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INVITED COMMENTARY

Bariatric Surgery as Treatment for Type 2 Diabetes

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Over a decade ago, Walter Pories published "Who would have thought it? An operation proves to be the most effective therapy for adult-onset diabetes mellitus" [1]. He demonstrated that weight loss surgery (WLS) was the most effective, durable treatment for diabetes available.

Dr. Pories captures the essence of his paper in his published cartoons. In one, a man meets a woman for the first time [2]. She asks, "What do you do?" and he answers, "I'm a bariatric surgeon." She then says, "Oh, you make people thin?" He responds. "No, I make them well." Dr. Pories in his research, publications, and cartoons has refocused bariatric surgery from issues of weight loss to metabolic improvements in health.

Gastric bypass can reduce the dose of insulin within days and off all hypoglycemic medications in 1 year. In a meta-analysis, Buchwald et al. [3] compared morbidity and resolution of weight-related conditions with restrictive and malabsorptive procedures. On average, postoperative weight loss was 38.5 kg or 55.9% excess body weight loss. Overall, 78.1% of diabetic patients had complete resolution, and diabetes was improved or resolved in 86.6% of patients [3]. A recent retrospective analysis of bariatric surgery outcomes found that laparoscopic adjustable gastric banding (AGB) reduced homeostatic model assessment for insulin resistance (HOMA IR) from 3.6 to 2.3 and laparoscopic Roux-en-Y gastric bypass (RYGB) reduced HOMA IR from 4.4 (0.6–56.5) to 1.4 (0.3–15.2) [4].

WLS can also be a cost-effective treatment for type 2 diabetes mellitus (T2DM). A recent study by the National Institute of Health Research in the United Kingdom confirmed that bariatric surgery is cost effective compared with nonsurgical treatment, although the variability in estimates of costs and outcomes is large [5].

The various operations appear to work by different mechanisms and variations of bypass have led to several new concepts. The RYGB seems to ameliorate T2DM through two mechanisms: 1) early augmentation of β-cell function at 1 month, and 2) attenuation of peripheral insulin resistance at 6 months. Conversely, patients undergoing AGB experience only the latter benefit but no changes in insulin secretion [6]. Generally speaking, restrictive procedures such as AGB control diabetes exclusively through weight loss-induced improvements in peripheral insulin sensitivity. Conversely, the antidiabetic effects of malabsorptive procedures (gastric biliopancreatic diversion bypass, duodenal-jejunal bypass) begin almost immediately, and are not simply related to the effects of reduced food intake and lower body weight.

In the past few years, hindgut and foregut theories have focused on a few key gut hormones called incretins [7]. Glucagon-like peptide-1 has received attention for its possible central role in improving impaired glucose

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tolerance. GLP-1 is released in response to nutrient ingestion from endocrine L cells, most densely located in the distal ileum. Under physiologic conditions, GLP-1 acts primarily to augment insulin secretion after an oral glucose load. An enlarged GLP-1 response to meal intake after RYGB may cause an acceleration of gastric emptying and intestinal transit time after this type of bariatric surgery technique [8].

Investigational weight loss operations gaining popularity internationally will likely increase our understanding of type 2 diabetes in the future. The endoluminal sleeve (ELS) runs a plastic tubing from the stomach to the jejunum essentially preventing absorption and signaling of nutrients in the duodenum. In rat models, ELS treatment enhanced insulin sensitivity, as demonstrated by decreased fasting and glucose-stimulated insulin levels and confirmed by calculation of HOMA IR [9]. Selective bypass of the proximal intestine by ELS seems to mimic many of the effects of RYGB on body weight and glucose metabolism. A modification studied abroad is the duodenal-jejunal bypass. From these investigational procedures, more will be learned about signaling, metabolism, weight loss, and regulation of diabetes.

Notwithstanding the efficacy of WLS in resolving T2DM, it is not a "cure" for T2DM. Instead, WLS is a proven method to cause T2DM "remission." Percent excess weight loss significantly predicts postoperative insulin resistance (HOMA IR) during the first year following both RYGB and AGB [4]. If the weight goes back up, you can count on type T2DM to rear itself again. WLS involves a uniquely vulnerable population in need of specialized resources and ongoing multidisciplinary care. Timely best practice updates are required to identify new risks, develop strategies to address them, and optimize treatment [10].

WLS is also not without inherent risks and perioperative mortality. With the upswing in the number of bariatric procedures, patient safety has become a high priority. In the state of Massachusetts, more than 100 specialists across the many disciplines involved in WLS came together to develop new standards in patient care and patient safety. In 2004, the Betsy Lehman Center for Patient Safety and Medical Error Reduction (Lehman Center) formed an Expert Panel to assess WLS procedures, identify issues related to patient safety, and develop evidence-based best practice recommendations to address those issues [11]. Recently, the panel reconvened to update the evidence-based best practices [10].

With more than 9 million Americans suffering from class III obesity, the 200,000 bariatric operations performed each year are not enough to contain the severe obesity epidemic [12]. Practitioners must be judicious in determining which patients are most in need. A recent study validated the US National Institutes of Health guidelines for bariatric surgery using the UCLA/RAND analysis [13]. For patients in the 19- to 64-age group, the study confirmed a body mass index (BMI) $\geq$40 kg/m^2, without comorbidities, is an appropriate criterion for surgery in and of itself. For patients in the 35 to 39 BMI range in this age group, the presence of most of the obesity-related comorbidities is considered appropriate for surgery. For patients who fall in the lower BMI category of 32 to 34, surgery is considered appropriate only for the most severe of obesity-related comorbidities such as poorly controlled diabetes (despite maximal medical therapy).

To redefine bariatric surgery as a verifiable "metabolic" treatment for T2DM, large clinical trials comparing bariatric surgery versus optimal medical care of patients with T2DM should be given priority to define the role of surgery in the management of diabetes [14]. As an example, the Swedish Obesity Study compared diet and exercise lifestyle interventions to surgical interventions and demonstrated a measurable survival advantage for patients who had WLS [15]. Clinical trials to investigate the exact role of surgery in T2DM patients, especially in cases of less severe obesity, are now a priority for the Diabetes Surgery Summit delegates [16]. Clinical trial evidence paired with further basic research on mechanisms for surgically induced diabetes remission will lay strong foundations for transforming WLS into "diabetes surgery." WLS not only improves the human condition today, but it is also allowing investigators to better understand normal physiology and better treat diabetes.

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