diversion/duodenal switch, followed by those undergoing GBP, and was least for banding procedures. Insulin levels declined significantly postoperatively, as HbA1c, and fasting glucose values. Weight and diabetes parameters showed little differences at both < 2 years and ≥ 2 years [14]. However, long-term weight loss and improvement or remission of metabolic and respiratory complications has been well documented in two major studies [12,13]. In the SOS study, the rate of recovery of diabetes was 72% at 2 years and 36% at 10 years. Moreover, the incidence of diabetes at 2 years was 30 times lower than in the controls, a benefit that was still evident at 10 years.

Based on such results, bariatric surgery in now considered a therapeutic option for the treatment of T2DM. In fact, T2DM is among the indications for bariatric surgery in patients with a BMI < 40 kg/m² [15–17]. It also appears that malabsorptive bariatric procedures are the most efficient: in the meta-analysis by Buchwald et al. [14], the highest rate of T2DM recovery was observed in the biliopancreatic diversion/duodenal switch and GBP groups (98% and 83%, respectively) compared with AGB (49%). Nevertheless, the issue remains debatable: in the meta-analysis by Parikh et al. [16] of only diabetic patients,
the rate of patients requiring antidiabetic drugs at 1 and 2 years was 39% and 34%, respectively, for AGB, and 22% for GBP with no significant differences.

The mechanism of metabolic improvement after bariatric surgery is currently under study. Weight loss certainly plays a role: in the SOS study, weight relapse was associated with a higher risk of diabetes relapse. Reduction of food intake may also play a role. However, after GBP, the improvement in metabolic control is seen early after the intervention, whereas it takes several weeks after AGB. Clearly, the kinetics of such an improvement suggest other explanations. The unusual improvement in T2D after GBP compared with equivalent weight losses due to medical treatment suggests a specific effect of surgery on glucose homoeostasis that is independent of weight loss. The surgical procedure itself may explain the differences observed, with exclusion of the proximal part of the duodenum necessary for rapid metabolic improvement to occur. Other potential mechanisms include the effect of the surgical procedure on adiponectin, ghrelin, incretins (such as glucagon-like peptide-1, or GLP-1) and intestinal nutrient-sensing. In animals, the beneficial effects of enterogastric-anastomosis (EGA) procedures on food intake and glucose homeostasis involve intestinal gluconeogenesis and its detection via the GLUT2 and hepatoporal sensory pathway. In addition, ghrelin levels are decreased following GBP despite decreases in weight loss and food intake in some studies. Higher levels of GLP-1, an intestinal peptide involved in the control of food intake and insulin secretion, may also play a role. Furthermore, modification of the gut flora may be yet another potential explanation for the observed metabolic improvement [18–20].

4. Benefits and risks of bariatric surgery in adolescents

Little is known of the benefits and risks of bariatric surgery in children and adolescents. For this reason, the data from 17 studies, involving 553, mostly consecutive, morbidly obese adolescent patients, were reviewed by Treadwell et al. [21] as part of a health-technology assessment for the Washington State Health Care Authority. The panel of experts concluded that: (1) GBP and AGB both resulted in clinically significant weight loss—defined as a loss of 7% of body weight—corresponding to a decrease in BMI of 4 kg/m² after roux-en-Y GBP (follow-up of 1–6.3 years) and of 3.5 kg/m² after AGB (follow-up of 1.7–3.3 years); (2) laparoscopic AGB resolved the co-morbid conditions of diabetes and hypertension, whereas Roux-en-Y GBP resolved hypertension, with insufficient data to rate the evolution of other co-morbidities; (3) the safety profile (moderate evidence) for laparoscopic AGB after a follow-up period of 1–85 months revealed no peri- or postoperative deaths, although 26 of 328 patients required repeat surgery to correct complications (band slippage, intragastric migration and port/tubing problems); (4) the safety profile (moderate evidence) for Roux-en-Y GBP after a follow-up period of 2 weeks to 6 years revealed a combination of mild (slight malnutrition) and severe (pulmonary embolism, severe malnutrition, postoperative bleeding and gastrointestinal obstruction) complications [21,22].

In a longitudinal assessment of clinical characteristics in 61 adolescents who underwent laparoscopic roux-en-Y GBP, Inge et al. [23] showed that it resulted in improvement or reversal of cardiovascular risk factors and a decrease in BMI in approximately 37% of all patients, regardless of the initial BMI, at 1 year after the surgery. They also concluded that ‘late’ referral for bariatric surgery in those with the highest BMI values may preclude reversal of obesity. This suggests that the timing of referral for and the decision to undergo bariatric surgery in adolescents is a key issue.

Nevertheless, a number of questions have yet to be answered:
Are the improvements in quality of life and co-morbid conditions due to surgery-induced weight loss long-lasting? Are the results collected in academic centres using multidisciplinary teams representative of the general population? What are the predictors of bariatric surgery success and safety?

Given these uncertainties, it appears necessary to be extremely prudent before considering bariatric surgery in younger patients. Indeed, bariatric surgery in such cases should only be considered in the presence of obesity-related health-threatening co-morbidities (BMI >40 kg/m² plus a severe co-morbidity, or a BMI >50 kg/m² and a less severe co-morbidity) after failure of a well-conducted medical treatment that includes psychological and social support. Also, the decision should involve a skilled, multidisciplinary team, and the patient needs to demonstrate good compliance with a family-based lifestyle-modification programme. It must be made clear that obesity surgery is a trade-off: surgery creates a new lifelong ‘digestive disorder’ in the hopes that the altered gastrointestinal tract will improve the primary behavioural disorder (obesity) and its consequences without inducing new risks (such as malnutrition, micronutrient deficiency and osteopenia). It should also be clear that bariatric surgery is not a cure, but merely an intervention that only helps the patient to keep a commitment to lifestyle changes. To create anatomical and functional changes in developing children is not a harmless act, and a lifelong exposure to such changes may result in unforeseen complications [22–27].

