Is type 2 diabetes a surgical disease?

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Diabetes mellitus (DM) affects more than 2 million people in Canada and an estimated 150 million people around the world. Owing at least partly to the rising epidemic of obesity in most countries around the world, this number is expected to double by the year 2025. Diabetes is the seventh cause of death among Canadians,1 and the cost to society is expected to reach $15.6 billion by 2010. Most (90%) patients have type 2 DM, which is closely associated with obesity and lack of exercise.

Across Canada, people with diabetes continue to face difficult and significant challenges accessing the medication, service and support they need to live well with diabetes. This problem is particularly acute among the First Nations and indigenous populations of Canada. According to the Canadian Diabetes Association, diabetes can lead to a host of serious complications, including heart disease, stroke, kidney disease, blindness, and amputation. Also, infectious diseases such as colds, flu, and severe acute respiratory syndrome affect people living with diabetes more virulently than other Canadians.1

For these reasons, it is imperative that we find a more definitive solution to this ever-increasing problem. Medical or conservative measures to deal with obesity in patients with a body mass index (BMI) over 40 kg/m² have been found to be ineffective, and in many countries, anti-obesity (bariatric) surgery is recognized as the only viable treatment option.2 The advent of the laparoscopic approach to bariatric surgery, which has significantly reduced the morbidity, mortality and recovery time from surgery, has also significantly added to the attractiveness of this option.2 Laparoscopic bariatric surgery has recently become the fastest growing surgical specialty in many countries. However, unlike earlier experiences with antiobesity operations, the recent series of patients undergoing surgery have been better selected, prepared and studied. Thus, the results of surgery have been significantly better, and patient follow-up has been more comprehensive than studies published in the 1980s and even 1990s.3 As such, we are now in a position to provide a much better level of evidence in support of surgical roles in the treatment of morbid obesity.

According to a recent metaanalysis, patients undergoing gastric bypass procedures lose an average of 62% of their excess weight and experience marked improvements in associated conditions, including diabetes, hyperlipidemia, hypertension and obstructive sleep apnea.4 However, these procedures are not without substantial risks, including a mortality rate of 0.5%.4 Late complications of gastric bypass include anastomotic stricture and bowel obstruction. Incisional hernias, another late complication, can be greatly reduced with a laparoscopic approach.5 Patients may also experience dumping syndrome and nutritional deficiencies after Roux-en-Y gastric bypass (RYGB).

In several recently published studies, there has been an observation that, in addition to significant weight loss after surgery, many (80%–100%) patients with type 2 DM have experienced complete or partial resolution of their glucose intolerance.6-8 Although this effect has been reported with all antiobesity surgeries, 2 procedures (RYGB9,10 and biliopancreatic diversion11) have been shown to be more effective in controlling diabetes than other purely restrictive procedures.12

Because BMI is the dominant risk factor for diabetes, and because weight loss and hypocaloric diet have been shown to reduce plasma glucose and improve insulin sensitivity in people with obesity, the antidiabetic effect of surgery has been interpreted by some to be the result of surgically induced weight loss and decreased caloric intake.13,14 However, glycemic control is often observed within days of surgery,9,15 long before significant weight loss occurs, suggesting that the control of diabetes may be a direct effect of the surgical interventions, rather than a secondary outcome of weight loss. Some possible mechanisms have been proposed.16,17

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Several investigators have postulated that the control of diabetes after such surgeries is not a secondary outcome of obesity treatment alone, but is caused at least partly by anatomic rearrangements of the gastrointestinal tract.\textsuperscript{10,15-17} The “hindgut hypothesis” proposes that more rapid delivery of nutrients to the distal intestine results in improved glucose metabolism, potentially mediated via glucagon-like peptide 1 (GLP-1) or other distal gut peptides.\textsuperscript{18} In contrast, the “foregut hypothesis” proposes that improved diabetic control results from excluding the duodenum and proximal jejunum from nutrient flow. This exclusion may interfere with production of a factor (as yet unidentified) involved in the development of insulin resistance and diabetes. Recent studies in nonobese rats have supported this latter theory.\textsuperscript{19}

A recent symposium was held at the University of Strasbourg, in Strasbourg, France (Institut de Recherche contre les Cancers de l’Appareil Digestif [IRCAD], June 2006) to review the clinical evidence on possible use of bypass surgery in treatment of type 2 DM in nonobese or marginally obese patients. Preliminary data were presented from 3 nonrandomized trials underway in Chile, Mexico and Brazil, evaluating the effect of duodeno-jejunal exclusion on drug- or insulin-dependent type 2 DM patients with a BMI less than 35. All 3 studies observed similar improvements in glycemic control in 70% to 80% of patients after bypass surgery. The determinant of success appeared to be a history of medical therapy of less than 10 years.

In view of mounting evidence in support of duodenal exclusion as a potential long-term therapy for type 2 DM, we believe that a randomized controlled trial (RCT) of laparoscopic RYGB versus intensive medical management (combined lifestyle and medical intervention)\textsuperscript{20} in patients with type 2 DM is now indicated. This study would enable us to assess the viability and acceptance of this invasive therapy as a possible long-term control or even cure for an increasingly prevalent chronic disease. Attempts are currently underway to conduct such an RCT in Europe and the United States. In view of the recent experience with the conduct of surgical RCTs and willingness of patients to accept the required study protocol and comply with the follow-up necessary, Canada is uniquely positioned to contribute to this field. At least 1 site (McMaster University, Hamilton Ont.) is currently exploring the launch of such a study.

At a time when the outlook for controlling this increasingly prevalent world epidemic looks bleak, this surgical solution may offer hope to the millions of patients affected. The surgery proposed is not easy and has significant potential risks, however, medically treated type 2 DM is associated with a morbidity and mortality of its own, which may persuade patients to consider this apparently drastic measure to find a cure.

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References