# Editorial
# Bariatric surgery: three remarks and an addendum at the begining of 2010

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**First remark**

Surgical methods of loosing weight have been initially almost exclusively used in "morbid" obesity, a special phenotype of this syndrome beyond the possibilities of traditional therapeutic resources. The number of surgical interventions ( the ~ 300.000/year in USA) may seem impressive, although the calculated percent of obese patients treated by this procedures may seem insignificant. I am sure that the failures of this procedure or at least partial failures (a drop in weight from 160 to 130 kg for instance, which might be considered a major success!) are more numerous than some statistics report (1-6). Not to speak of malabsorbtion syndrom or reccurent hypoglycaemia, that may raise medical issues, even more serious than treated obesity itself. This point of view should not be regarded as a dismissal of this type of procedure which is apparently the only solution in this phenotype of obesity.

**Second remark**

The interest roused by the surgical approach to obesity is justified by an important collateral information: the favorable effect of the bariatric surgical intervention on the metabolic control of diabetes, which was quite a surprising finding (7,8,9,10). Obesity almost always induces an increase in β-cell function. This is an adaptative reaction to the overload due to the increase in the number of insulin-dependent cells, not only adipocytes, but also miocytes and hepatocytes. This subset of hyperobese diabetics is a subphenotype, which thanks to bariatric surgery is going to get a lot of scrutiny in order to understand the pathogeny of some types of glucoregulation disorders that can quickly improve or dissapear after the surgical procedure.

**Third remark**

The different metabolic effects of the various bariatric surgical methods on the "remission" of diabetes raised the interest in the potential mechanism involved in this (10). The already described incretinic effect was the first option for an explanation. It is known that some intestinal hormons like GIP (glucoso-dependent insulinotrope peptide) and GLP 1 (glucagon-like peptide) establish a hormonal link between the intestinal epithelium and the β-cell. GIP is secreted in the K-cells from the duodenum and the proximal portion of jejunum ("fore-gut" intestine), whereas GLP1 is secreted by the L-cells from the distal ileonum and the colon ("hinde-gut" intestine) (11,12,13). The existence of the "entero-insular" axis is a certainty. However, the regenerative effect of the intestinal hormones on the β-cell mass/function is difficult to asses, due to the extremely limited access of the investigators to the endocrine pancreas, both *in situ* and *in vivo*. The extrapolation in

humans of data obtained in some animal models showing an increase in the number of the β-cells, is premature.

**Adendum**

For the last few years I promoted a pathogenetic hypothesis related to type 2 diabetes which is associated with overweight/obesity (about 90% of the cases), suggesting that in these cases the main disturbance is induced by the "*increased biochemical pressure*" of the various fuels in the energy system of the human body (14,15). In essence, the quantity of energetic fuels from the adipose tissue and the ectopic lipid deposits is almost always increased in type 2 diabetic patients (14, 15,18,19). The increase may be moderate (10-20%) to large (20-50%) and very large (over 50%). The high biochemical pressure in energy sistems is due to all types of fuels, both lipids (permanently stored in fat deposits and intermitently in systemic circulation) and carbohydrates (sometimes stored in deposits as glycogen but permanently present in systemic circulation as glucose). Even less is known about protein fuels, but the increase of their circulating levels as amino acids is obvious when the intake is very high, exceeding the need for continuos structural protein renewal. In this condition, more than half of the protein intake would be used for producing energy via neoglucogenesis. Little is known about the effect of glucogenic amino acids on the increased hepatic production of glucose.

Regarding the spectacular effect of bariatric surgery on the metabolic control, it may have a simpler explanation than it currently has, involving a strong activation of the entero-insular axis leading to a regeneration of β-cell mass (1, 4, 6, 11). In an energy system in which the biochemical pressure is increased, any rapid decrease in bodyweight which induces a drop in the biochemical pressure from the system, may explain the rapid correction of the various biochemical disturbances, determined by the improvement of the utilisation of glucose and fatty acids as fuels (20,21).

In our view, the metabolic improvement appears irrespective of the modality by which a decrease in body weight is obtained. In this respect we can exemplify the following case: pacient aged 53, with type 2 diabetes associated with important ponderal excess (BMI 39), hypertriglyceridemia (876mg/dl), HDL-cholesterol (34mg/dl) and HbA1c 11.5%, on treatement with metformin and sulfonilureic derivative, is imprisoned for 9 months, period in which he lost 27kg. After his conditioned parole, in need of a medical certificate, I found to my surprise that all determined biological parameters (blood glucose, triglycerids, HDL-cholesterol, HbA1c) were entirely normalised. Consulting his medical record with the previous disastruous metabolic derangement, I asked for a new assessment of his biological profile on the next day. Once again, all parameters were normal! However, based on the data inscribed in his file, I maintained the diagnosis of type 2 diabetes.

Such a normalisation of the biochemical profile as obtained in our patient is, as a rule, labeled by bariatric surgeons as a "total remission" of diabetes (1-6,10). This was not the case in our patient, which after dealing with the legal issues regained weight quite rapidly, and the biochemical profile deteriorated as before. Later the patient passed

through all the therapeutical steps, using all the new drugs, arriving finally to insulin therapy. However, this accelerated his weight gain without obtaining β-metabolic control. After 15 years since the apparent "total remission of diabetes" the patient with florid metabolic alterations developed all the chronical complications of diabetes. In order to admit a "total remission of diabetes", a long-term follow-up of post-surgical intervention is necessary.

The positive effect of losing weight on the metabolic profile of the diabetic patients and on β-cell function has been known for a long time (14,15, 22-25). The fact that by bariatric surgery, also called nowadays "*metabolic surgery*" (1), this effect is almost always obtained rapidly, led to the idea that its spectacular outcome is mediated by other mechanisms related to the activation of the entero-insular axis (11-13). Indeed, such a mechanism could be involved. However, the main reason for such a rapid biochemical normalization depends on the sharp decrease in body weight, which, of course, could be obtained in most cases after bariatric surgery, but also in patients who have had a similar weight-loss using other non-surgical methods. We believe tha the main goal in obesity treatment is the weight loss itself and not the method through which it was obtained.

The great debate commenced by bariatric surgeons reminded me of the unsolved problems with which modern diabetology must deal with. The first one is the change in the definition of diabetes and its diagnostic criteria, ranging from the epiphenomenon *hyperglycemia* (presently as the only criterium for the diagnosis of diabetes) to its *cause*, which is the loss of *the β-cell mass/function*. The second one is to reconsider the *classification of diabetes* in order to include the genetic and pathophysiological progress noted in the last decade. The third, to clarify *the role of obesity* in the ethiopathogenesis of type 2 diabetes and for the fourth, clearing-up what is and what is not the mechanism of the so-called *" peripheral insulin resistance"*, whether this mechanism really does exist as a primary cause of diabetes. According to the last genetic data, from the 20 genes found to be associated with diabetes, 17 express several β-cell molecules and 3 are related to body weight (30). No gene was associated with so-called insulin-resistance (33). Moreover, bariatric surgery results show that this so-called insulin-resistance documented by its "golden standard" of euglycaemic/ hyperinsulinaemic clamp (32), disappeared in several days-weeks. This cannot happen if the insulin-resistance is considered to be based on one or more genetic molecular defects as sustained by the ardent advocates of the concept of insulin-resistance as primary cause of diabetes (30,34).

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