

# The place of bariatric surgery in the management of the obese Type 2 diabetic patient

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### Introduction

Most patients with Type 2 diabetes are significantly overweight and obesity certainly plays a major role in the pathophysiology of the disease [1–3]. This deleterious effect of fat mass is generally attributed to insulin resistance, especially in the presence of visceral adiposity [4–6]. Furthermore, obese diabetic patients have a higher prevalence of associated vascular risk factors, such as arterial hypertension and dyslipidaemia, and are exposed to higher morbidity and mortality rates [7]. Conversely, studies with low- or very-low-calorie diets have demonstrated that weight loss markedly and rapidly improves the glycaemic control of obese diabetic patients [8–11] and also reduces the severity of associated vascular risk factors [12]. Weight reduction should thus represent a major target in the treatment of the obese patient with Type 2 diabetes [8, 9, 13–17]. Unfortunately, conventional therapy combining diet and exercise, or even pharmacological intervention using various antiobesity compounds, have a poor long-term success rate in most cases [18, 19], so that more aggressive strategies, such as bariatric surgery, may be considered in well-selected patients [20].

The aims of this concise review are: (1) to summarize the arguments in favour of a surgical approach in severely obese individuals with Type 2 diabetes; and (2) to analyse the efficacy of bariatric surgery on body weight reduction, quality of blood glucose control and improvement of associated risk factors in such patients.

### Benefits and limits of weight loss in obese patients with Type 2 diabetes

Beneficial effects of weight loss have been demonstrated in studies focusing on prevention, treatment and prognosis of diabetes in obese

individuals (review in [8, 9]). Most importantly, intentional moderate weight loss (<10 kg) has been shown to reduce (–44%) the risk of death from comorbid diabetes in overweight women [21]. Furthermore, each decrease of 1 kg has been estimated to increase life-expectancy by 3–4 months in obese patients with Type 2 diabetes [22]. Such observations should encourage the search for successful treatments to reduce weight excess in these patients.

A recent study compared the results of four classical strategies of weight reduction in overweight diabetic patients: regular clinic visits; behavioural group therapy; administration of the serotonergic anorectic agent dexfenfluramine (for an initial 3-month period); or combined home and clinic visits [23]. Only 103 of the 147 patients completed the 12-month study. Mean weight loss, whatever the strategy, was rather modest after 1 year of follow-up (between 1 and 3 kg) and indeed not sufficient to improve HbA<sub>1c</sub> levels, which remained quite stable or even tended to slightly increase in almost all groups. In a study performed on 114 obese patients with diabetes who had 12 months of follow-up after a 10- to 16-week behavioural weight control programme [24], only the very small ( $n = 6$ ) subgroup of patients who showed a marked and prolonged weight reduction above 13.6 kg exhibited a substantial reduction in both fasting blood glucose (from 10.3 to 6.1 mmol/l) and HbA<sub>1c</sub> (from 9.7 to 7.1%) levels. In 21 patients who achieved a less marked weight loss (between 6.8 and 13.6 kg), only a modest reduction in fasting blood glucose (–1.6 mmol/l) and in HbA<sub>1c</sub> (–1.1%) levels was observed after 1 year of follow-up. In the vast majority of patients (76%), who were less successful in losing weight, the parameters of glucose control did not improve, or even worsened. Thus, even if several studies have demonstrated that a modest weight loss could improve the metabolic

control of obese diabetic patients in the short term [25–27], only a major weight reduction can drastically reverse hyperglycaemia in the long term.

