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In This Issue of *Diabetes Care*

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International Diabetes Organizations: New Clinical Guidelines and Recommendations for Metabolic Surgery in Type 2 Diabetes

A set of 32 recommendations related to the use of metabolic surgery for treatment of type 2 diabetes are published in this issue of *Diabetes Care* (**p. 861**). This follows the completion of the multiple stages of the 2nd Diabetes Surgery Summit (DSS-II), an international consensus conference finalized at the end of September 2015. The topline outcomes, as reported in the consensus report by Rubino et al., are that forms of bariatric surgery, which the authors termed "metabolic surgery," should be either considered or recommended to treat type 2 diabetes depending on the severity of obesity present and the success or otherwise of prior lifestyle or medical interventions. The recommendations are supported by high-quality evidence, including randomized controlled trials and systematic reviews/meta-analyses that show that gastrointestinal procedures used for many years in bariatric surgery promote dramatic and durable improvements in type 2 diabetes. The biological rationale behind the recommendations is based on the recognition of an important role of the gut in metabolic regulation and experimental evidence that some of the surgical procedures have direct effects on glucose homeostasis. The summit involved 48 international clinicians and scholars from multiple disciplines, including representatives of leading diabetes organizations. The process involved evidence-appraisal stages and systematic consensus building. According to the authors, despite evidence being available for the powerful antidiabetes effects of surgery on type 2 diabetes, no guidelines for diabetes care included surgical options. Concluding, they report that "there is sufficient clinical and mechanistic evidence to support inclusion of metabolic surgery among antidiabetes interventions for people with [type 2 diabetes] and obesity." The statements and guidance of DSS-II have already been endorsed or ratified by over 30 professional organizations with interests in diabetes and obesity, an unprecedented level of support for new clinical guidelines. More organizations are expected to endorse the recommendations shortly. Commenting more widely on the report, Prof. Rubino stated: "The new guidelines recognize for the first time surgery as a legitimate diabetes treatment and should inform physicians and policymakers about the appropriate selection of patients for surgical treatment. Both practically and conceptually it is one of the greatest innovations in diabetes care in recent times."

Rubino et al. Metabolic surgery in the treatment algorithm for type 2 diabetes: a joint statement by international diabetes organizations. Diabetes Care 2016;39:861–877

Improved Outcomes Following Bariatric Surgery in Patients With Obesity and Type 1 Diabetes

Bariatric surgery can result in remarkable weight loss in patients with obesity. On top of this, multiple randomized clinical trials and long-term studies have shown durable and significant metabolic effects of surgery, even to the extent that remission of type 2 diabetes is sometimes possible. Against the background of the recommendations of the 2nd Diabetes Surgery Summit (DSS-II) and many other studies, it is perhaps surprising that there are relatively few data on the effects of bariatric surgery in type 1 diabetes. Kirwan et al. (**p. 941**) report the results of a systematic literature review up to December 2015 designed to identify all relevant studies related to bariatric surgery in adult obese patients with type 1 diabetes. They reportedly were able to identify 17 studies, all either case series or case reports, that in total provided information on outcomes in 107 individuals with both obesity and type 1 diabetes. The overall majority of studies reported significant weight loss and reductions in the use of insulin as a result of surgery. Calculated means of pre- and postoperative HbA_{1c} for the entire cohort also suggest that significant reductions might be possible. Although the precise mechanisms involved are unclear, the authors also propose a series of pathways that may be involved in the apparent effects. Taken together, they suggest, available data are promising, but additional experimental and prospective clinical studies are still necessary. Commenting more widely on the outcome, Dr. Aminian stated: "Management of type 1 diabetes in patients with severe obesity can be a challenge, since insulin therapy can lead to more weight gain, which further exacerbates insulin resistance. Therefore, the observed metabolic effects of bariatric surgery in patients with type 1 diabetes can facilitate medical management of this disease. In addition to the positive impact on weight and glycemic control, bariatric surgery can also improve other obesity-related comorbidities including hypertension, dyslipidemia, sleep apnea, gastroesophageal reflux disease, fatty liver, urinary incontinence, and musculoskeletal problems in obese patients with type 1 diabetes."