5. Effect of bariatric surgery on diabetes in adolescents

The balance between the benefits and risks of bariatric surgery in adolescents is poorly documented, particularly in the long term, with little data available on the effects of bariatric surgery on diabetes in this patient population. However, Inge et al. [23] studied T2D reversal after surgery-induced weight loss in 11 adolescents who had undergone GBP and whose metabolic outcomes were compared with those of 67 diabetic adolescents treated medically. After surgery, there was evidence of diabetes remission associated with massive weight loss in all but one patient in the surgery group. In comparison, adolescents who were followed during 1 year of medical treatment demonstrated stable weight and no significant change in diabetic medication use. In addition, in the surgery
group, HbA1c decreased from 7.3% to 5.6% compared with 7.8% to 7.1% in the medical group. Furthermore, in another series of 30 cases, GBP resulted in improvement of fasting blood glucose and insulin after 1 year [27]. Interestingly, bariatric surgery also brought about major improvement in sleep apnoea syndrome in adolescents [28,29].

In a retrospective study in 76 adolescents who underwent biliopancreatic diversion (BPD) with a mean follow-up period of 11 years (range 2–23 years), Scopinaro et al. [29] found that the mean percentage of initial excess weight loss at each patient’s longest follow-up was 78%. Prior to surgery, two patients had T2DM but, at the longest follow-up period after surgery, none were diabetic. However, 11 patients developed protein malnutrition 1–10 years after BPD, and the long-term mortality rate was 4%.

6. Practical guidelines

Considering the effects of bariatric surgery on the overall co-morbidities linked with obesity, the expert panel of the health technology assessment for the Washington State Health Care Authority concluded that: (1) AGB and GBP for morbidly patients aged 21 or less can resolve co-morbid conditions (diabetes and hypertension) compared with non-surgical approaches (strength of evidence: weak), and two studies of AGB indicate a diabetes resolution rate of 80% and 100%, respectively (strength of evidence: weak); and (2) the evidence is insufficient to permit quantitative estimates of the likelihood of co-morbidity resolution and survival [21].

Pratt et al. [30] carried out a systematic search to update the evidence-based best-practice guidelines for paediatric/adolescent bariatric surgery, and recommended the inclusion of adolescents with BMI scores > 35 kg/m² plus specific obesity-related co-morbid conditions for which there is clear evidence of serious short-term morbidity (such as T2DM, severe steatohepatitis, pseudotumour cerebri and moderate-to-severe obstructive sleep apnoea), and those with extreme obesity (BMI ≥ 40 kg/m²) plus other co-morbidities associated with long-term risks. On identifying more than 1085 reports, and reviewing 186 of the most relevant in detail, they recommend that the preoperative multidisciplinary evaluation should take into consideration carefully designed criteria for patient selection, choice of appropriate procedure, thorough screening and management of co-morbidities, optimization of long-term compliance and age-appropriate, fully informed consent.

In patients with genetic disorders associated with major obesity such as Prader–Willi syndrome, the fact that bariatric surgery yields a high risk of complications is problematic [31].

7. Conclusion

Should bariatric surgery be considered for young, massively obese, diabetic patients? The answer to the first part of the question is that, in exceptional circumstances, bariatric surgery can be considered in young obese patients with a BMI > 35 kg/m² with life-threatening complications as a result. This means that diabetes that is inadequately controlled by medical treatment is one co-morbid condition that justifies a discussion on the appropriateness of bariatric surgery, especially in a young patient who has not responded to intensive obesity care. Albeit based on scant data, it appears that bariatric surgery may be just as effective for T2DM improvement or recovery in adolescents as it is in adults. However, it is not yet known, in the absence of long-term data, whether or not bariatric surgery can cure T2DM in such patients in the long term.

Bariatric surgery in children and adolescents should only be performed in reference academic centres with long-term follow-ups and in relation to clinical research. The multidisciplinary paediatric team should include medical (nutritional, endocrinological, metabolic, gastrointestinal, sleep and pulmonary) expertise, as well as psychological and surgical expertise, and an anaesthetic-care team experienced in obesity management. Also, only strongly motivated and well-informed patients (and their families) capable of providing favourable social and psychological support, and good preoperative care and counselling, should be considered for such surgery. In addition, both patients and their families need to be well informed as to the risks and complications of bariatric surgery.

The postoperative follow-up should take into account growth and development. Compliance is also essential to prevent and treat the potential risks of the procedure, adapt the treatment (insulin, antidiabetic drugs), and manage the physical and psychosocial responses to any dramatic weight loss. In addition, lifelong surveillance of micro- and macronutrient intakes, and nutritional, weight and digestive status has to be undertaken postoperatively.

Data on the effects and complications of bariatric surgery in children and adolescents are currently scanty, so the multidisciplinary teams involved in the management of these patients are encouraged to contribute their findings to a database.

Conflicts of interests

The authors have reported no conflict of interests.

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