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Editorial

Evolving Concept of Bariatric–Metabolic Surgery in Treatment and Prevention of Type 2 Diabetes Mellitus

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Type 2 Diabetes mellitus (T2DM) represents an expanding pandemic chronic illness. Currently, 285 million people have T2DM, and this number is predicted to increase to 439 million by 2030 [1]. It is a risk factor for vascular damage [2]. Uncontrolled diabetes leads to macrovascular and microvascular complications, including myocardial infarction, stroke, blindness, neuropathy, and renal failure in many patients [3]. However, despite substantial advances in pharmacotherapy and disease management, less than 50% moderate-to-severe T2DM patients remain inadequately controlled [4], and complete remission of hyperglycemia and the associated metabolic alterations is rare [5].

Obesity is also a serious global health problem associated with important morbidity and mortality [6,7]. The increased morbidity is assumed to be mediated mainly by insulin resistance, T2DM, hypertension, and lipid disturbances [8]. The prevalence of T2DM among severely obese patients is high, and despite medical treatment, T2DM is a leading cause of an overall increased mortality in obesity [9]. Virtually all morbidly obese adults have a measurably impaired glucose tolerance; 36% of individuals with impaired glucose tolerance will progress to T2DM within 10 years [10]. Even in the preclinical state, the steady-state plasma glucose concentration is statistically significantly correlated with the body mass index (BMI) [11].

Obesity with T2DM is highly relevant not only in terms of quality-of-life impairment but also in terms of medical costs incurred over time [12]. Multiple studies have shown associations between obesity and T2DM [13-18] and between changes in body weight and incident T2DM [19-21]. The benefit of weight loss on glycemic control in T2DM is well. Intensive lifestyle intervention and strict compliance to diet, which produce modest (5–10%) weight loss has been reported to produce durable (demonstrated up to 4 years) improvement in HbA1c and some cardiovascular risk factors [22,23].

However, management of T2DM is particularly challenging in obese patients. With the noted exception of agonists of the glucagon-like peptide 1 (GLP-1) receptor and inhibitors of dipeptidyl peptidase 4 (DPP-4), oral hypoglycemic agents and insulin therapy may result in weight gain, which may further impair metabolic control [24].

In 1980, bariatric surgeon Walter Pories started to perform gastric bypass surgery on obese patients with T2DM, and later he noticed right away that the patients no longer needed insulin [25]. Since then, various types of bariatric surgery on the gastrointestinal tract develop and constitute extremely powerful options to ameliorate T2DM in severely obese patients, often normalizing blood glucose levels without diabetes medications [5]. A recent systematic review and meta-analysis of 621 bariatric surgery studies (>135,000 patients) reported that diabetes "improved or resolved" effectively [26]. Although, there is a growing appreciation for the role of bariatric surgery as a tool in diabetes management [27], level 1 clinical evidence to support such surgery as an alternative treatment option of T2DM is still lacking [24].

Bariatric surgery can be basically divided into 3 categories: restrictive procedures (laparoscopic adjustable gastric banding, sleeve gastrectomy and vertical banded gastroplasty) that reduce the ability to consume large amounts of food, malabsorptive procedures (duodenal switch and biliopancreatic diversion) that reduce intestinal uptake of nutrients, and procedures (Roux-en-Y or other type gastric bypass) that combine these two aspects [28]. The mechanisms involved in surgical resolution of T2DM in morbidly obese patients primarily incorporate the action of weight loss, the role of hormones, intestinal malabsorption, and the role of gastrointestinal rearrangement. Besides, different types of gastrointestinal rearrangements in different surgical procedures contribute differently to improved insulin secretion and improved sensitivity in diabetes [12]. From the laboratory data, we could also observe the improvement in insulin sensitivity, with a marked reduction in insulin levels and improvement in the homeostasis model assessment of insulin resistance (HOMA-IR) index, which may be linked to the attenuation of chronic inflammation, as suggested by the greater reduction in high-sensitivity C-reactive protein (CRP) in the surgery patients than in the medical-therapy ones [3]. In the meta-analysis of 621 bariatric surgery studies, weight loss was found greatest for the duodenal switch and biliopancreatic diversion groups followed by gastric bypass, gastroplasty, and laparoscopic adjustable gastric banding. Diabetes resolution was greatest for patients undergoing duodenal switch and biliopancreatic diversion (95.1% resolved), followed by gastric bypass (80.3%), gastroplasty (79.7%), and then laparoscopic adjustable gastric banding (56.7%). Conclusively, 82% of patients had resolution of the clinical and laboratory manifestations of diabetes in the first 2 years after surgery, and 62% remained free of diabetes more than 2 years after surgery [26]. The 30-day mortality associated with bariatric surgery is estimated at 0.1–0.3%, a rate similar to that for laparoscopic cholecystectomy and described as 'low' [29]. However, only limited data from studies with varying results are available on long-term mortality after bariatric surgery [30]. One retrospective cohort study among 7,925 severely obese after gastric bypass surgery showed the long-term mortality was significantly reduced, particularly deaths

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from diabetes, heart disease, and cancer [31].

In order to clear up the confusion and state down consensus for indications of bariatric surgery, there have been several summits and conferences held by related institutions these years, e.g. Diabetic Surgery Summit (DSS), American Diabetes Association (ADA) and International Diabetes Federation (IDF). The latest guidelines recommend gastrointestinal surgery in treatment of T2DM patients with severe obesity (BMI ≥ 35 kg/m^2) as well as in carefully selected, moderately obese patients (BMI: 30–35 kg/m^2) who are inadequately controlled by conventional medical and behavioral therapies. However, there are some differences between the Western and Asian. Asians have a higher risk of developing diabetes and cardiovascular diseases than the Western population with the same BMI. Hence, BMI action points may be reduced by 2.5 kg/m^2 in the Asian with increased risk [2].

Due to extensive weight loss after bariatric surgery and even a modest weight loss of 5% to 10% conferring metabolic benefits, a preventive effect of bariatric surgery on the development of T2DM would be expected [32]. In a prospective, controlled study of 4,047 obese subjects, the incidence of new T2DM was 24% in the control group and 7% in the surgery group at a follow-up of 10 years, translating into a relative risk reduction of no less than 71% [8]. Although the current guidelines do not recommend bariatric surgery for the prevention of T2DM, some experts still advocate that disturbances of glucose metabolism might be treated early, even beforeT2DM is diagnosed [21].

Bariatric surgery is beyond weight loss and has specific metabolic effects on T2DM. It is also associated with substantial other health benefits, including improvement or normalization of hyperlipidemia, blood pressure, obstructive sleep apnea and improved quality of life [33]. So the name "Bariatric surgery" should be evolved to "Bariatric-metabolic surgery", which reflects its medical reality. In future, disease specific end-points would be more important factors in consideration of the guidelines, besides the BMI level.

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