## Trial Backs Metabolic Surgery as Long-Term Diabetes Cure

 Alternative to medical therapy gets harder to ignore

For long-term diabetes remission, metabolic surgery is an effective option, 10-year data suggested.

In a randomized trial of 60 patients with type 2 diabetes and obesity, diabetes remission rates were significantly higher in the years following surgery versus conventional medical therapy, Geltrude Mingrone, MD, PhD, of King's College London in the U.K., and colleagues reported in The Lancet.

In previously reported 2-year outcomes, 75% of patients who underwent Roux-en-Y gastric bypass (RYGB) and 95% of patients who underwent biliopancreatic diversion (BPD) achieved diabetes remission, defined as an HbA1c under 6.5% and fasting glucose under 100 mg/dL (5.55 mmol/L) without ongoing pharmacological medication for at least 1 year.

In the newly reported 10-year outcomes of the same patients, 50% of those who underwent BPD were able to maintain their diabetes remission by year 10 (50%, 95% CI 29.9-70.1%), while a quarter of those who underwent RYGB maintained their remission 10 years after surgery (25%, 95% CI 11.2-46.9%, P=0.0082).

On the other hand, only 5.5% (95% CI 1.0-25.7%) of those who received nonsurgical medical therapy for their diabetes achieved and maintained long-term remission a decade later. Of note, this actually included only one participant who went into diabetes remission after crossing over to the surgery group.

"No patient was shown to be in diabetes remission after medical therapy," the researchers explained.

Overall, about 38% of all patients who underwent surgery maintained their diabetes remission throughout the decade-long follow-up. Also, no patient who didn't achieve remission within the initial 2 years achieved it later on. "This factor might help us to intensify modern and potent glucose-lowering therapies like SGLT2 inhibitors and GLP-1 receptor agonists earlier after metabolic surgery," suggested the authors of an accompanying commentary, Alexander Miras, MRCP, PhD, of Imperial College London, and Carel le Roux, MBChB, MSc, PhD, of University College Dublin in Ireland. "The combination of metabolic surgery and glucoselowering agents could have a positive effect not only on glycemic outcomes but also on the prevention of the macrovascular and microvascular complications of type 2 diabetes," Miras and le Roux added.

Among the surgical patients who did achieve diabetes remission 2 years after surgery, a larger percentage of RYGB patients had a relapse into hyperglycemia versus BPD patients.

After 2-year remission, about 67% (95% CI 41.7-84.8%) of RYGB patients had a relapse vs 53% (95% CI 41.7-84.8%) of RPD patients. Importantly though the team

31.7-72.7%) of BPD patients. Importantly though, the team said, all these patients who had a relapse in diabetes 2 years later were able to maintain "adequate" glucose control by year 10, with an average HbA1c of 6.7%.

The median diabetes-free survival time was 9 years for the BPD patients and 5 years for the RYGB patients.

Not surprisingly, patients who underwent either type of metabolic surgery saw far fewer diabetes-related complications throughout the years, including macrovascular complications -- specifically myocardial infarctions -- and microvascular diabetic complications

including retinopathy, nephropathy, and neuropathy.

Surgery patients also had significantly lower body weight, body mass index (BMI), waist circumference, Homeostatic Model Assessment for Insulin Resistance scores, plasma triglycerides, and higher quality-of-life scores; no differences were seen in blood pressure, however. "Metabolic surgery is arguably the most effective available therapy for type 2 diabetes and can be a life-saving option for many patients. It should be appropriately prioritized in times of pandemic and beyond," said the study's senior author, Francesco Rubino, MD, of King's College London, in a statement.

The findings "provide the most robust scientific evidence yet that full-blown type 2 diabetes is a curable disease, not inevitably progressive and irreversible. In addition to represent[ing] a major advance in the treatment of diabetes, metabolic surgery is our best lead to the elusive cause of the disease," he added.

The open-label, single-center trial included 60 Italian patients -- 20 patients randomized to laparoscopic RYGB, BPD, or conventional medical therapy plus lifestyle interventions. The BPD was performed with an opensurgery approach with the Scopinaro procedure, which uses a horizontal gastrectomy and not a sleeve gastrectomy, the researchers explained. "The BPD used in this study leaves behind a larger gastric remnant and has a lesser effect on restriction of calorie intake than the duodenal switch variant." Participants were ages 30 to 60, had a BMI of 35 or higher, had at least a 5-year history of type 2 diabetes, had an HbA1c of 7% or higher, and about half were female. After 10 years, the average HbA1c levels were 6.4% in the BPD group, 6.7% in the RYGB group, and 7.6% in the medical therapy group.

Miras and le Roux praised the study for not only its long follow-up, but also that it included patients with largely advanced type 2 diabetes as half of the participants were taking insulin at the time of surgery.

However, one limitation was that the sample size was small, meaning there was a lack of power to really quantify the benefits of surgery on type 2 diabetes complications. In addition, the team said, the BPD procedure is actually seldomly performed, whereas the sleeve gastrectomy procedure is currently the most popular metabolic surgery performed in the U.S. today.

"The 10-year data from STAMPEDE are now eagerly awaited to see how the sleeve gastrectomy performed over 10 years, but we hope also to gain more insight into the rates of hypoglycemia and long-term surgical and nutritional complications for all surgical procedures," the team noted.