Kirwan et al. Bariatric surgery in obese patients with type 1 diabetes. Diabetes Care 2016;39:941–948

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Modest Glycemic Benefits of Liraglutide in Overweight/Obese Patients With Type 1 Diabetes

Liraglutide (a GLP-1 receptor agonist) in addition to insulin treatment for overweight/obese patients with type 1 diabetes likely results in modest improvements in glucose control and weight loss. According to the authors of the study, Kuhadiya et al. (**p. 1027**), its use in all patients with type 1 diabetes is probably not justified at this stage on the basis of additional expense, the modest outcomes, and likely gastrointestinal side effects. Their conclusions are based on the outcome of a prospective randomized trial that investigated the effects on blood glucose parameters of placebo or three different doses of liraglutide daily for 12 weeks. Blood glucose in this case was monitored with a continuous glucose monitoring system. The primary outcome was the difference from baseline of mean weekly blood glucose concentrations before and after the trial period in each of the groups in comparison with changes seen in the placebo group. Other outcomes included changes in HbA_{1c}, insulin doses, percent time spent in different glycemic ranges, body weight, blood pressure, carbohydrate intake, and glucagon levels. In the groups that received the two highest doses (1.2 mg and 1.8 mg), mean weekly blood glucose dropped by about 0.55 mmol/L, while in the low-dose group (0.6 mg) and in the placebo group blood glucose did not change. Other significant reductions in one or both of the highest doses were observed for many of the secondary outcomes. Liraglutide also led to significantly more gastrointestinal adverse events in comparison with placebo. While acknowledging the potential issues of liraglutide intervention, the authors suggest that the effects seen pave "the way for larger multicenter clinical trials over longer periods in overweight and obese patients with [type 1 diabetes] to establish the durability and consistency of effects of liraglutide in [type 1 diabetes]." Highlighting the potential benefits and where this research should go, Prof. Dandona stated that "the benefit of improved diabetic control was best seen in patients with the highest HbA_{1c} and BMI, and hence future studies should target such a population."

Kuhadiya et al. Addition of liraglutide to insulin in patients with type 1 diabetes: a randomized placebo-controlled clinical trial of 12 weeks. Diabetes Care 2016;39:1027–1035

Exenatide Reduces Glucose Variability in Type 2 Diabetes

A proof-of-concept study into another GLP-1 agonist, exenatide, taken with meals in addition to basal insulin and metformin, suggests that the intervention can reduce glycemic variability, weight, and certain cardiometabolic risk markers in patients with type 2 diabetes and high cardiovascular risk. Significantly, this was in comparison with basal-bolus insulin alone and while HbA_{1c} was maintained at the same level over the course of the study. Using a two-arm comparison design, the FLAT-SUGAR study by Probstfield et al. (**p. 973**) compared glucose variability (and a number of secondary outcomes) over a 26-week intervention period. After a run-in period of 8–12 weeks where all volunteers received metformin and basal-bolus insulin, about half of the volunteers then received exenatide instead of mealtime insulin (the GLIPULIN group) with the remainder staying on the run-in regimen (BBI group). The total population studied was ~100 volunteers. Glucose variability was assessed by continuous glucose monitoring. According to the authors, exenatide intervention resulted in glucose coefficients of variation (CV) dropping by 2.4. In contrast, the BBI group had a CV increase of 0.4. Other glycemic variability indices followed this pattern of improvement, although were not statistically significant. There were also no differences in hypoglycemia or arrhythmia rates between the groups, and, according to the authors, changes in body weight and certain other factors favored the GLIPULIN group. Commenting more widely on the study, Prof. Probstfield and Prof. Hirsch stated: "How high-risk type 2 diabetes is best treated is still being debated, partly due to the unclear impact of glycemic variability. Our results show that, added to basal insulin, short-acting exenatide given with meals is at least as effective as the previous gold standard treatment, basal-bolus insulin. Further, this regimen has the advantage of reducing weight and glycemic variability, two potential contributors to cardiovascular risk. Our findings from FLAT-SUGAR allow us to design future more definitive studies."

The FLAT-SUGAR Trial Investigators. Glucose variability in a 26-week randomized comparison of mealtime treatment with rapid-acting insulin versus GLP-1 agonist in participants with type 2 diabetes at high cardiovascular risk. Diabetes Care 2016;39:973–981

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