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Editorial

Type 2 diabetes surgery: A casual finding?

Cirugía de la diabetes tipo II: ¿un descubrimiento casual?

And so it is. Just as Walter Pories said, we surgeons were unprepared to adequately assess the observation that gastric bypass surgery cured type 2 *diabetes mellitus* (IIDM). Indeed, it is a matter that is currently the subject of great debate among surgeons, endocrinologists, and general scientists, it was already touched on in 1982 after remission of diabetes was observed for the first time following a gastric bypass.² Remission had in fact been observed many years earlier in diabetic patients that underwent subtotal gastrectomies, however, its practical importance was never valued.¹ After a 16-year study comparing two cohorts that had similar original characteristics (one that underwent bypass surgery and one that refused surgery), the remission rate of IIDM for the surgery group was confirmed at 83%, with improvement in complications, and a reduced mortality from 4.5% to 1% ($P<.0001$).³

Twenty-five years have had to pass for those preliminary observations, along with those from other bariatric surgery units that also reviewed their own experiences in light of the initial findings, to be formally analysed by an international group of 50 experts in March 2007 in Rome. The results from this conference were then released for discussion by the scientific community. In the First World Congress on Interventional Therapies for Type 2 Diabetes, which was held in New York in September 2008,⁴ a series of recommendations were put together for performing the surgery safely and so to achieve better results. In other words, the accidental discovery was later subjected to standard scientific methodology in order to ensure that, when offering surgical treatment for IIDM to a patient, this is based on rigorous tests that ensure its effectiveness.

The bariatric surgery results observed in obese patients with IIDM attest to the fact that the resolution of diabetes does not depend on weight loss,⁵ since this is almost instantaneous. Most of the patients who are discharged from hospital no longer need insulin, and some do not require insulin or oral anti-diabetic drugs following procedures that include a biliopancreatic diversion, whether by a Roux-en-Y gastric bypass,⁵ an anastomosis,^{6,10} or a Scopinaro biliopancreatic diversion.⁵ The results from restrictive surgery are mainly related to weight-loss, since hormonal changes are minimal

or non-existent, and so the resolution of the diabetes is not so immediate. The meta-analysis carried out by Buchwald⁵ concerning diabetes obese patients ($BMI>35$) showed a global percentage of IIDM resolution of 56% when using gastric bands, 80% for Roux-en-Y gastric bypass, and 95% for Scopinaro biliopancreatic diversion and duodenal switch. Furthermore, Roux-en-Y gastric bypass, gastric bypass with an anastomosis, and biliopancreatic diversions resulted in better long-term percentages of resolution than restrictive bariatric surgery.⁵⁻⁷

Based primarily on these results, the New York Consensus Conference supports the gastric bypass as a procedure for treating IIDM patients with a BMI of 30-35 that are carefully selected and who have poor control of their condition. The Consensus also established as a priority for future development clinical studies for researching the role of surgery in patients with IIDM and a $BMI<30$. However, the 2008 New York Consensus failed to clarify the significance of “carefully selected patients with a $BMI<35$.”⁴ This was the main objective of the *Jornadas Internacionales sobre Cirugía de Diabetes* (International Conference on Surgery in Diabetes) that took place at the University of Malaga, where bariatric surgery experts, endocrinologists, and general scientists analysed when non-obese patients with type II diabetes should undergo surgery and which surgical technique to use.⁸

Because this is the authentic surgery for diabetes. Until now, only diabetes patients underwent obesity surgery. The challenge lies in surgically treating patients with type II diabetes and a BMI less than 30, not even corresponding to simple obesity, or patients with a BMI between 30 and 35, which is a subgroup for which the existing data indicate similar improvement or resolution of diabetes to those patients with a $BMI>35$.^{6,9} The experience attained up until now in the surgical treatment of patients with IIDM and BMI of 30-35 or 25-30 was reviewed by Fried et al.⁹ Using the most stringent criteria for surgical success (baseline glycaemia <99 mg/dl and glycosylated Hb $<6\%$ with no anti-IIDM treatment), the mean rate of resolution was 85.3% (81.8% in IIDM with BMI of 25-30, and 89.1% in IIDM with BMI of 30-35). In other words, identical results to those presented by Pories² in the

