Bariatric Surgery in Type 2 Diabetes

Written by **Brian Hoyle**

Ele Ferrannini, MD, University of Pisa School of Medicine, Pisa, Italy, discussed the pathophysiology of bariatric surgery, which he described as a hybrid of Roux-En-Y gastric bypass (RYGB) and biliopancreatic diversion (BPD).

One possible explanation for the improvement in insulin resistance with RYGB is the "foregut hypothesis", which posits that the exclusion of the duodenum removes the release of a factor(s) that antagonizes insulin sensitivity.

However, the available data do not support the foregut hypothesis and the involvement of weight-independent effects with respect to insulin resistance with RYGB. In morbidly obese patients, this operation improves liver, adipose tissue, and muscle insulin sensitivity essentially in proportion to weight loss. Early after surgery calorie deprivation decreases endogenous glucose release and plasma glucose levels. On the other hand, both early and late after RYGB ß-cell function improves as a result of the augmented release of gut hormones (principally, glucagon-like peptide-1 [GLP-1]) that potentiate insulin secretion as well as the abatement of glucotoxicity [Camastra S et al. *Diabetologia* 2011; Bradley D et al. *J Clin Invest* 2012; Lingvay I et al. *Diabetes Care* 2013].

Furthermore, it has been demonstrated that in response to a mixed meal, gastric bypass creates a state of improved peripheral insulin sensitivity but impaired hepatic response to a meal because of changes in the prehepatic insulin-to-glucagon ratio [Camastra S et al. *Diabetes* 2013] Diabetes remission (or nonremission) may depend on the initial degree of β-cell dysfunction, rather than on insulin sensitivity, although confirmation will require studies in larger numbers of patients. [Nannipieri M et al. *J Clin Endocrinol Metab* 2011].

In BPD, the "hindgut hypothesis" posits that ileal mucosal cells releases factor(s) that enhance the action of insulin and that the surgical diversion elicits weight-independent effects. Results from a number of studies indicate that in morbidly obese patients, BPD normalizes insulin sensitivity and this effect occurs prior to significant post-surgery weight loss [Camastra S et al. *Diabetes Care* 2007; Astiarraga B et al. *J Clin Endocrinol Metab* 2013].

Regarding the foregut and hindgut hypotheses, several conclusions can be drawn:

- Bypassing the duodenum and initial jejunum does not involve metabolic mechanisms impacting on insulin resistance
- Contact of biliopancreatic secretions with the mucosa of the terminal ileum improves insulin sensitivity in a partially weight-independent manner
- The weight of evidence supports the hindgut hypothesis over the foregut hypothesis

Dimitrios Pournaras, MD, Musgrove Park Hospital, Tauton, England, United Kingdom, discussed the methods and results of bariatric surgery. The surgery is done as a means of diabetes control in the morbidly obese, with the aims of extending lifespan and improving quality of life. The principle aim of bariatric surgery in these patients is not strictly weight loss.

The approach is safe. Exemplifying this, Table 1 summarizes data of 5612 patients from the National Bariatric Surgery Registry for 2012 in the United Kingdom for 3 types of bariatric surgery. The in-hospital mortality rate was very low.

Table 1. Outcomes in the 2012 UK National Bariatric Surgery Registry

Type of Surgery	Adjustable Gastric Banding (n=2132)	Roux-En-Y Gastric Bypass (n=2892)	Sleeve Gastrectomy (n=588)
Mean body mass index (kg/m2)	47.7	50.1	53.9
Mortality (%)	0.0	0.22	0.0
30-day reoperation (%)	0.9	3.4	3.1
In-hospital mortality (n=4389)	0.07%		

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The safety of bariatric surgery is especially bolstered when performed in a facility with high volume experience. Despite this, bariatric surgery performed in the morbidly obese should not be regarded as a means of achieving complete remission of diabetes, which is defined as a glycated hemoglobin (HbA1C) level <6% and fasting glucose <5.6 mmol/L for at least 1 year after surgery, and no active hypoglycemic pharmacologic therapy or ongoing procedures [Buse JB et al. *Diabetes Care* 2009]. However, the procedures are excellent in achieving glycemic control (Table 2) [Pournaras DJ et al. *Brit J Surg* 2012].

Table 2. Glycemic Control Following Bariatric Surgery

	Roux-En-Y Gastric Bypass	Sleeve Gastrectomy	Adjustable Gastric Banding	p Value
HbA1C (%) preoperative	8.1±1.9	7.5±1.5	7.7±1.5	0.46
HbA1C (%) postoperative	6.2±1.2*	6.8±1.7*	6.3±0.7*	0.08

*p<0.001 compared with preoperative.

A number of randomized controlled trials have demonstrated the ability of bariatric surgery to produce long-term reductions in HbA1C. One trial randomized 60 patients with type 2 diabetes mellitus (T2DM; body mass index [BMI] ≥35 kg/m^2) to medical therapy, gastric bypass, or BPD. The change in HbA1C from randomization to 24 months was assessed to determine diabetes remission. All 3 treatments produced an initial drop in HbA1C in the first 3 months with a subsequent plateau at marginally higher or lower levels. The overall decrease in HbA1C from Month 3 to Month 24 was greatest for BPD, followed by gastric bypass and then medical therapy [Mingrone G et al. *N Engl J Med* 2012]. Another trial that randomized 150 patients (BMI 27-43 kg/m^2) to intensive medical therapy with or without RYGB or sleeve gastrectomy reported a significantly greater and sustained reduction in HbA1C with combined medical therapy and surgery [Schauer PR et al. *N Engl J Med* 2012].

Another option for patients with T2DM and obesity is implanting an impermeable duodenal-jejunal bypass liner. A study involving 16 patients with T2DM reported a lower HbA1C with the liner at 52 weeks compared with no liner (7.5±0.4% vs 8.6±0.2%; p<0.001) [Cohen R et al. *Diabet Med* 2013]. The mean duration of diabetes was 2 to 10 years and HbA1C ranged between 7.5% and 10.2% at baseline. All patients were on metformin, but none were taking insulin, a GLP-1 analogue, or dipeptidyl peptidase-4 inhibitor.

According to Prof. Pournaras, the collective data allow the following conclusions:

- Bariatric surgery is a safe weight loss approach for obese diabetics
- Remission of T2DM is possible
- Diabetes-related complications can be reduced
- Diabetes can recur
- Combinational treatment incorporating surgery can be advantageous
- Outcome is optimized by identifying patients who will benefit most and when benefits are achieved