

## Bariatric surgery. *Its role in “curing” diabetes*

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Obesity is a major independent risk factor for type 2 diabetes mellitus and is also associated with rapidly increasing prevalence of diabetes worldwide. The twin epidemic of obesity and diabetes has increased the cardiovascular morbidity and premature mortality.<sup>1</sup> Different modalities were tried to tackle the problem of “central” obesity as an indicator of a higher chance of metabolic derangement and the potential risk for future diabetes. Typically, lifestyle modifications are tried first followed by medications and behavioral therapy, but what is gaining popularity recently is the surgical treatment of obesity for those with higher body mass index (BMI) as more patients start losing faith in their ability to lose weight significantly or to maintain their reduced weight.

Bariatric surgery has emerged as an opportunity for greater and more persistent weight loss that results in improved quality of life, self-image, psychosocial health, and functional status.<sup>2</sup> Those that lose significant weight become more employable, physically more active and sociable, and acquire a more gregarious outlook on life. Women who underwent bariatric surgery showed better maternal, and neonatal pregnancy outcome compared with those who remain obese.<sup>3</sup>

According to the 2012 Health Statistics, a survey conducted by the Health Authority of Abu Dhabi found that 36% of United Arab Emirates Nationals are obese.<sup>4</sup> This has its consequences both medically by raising the chance of having diabetes, hypertension, and heart disease, as well as socially by worsening body image and quality of life. For type 2 diabetics, bariatric surgery offers a chance of “cure” and favorably improves cardiovascular risk status while reducing reliance on medications to achieve glycemic control.<sup>5</sup> The Swedish Obese Subjects study<sup>6</sup> demonstrated that bariatric surgery in patients with a BMI  $\geq 35$  kg/m<sup>2</sup> reduced cardiovascular risk factors for more than a decade after surgery, and this was translated into a reduction in cardiovascular and total mortality. There are a variety of surgical techniques that aim at improving metabolic and organ function in diabetics. Several studies have shown that patients after bariatric surgery witness complete resolution or improvement of obesity-related co morbidities like hypertension, dyslipidemia, and obstructive sleep apnea.<sup>7</sup> Evidence supporting the benefit

of bariatric surgery was strongest in patients with a BMI of  $>40$ , while the benefits in those with BMI of 35 to 39 were less clear.<sup>8</sup> In a position statement released in 2011,<sup>9</sup> the International Diabetes Federation recognized that bariatric surgery is suitable for obese patients with type 2 diabetes in whom glycemic targets are not reached with available medical therapies, especially when the patient has major coexisting illnesses such as hypertension and dyslipidemia. It also recommended the inclusion of bariatric surgery in future algorithms for the treatment of type 2 diabetes. More recently, the 2013 updated guidelines<sup>10</sup> issued by the American Association of Clinical Endocrinologists in cooperation with the Obesity Society and the American Society for Metabolic & Bariatric Surgery advise that bariatric surgery is suggested for patients with a BMI of 40 kg/m<sup>2</sup> or more in absence of coexisting medical problems, and for those with a BMI of 35 kg/m<sup>2</sup> or greater with comorbidities such as type 2 diabetes, hypertension, hyperlipidemia, or obstructive sleep apnea.

Bariatric surgery proved its efficacy in obtaining marked and sustained weight loss. This was associated with a significant improvement in glucose control and even resolution of the clinical and laboratory manifestations of diabetes. The bad companions of type 2 diabetes that accelerate atherosclerosis could improve as well. Besides the effect on glucose control, bariatric surgery also leads to significant improvement of cardiovascular risk factors, especially those linked with metabolic syndrome, including inflammation markers, improves glucose, lipid and blood pressure control in surgically compared with medically treated obese individuals.<sup>1</sup>

Data from randomized clinical trials<sup>5</sup> comparing surgical versus medical therapy, specifically in obese patients with diabetes, reported a significant rate of remission of diabetes. The cure rates were variable and influenced by the procedure utilized as well as how they defined cure. Earlier reports for those underwent vertical banded gastroplasty showed that remission of diabetes may be transient, with 72% having impaired fasting glycemia or normoglycemia 2 years after bariatric surgery, but only 36% remaining free of diabetes at 10 years.<sup>11</sup> In that study, none of the patients that underwent biliopancreatic diversion or sleeve gastrectomy were included, which could explain the lower remission rate as these procedures are technically more difficult but followed by more persistent weight loss.

