

# Diabetes remission and relapse after metabolic surgery

Obesity and type 2 diabetes mellitus are prevalent worldwide. Obese patients with more visceral fat are more likely to suffer from type 2 diabetes mellitus, hypertension, dyslipidemia and obstructive sleep apnea. Obese patients with type 2 diabetes mellitus have a higher risk of obesity- and diabetes-related complications (especially arteriosclerotic cardiovascular disease). The goal of diabetes management is not only to maintain ideal weight and tight glycemic control, but also to prevent or decrease the incidence of related macrovascular and microvascular complications. However, it is rather difficult to achieve these goals by pharmacotherapy alone in obese individuals with diabetes.

Metabolic surgery, formerly known as bariatric surgery, has been shown by numerous studies to improve and even resolve weight-related metabolic comorbidities, in addition to its remarkable weight reduction. Metabolic surgery has also shown a striking ability to ameliorate glycemic control and metabolic risk factors, and reduce cardiovascular events and even mortality. A 3-year study carried out in uncontrolled obese patients with diabetes showed profound efficiency of blood glucose control and quality of life in the metabolic surgery group, as compared with the antidiabetic drug intensive treatment group alone<sup>1</sup>. Based on mounting evidence, metabolic surgery is recommended by many guidelines as an effective treatment for people with type 2 diabetes mellitus and obesity, especially severe obesity<sup>2</sup>.

However, metabolic surgery cannot cure all obese patients with diabetes. The extent of diabetes remission varies from person to person. This should be taken into account to establish a complete prediction model of diabetes remission in the preoperative assessment, and the predictors of diabetes relapse after the operation. This will be helpful for patient selection, preoperative assessment and postoperative management.

## DIABETES REMISSION AND RELAPSE

Metabolic surgery has been shown to result in a high remission rate of type 2 diabetes mellitus. Diabetes remission criteria are characterized as partial or complete based on published consensus definitions<sup>3</sup>. Partial remission means glycosylated hemoglobin is <6.5% and fasting plasma glucose value is 5.6–6.9 mmol/L, in the absence of glucose-lowering medications for at least 1 year. Complete remission refers to normal glycosylated hemoglobin level and fasting plasma glucose <5.6 mmol/L for 1 year of medication-free therapy. The prospective Swedish Obese Subjects study reported that the remission rates of type 2

diabetes mellitus at 2, 10 and 15 years of follow up were 72.3%, 38.1% and 30.4%, respectively<sup>4</sup>. The results of a retrospective cohort study including 4,434 obese patients with diabetes who underwent gastric bypass were consistent with those prior studies. The 5-year rate of complete and partial diabetes remission was 68.2% and 76.9%, respectively. The average remission time was 8.3 years, and 35.1% suffered from type 2 diabetes mellitus relapse at year 5 after complete remission<sup>5</sup>.

As described in previous studies, a younger age, shorter diabetes duration, lower glycosylated hemoglobin level, appropriate fasting C-peptide and no insulin use are the main preoperative predictive factors of type 2 diabetes mellitus remission through metabolic surgery<sup>6</sup>. Among these factors, short diabetes duration is more closely related to the long-term remission of diabetes, and with stronger prevention of diabetes-related microvascular and macrovascular complications for up to 25 years<sup>4</sup>. Less is known about the factors leading to subsequent recurrence. For those with diabetes relapse after remission, the prevalence and severity of diabetes-related complications remain unclear.

## OUTLOOK

Previous studies have emphasized that predictors of diabetes remission and relapse are mainly concentrated in some clinical characteristics. Putative predictive factors on diabetes remission and relapse have gained growing interest during recent years, including the surgery procedure, insulin sensitivity, weight regain, bile acids, changes of gut microbiota and gastrointestinal hormones, particularly ghrelin, glucagon-like-peptide-1, gastric inhibitory polypeptide and peptide YY<sup>7</sup>.

However, the specific mechanisms determining the outcome of diabetes after surgery in different individuals are not yet clear, especially in those who have had a relapse of diabetes early after the operation. Further concern is warranted regarding the predictors responsible for the durable remission and relapse of type 2 diabetes mellitus after metabolic surgery in obese patients, including insulin, glucagon, gastrointestinal hormones and the metabolic profile of type 2 diabetes mellitus (Table 1).

Furthermore, the roles of some pro-inflammatory and anti-inflammatory adipokines, such as adiponectin, leptin, tumor necrosis factor- $\alpha$ , interleukin-6, resistin, visfatin, chemerin, omentin and nesfatin<sup>8</sup>, as well as fibroblast growth factor-19, needed to be investigated to gain a better understanding (Table 1). These obesity-related biomarkers have the potential

**Table 1** | Possible factors involved in the evaluation of diabetes remission and relapse after metabolic surgery

Gastrointestinal hormones and metabolites	Glucagon-like peptide 1, gastric inhibitory peptide, ghrelin, peptide YY, fibroblast growth factor-19, bile acids
Islet hormones	Insulin, glucagon
Adipokines	Adiponectin, leptin, tumor necrosis factor- $\alpha$ , interleukin-6, resistin, visfatin, chemerin, omentin, nesfatin

to be used in the prediction of diabetes remission and relapse after metabolic surgery. Furthermore, these factors, and both their baseline level and dynamic changes, need to be verified in prospective, randomized controlled studies and long-term follow up in the future. Appropriate patient selection before operation might produce better outcomes.

#### DISCLOSURE

The authors declare no conflict of interest.

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Doi: 10.1111/jdi.12871