very first observations made in 1982 (resolution of IIDM in 83% of obese patients). After a follow-up period of 6-216 months, the gastric bypass technique (Roux-en-Y or an anastomosis) obtained the best results (97.7%), followed by biliopancreatic derivation (72.9%), and gastric band (72.2%).⁹ However, this review did not study the relationship between the rate of resolution and the progression of the IIDM before surgery in terms of total number of years under IIDM treatment, and especially, years of insulin treatment. Nor did this review investigate the relationship between the rate of resolution and the level of pancreatic reserve.

The main lack of information regarding IIDM patients with a BMI<30, based on the data currently available, is whether the mechanisms of development and progression of IIDM are different from patients with a BMI>30. The improvement in IIDM and secondary effects from the surgery could be worse than in patients with a BMI greater than 30, in which the excess weight of the patient plays a central role in the development and progression of IIDM.¹¹ Meanwhile, almost all studies agree on the finding that worse results are obtained in patients with a longer progression of the illness and more years on insulin treatment due to the deterioration of pancreatic beta-cells, compared to patients under treatment only with oral anti-diabetics and fewer than 5 years progression of the disease, in which resolution of IIDM is quick and complete. Therefore, it would seem logical to indicate surgical treatment in all patients with IIDM of short progression and receiving only oral anti-diabetics, above all in patients with BMI greater than 30.¹² However, this would mean operating on millions of IIDM patients all over the world, when many of these could adequately control their IIDM with oral anti-diabetic drugs, especially metformin, which has also been demonstrated to control the effects of IIDM on the cardiovascular system. Endocrinologists present at the meeting for Surgery in Diabetes at the University of Malaga⁸ agreed that surgery would be indicated in all insulin-dependent patients with difficulty in controlling their IIDM (determined by glycaemia and glycosylated haemoglobin levels), and in those in which metformin is unable to control glycaemia, requiring insulin supplementation. This would be the cut-off point for surgical treatment in patients between 18 and 65 years old.

It is also important to understand the long-term effects of this type of surgery. That is, whether it is a lasting solution or if hyperglycaemia reappears after a period of time. The only evidence that the effects are maintained comes from studies involving gastric bypass¹³ and biliopancreatic derivation techniques,⁷ while no long-term information exists for purely restrictive procedures, and the little data available indicates that the disease reappears in many patients after a year.¹⁴ The professional opinion agrees that the surgical procedure to be used should include a bypass in the duodenal area, this being an important mechanism for the resolution of IIDM, which does not involve any restrictive surgical procedures. This could be the source of the lower efficacy and long-term failure with these type of operations.¹³ The mechanisms that have been proposed as IIDM effective surgical techniques include duodenal bypass, which permits the early passage of undigested nutrients into the distal segments of the intestine,

which in turn stimulates the release of incretin hormones (such as GLP1 and GIP, proteins regulating postprandial insulin secretion) in the jejunum and ileum,¹⁵ a sustained caloric restriction,¹⁶ weight-loss,¹⁷ and poor absorption of nutrients.¹⁸

We are on the verge of a new era in the treatment of diabetes, although a long road still lies ahead. We have discovered a treatment for IIDM that was unthinkable only a few years ago. However, the application of this treatment is currently still under debate due to the fear of repeating past mistakes (by applying surgical techniques where not necessary) and the ethical doubts raised by the prospect of abandoning currently available knowledge and therapies used for resolving health problems with severe consequences. At the same time, the development and study of metabolic and endocrine alterations provoked by gastrointestinal are a source of information for their role in human nutrition and metabolism.¹⁹ The substances identified as key actors in the process of curing IIDM following bariatric surgery are aiding in the development of new drugs that will make a paradigm shift for diabetes: from treatment to reversal of the disease.¹³ For now though, as in obesity, surgery is the only viable option for achieving these results.

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