Trials that followed demonstrated higher cure rates. One study that looked at the rates of diabetes resolution of sleeve gastrectomy and gastric bypass concluded that both procedures provided long-lasting glycemic control when compared with intensive medical therapy at 2

years. It stated that despite similar weight loss of both procedures, gastric bypass uniquely restores pancreatic beta cell function and reduces truncal fat; thus, reversing the core defects in diabetes when compared to sleeve gastrectomy.<sup>11</sup>

Diabetes remission is more likely in those with lower glycated hemoglobin (HbA1c) levels and pre-operative insulin independence. In those who do not achieve remission, bariatric surgery results in better glycemic control and reduced pharmacotherapy use compared with intensive medical therapy.<sup>5</sup> Bariatric surgery may also facilitate remission of microvascular complications. Schauer et al<sup>5</sup> observed parameters of chronic kidney disease in diabetics. The urinary albumin-to-creatinine ratio was significantly better in the sleeve gastrectomy and gastric bypass groups when compared with intensive medical therapy. The only predictor of cardiovascular benefit after bariatric surgery appears to be raised fasting insulin levels, suggesting that patients with diabetes or insulin resistance may be the group who has most to gain in terms of cardiovascular risk reduction.<sup>12</sup>

The mechanism of diabetes resolution was a matter of debate. Early hypotheses regarding diabetes remission after Roux-en-Y gastric bypass centered on the effects of weight loss. However, this could not explain why diabetes resolution occurred within several days, occasionally before discharge from hospital while weight loss would take several months. It was subsequently recognized that these operations must offer direct metabolic effects independent of weight loss, and these procedures were renamed as 'metabolic operations'.<sup>13</sup> Diabetes improvement depends upon the type of surgery performed. In a meta-analysis of predominantly observational studies, diabetes resolution was highest after biliopancreatic diversion/duodenal switch being around 95%, and lowest after laparoscopic adjustable gastric banding at 57%.<sup>11</sup> Sleeve gastrectomy has a slightly lower remission rate compared with Roux-en-Y gastric bypass. Since normalization of blood glucose was not explained only by weight reduction, experts suggest that there are enteroendocrine effects following operations like Roux-en-Y gastric bypass, which alter gut hormone secretion leading to reduced food ingestion (due to lower levels of ghrelin and higher levels of postprandial peptide YY) plus superior insulin secretion in response to higher incretin levels, such as GLP-1.<sup>14</sup>

The optimal surgical approach for improvement and remission of diabetes has yet to be fully elucidated. The subject is advancing, and novel procedures are promising including the robotic-assisted laparoscopic approaches. Newer endoscopic techniques are in practice, such

as intra-gastric balloons and endoscopically placed synthetic duodenojejunal bypass liners, which have been developed as an alternative to bariatric surgery. Results of these newer techniques declared a mean weight loss of 10-20% of body weight, and a complication rate of up to 20%, mainly sleeve migration and bowel obstruction.<sup>11</sup>

Not all candidates are suitable for surgery as they should be highly motivated; mostly those who failed to achieve sustained weight reduction through extensive and repeated attempts at nonsurgical approaches, in the absence of underlying endocrine and psychological pathology. Most guidelines recommend against surgical procedures for those with serious concomitant medical and psychiatric diseases.<sup>15</sup> Late complications are related to the surgical procedure. Problems of Roux-en-Y gastric bypass are diverse, could be encountered during early postoperative periods or may present months following the surgery. These include anastomotic leak, gastrointestinal hemorrhage, bowel obstruction, and internal hernias, with the possibility of future nutritional deficiencies.<sup>16</sup> Laparoscopic adjustable gastric banding is associated with lower mortality rates. The most common complications include band slippage/gastric prolapse, pouch dilatation, and band erosion.<sup>16</sup> Laparoscopic sleeve gastrectomy has low complications rates, and these include stomal ulcer, dumping syndrome, and bowel obstruction. The most serious complication of biliopancreatic diversion is leaking from the gastric staple line and small bowel obstruction due to adhesions or internal hernias. Nutritional complications include significant protein calorie malnutrition, anemia, hypocalcemia and fat-soluble vitamin deficiencies that need lifelong supplementation.<sup>16</sup> After surgery, patients must be instructed to eat small amounts, eat slowly, chew carefully, avoid eating when not hungry and take no liquids with meals.

The remission of diabetes has recently been defined following bariatric surgery. The HbA1c levels should be measured between 3 and 6 months post-operatively, and glycemic therapy adjusted as appropriate. Patients are usually followed to evaluate retinopathy, neuropathy, and nephropathy for at least 5 years following surgery, as they can develop microvascular disease despite early remission of diabetes. Yearly fasting glucose and HbA1c measurements remain the best methods of monitoring long-term glycemic control.<sup>15</sup> Weight regain is often associated with a possibility of relapse of diabetes and screening frequency may therefore need to be adapted in patients with more than 2 kg in weight gain per year.<sup>17</sup>

In summary, it is worth mentioning that there is great interest in bariatric surgery in the medical community

these days with the evolution of newer procedures with less invasive techniques to help the growing numbers with obesity and diabetes mellitus. What is more important in my opinion, is comprehensive medical assessment along with psychological and dietetic evaluations for potential candidates. The consulting surgeon takes into account local surgical morbidity and mortality rates, availability of specialized follow up centers in addition to patient concerns, and weight loss expectations to assist in relieving the burden of obesity-related problems and improved overall life expectancy.

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