Findings

Good Long-Term Outcomes after Metabolic Surgery in Diabetes

Ten-year follow-up data in patients with type 2 diabetes show better outcomes in those undergoing metabolic surgery, compared to conventional medical therapy, reports a study in *The Lancet*.

The researchers analyzed data from a previous open-label, single-center trial in which 60 obese patients with type 2 diabetes were randomly assigned to medical therapy, Roux-en-Y gastric bypass (RYGB), or biliopancreatic diversion (BPD). The main outcome of interest was diabetes remission, defined as glycated hemoglobin less than 6.5% with a fasting blood glucose level of less than 5.5 mmol and no diabetes medications for at least 1 year. Fifty-seven patients were available for long-term follow-up.

On intention-to-treat analysis, 10-year remission rates were 50.0% in the BPD group, 25.0% in the RYGB group, and 5.5% in the medical therapy group. One patient initially assigned to medical therapy achieved remission after crossing over to surgery. Overall, type 2 diabetes remained in remission throughout a 10-year follow-up in 37.5% of patients who had either form of metabolic surgery.

Of the 34 patients whose diabetes was in remission at 2 years, 20 had a relapse of hyperglycemia during follow-up. Relapse rates were 52.6% in the BPD group and 66.7% in the RYGB group. However, all patients with relapse had adequate glycemic control at 10 years. Risk of diabetes-related complications was substantially lower in the two metabolic surgery groups: relative risk 0.07. Compared to patients receiving medical therapy, serious adverse events were more frequent in the BPD group (odds ratio 2.7) and less frequent in the RYGB group (odds ratio 0.7).

Bariatric or metabolic surgery has become an established treatment for type 2 diabetes, with clinical trials showing prolonged remission and reductions in cardiometabolic and chronic kidney disease risks, among other benefits. The new report presents the first randomized trial data on outcomes of metabolic surgery for diabetes beyond a 5-year follow-up.

The results add further support to the effectiveness of metabolic surgery over conventional medical therapy for long-term control of type 2 diabetes. The investigators conclude, "Clinicians and policy makers should ensure that metabolic surgery is appropriately considered in the management of patients with obesity and type 2 diabetes" [Mingrone G, et al. Metabolic surgery versus conventional medical therapy in patients with type 2 diabetes: 10-year follow-up of an open-label, single-centre, randomised controlled trial. *Lancet* 2021; 397:293–304. doi: 10.1016/S0140-6736(20)32649-0; https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32649-0/fulltext].

Corticosteroid Withdrawal after Kidney Transplant: 15-Year Follow-Up

Long-term corticosteroid therapy may not be necessary in kidney transplant recipients receiving calcineurin-based immunosuppressive therapy, according to a clinical trial report in *JAMA Surgery*.

The researchers analyzed long-term follow-up data from a previous multi-center, randomized, double-blind trial including 385 adult patients undergoing living or deceased kidney transplantation between 1999 and 2002. All patients were classified at low-to-moderate immune risk and were free of delayed graft function or short-term rejection within the first week.

Patients were assigned to tacrolimus and mycophenolate mofetil, with or without corticosteroids, 7 days after transplantation. Outcomes were assessed via linkage to the national Organ Procurement and Transplantation Network (OPTN) registry up to 2018–2019; median follow-up was 15.8 years. The primary outcome was all-cause kidney allograft failure including death, accounting for the need for long-term dialysis or repeat transplantation.

On intention-to-treat analysis, there was no significant difference in time-to-allograft failure from any cause, or in allograft failure censored for death, for patients assigned to corticosteroid withdrawal versus continuation. Similar patterns were seen in subgroup analyses, as well as on per-protocol analysis of 223 patients who stayed on their assigned treatment for at least 5 years. Outcomes were also comparable to those of 3540 patients from the OPTN registry who met the study eligibility criteria and received the same immunosuppressive drugs.

To avoid adverse effects, several studies have evaluated the effects of eliminating corticosteroids from immunosuppressive regimens after kidney transplantation. Despite positive results of clinical trials, only 30% of recipients are managed with corticosteroid withdrawal.

The new analysis supports the long-term safety of corticosteroid withdrawal in low-to-moderate immune-risk transplant recipients receiving calcineurin-based immunosuppression. At 15 years' follow-up, patients assigned to corticosteroid withdrawal versus continuation show no significant difference in outcomes. The authors note that the original trial showed no increase in moderate-to-severe short-term rejection events in the corticosteroid withdrawal group [Woodle ES, et al. Early corticosteroid cessation vs. long-term corticosteroid therapy in kidney transplant recipients. Long-term outcomes of a randomized clinical trial. *JAMA Surg*, published online ahead of print February 3, 2021. doi: 10.1001/jamasurg.2020.6929; https://jamanetwork.com/journals/jamasurgery/article-abstract/2775940].

Antibiotics Don't Reduce UTI in Transplant Patients with Bacteriuria

For kidney transplant recipients with screening-detected asymptomatic bacteriuria (ASB), antibiotic treatment does not reduce the risk of developing urinary tract infection (UTI) and may lead to emergence of antibiotic-resistant bacteria, reports a study in *Clinical Microbiology and Infection*.

The pragmatic, open-label Bacteriuria in Renal Transplantation (BiRT) trial included 199 patients with ASB detected by screening at least 2 months after transplantation. Patients were randomly assigned to receive antibiotic treatment, using a drug active against the causative bacteria, or no treatment. The incidence of symptomatic UTI over routine 1-year follow-up was compared between groups.

Fluoroquinolones and second- or third-generation cephalosporins were the most commonly prescribed antibiotics in the treatment group. Incidence of symptomatic UTI during follow-up was 29.1% overall, with no significant difference between groups: 27% with antibiotics and 31% with no treatment. Per-protocol analysis of 87 patients in the antibiotic group and 92 in the no-treatment group showed similar results.

Secondary outcomes of pyelonephritis and kidney function were not significantly different between groups. On urine cultures performed 1 month after randomization, prevalence of ASB was 29% in the antibiotic group versus 66% in the no-treatment group. Throughout the follow-up year, antibiotic use was fivefold higher in the antibiotic group: 30 days per patient compared to 6 days per patient in the no-treatment group.

On continued screening, 78% of patients had at least one more episode of bacteriuria. Patients assigned to antibiotic treatment for initial ASB were more likely to have bacteriuria caused by bacteria resistant to clinically relevant antibiotics: 18% versus 4%.

Screening and treatment of ASB are often performed as part of routine surveillance after kidney transplantation. This practice can lead to increased antibiotic exposure, with the potential for selection of antibiotic-resistant bacteria. There are also questions as to whether ASB screening and treatment actually reduce the incidence of symptomatic UTI.

The BiRT study finds no significant reduction in symptomatic UTI with antibiotic treatment for screening-detected ASB more than 2 months after kidney transplantation. "By contrast, this strategy drastically increased antibiotic use and promoted the emergence of more resistant organisms in the urine," the researchers write. They note that their study supports recent recommendations against systematic antibiotic use in kidney transplant recipients with ASB [Coussement J, et al. Antibiotics versus no therapy in kidney transplant recipients with asymptomatic bacteriuria (BiRT): A pragmatic, multicentre, randomized, controlled trial. *Clin Microbiol Infect*, published online ahead of print September 10, 2020, doi: 10.1016/j.cmi.2020.09.005; https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(20)30534-6/fulltext].