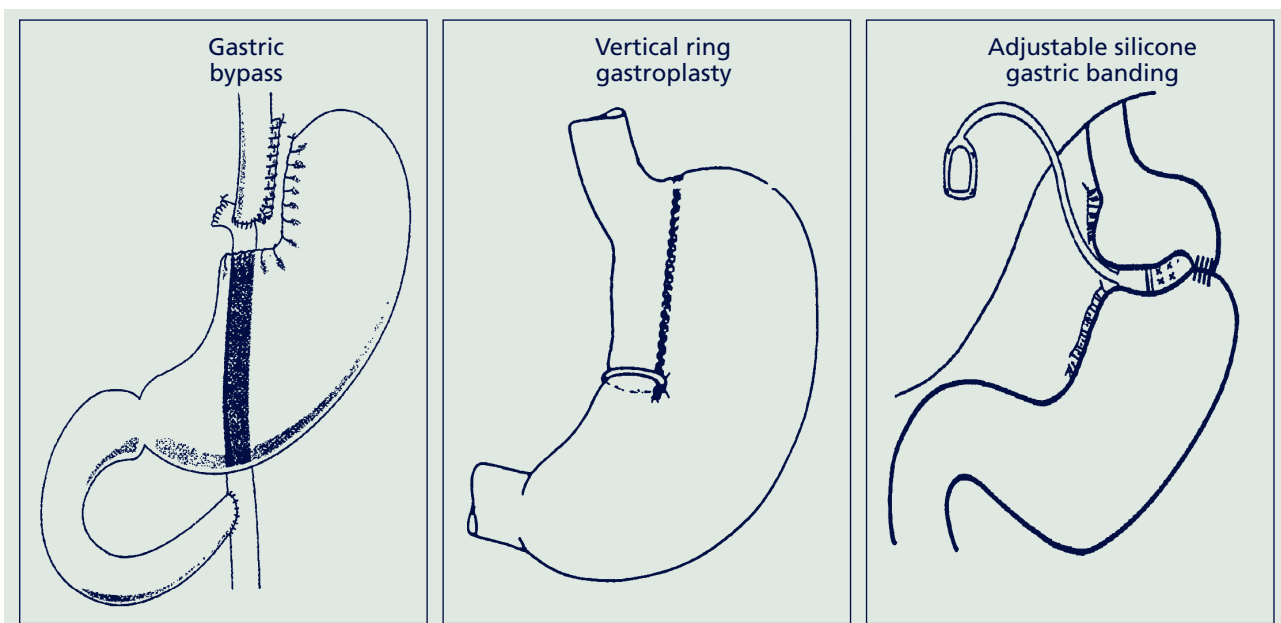
Theoretically, antiobesity drugs may represent a valuable help for the treatment of obese diabetic patients, providing that the treatment is effective, safe and may be maintained in the long term [28–32]. Unfortunately, the results of administering anorectic agents are usually disappointing, and probably not sufficient to improve glucose control and prognosis in the presence of severe or extreme obesity. In the *Desktop guide for the management of non-insulin-dependent diabetes mellitus* produced by the European NIDDM Policy Group [33], it was stated that effective management of Type 2 diabetes cannot be achieved without proper nutrition, and emphasis was put on weight control. However, there was no mention of any aggressive weight reduction therapy. In contrast, and interestingly, bariatric surgery was considered as a possible therapeutic approach in a recent review about the prevention and treatment of obesity and its application to Type 2 diabetes [9].

### Bariatric surgery as a therapeutic alternative

Most of the procedures currently used in bariatric surgery are based on inducing reductions in food intake: they include gastric bypass (GB) (Roux-en-Y), gastroplasty (essentially vertical ring gastroplasty, VRG) and gastric banding (adjustable silicone gastric banding, ASGB)

[34–37] (*Fig. 1*). The GB procedure involves constructing a proximal gastric pouch whose outlet is a Y-shaped limb of small bowel of varying lengths. VRG is designed to restrict food intake by the creation of a limited volume gastric pouch (20 ml) by stapling along the lesser curvature of the stomach. The small gastric reservoir empties through a narrow calibrated channel reinforced by a silastic catheter. In ASGB, a silicone elastomer banding forms a circular ring around the upper part of the stomach, delimiting a 25 ml gastric pouch. The inflatable part of the ring is connected to a self-sealing injection port which makes it possible to adjust postoperatively the diameter of the stomach, to avoid repetitive vomiting and warrant appropriate weight reduction. The latter technique has the advantages of being completely reversible, if necessary, and performed by laparoscopy.

In the National Institutes of Health Consensus Development Conference Statement [34], it was suggested that patients whose BMI exceeds  $40 \text{ kg/m}^2$  are potential candidates for surgery and that, ‘in certain instances, less severely obese patients (with BMIs between 35 and  $40 \text{ kg/m}^2$ ) also may be considered for surgery; included in this category are patients with ... severe diabetes mellitus’. It was also mentioned that ‘weight reduction surgery has been reported to improve several comorbid conditions such as ... glucose intolerance and frank diabetes mellitus’. The favourable effects of bariatric surgery on glucose metabolism could be so impressive that some authors, such as Pories et al., claimed that Type 2 diabetes may be considered



**Fig. 1:** Illustration of the three main surgical procedures currently used in bariatric surgery: Roux-en-Y gastric bypass, vertical ring gastroplasty and adjustable silicone gastric banding.

a surgical disease [38] and that 'an operation proves to be the most effective therapy for adult-onset diabetes mellitus' [39].

### Beneficial effects of bariatric surgery on glucose metabolism in non-diabetic obese subjects

Numerous studies performed during the last 15 years have clearly demonstrated that bariatric surgery, including jejuno-ileal bypass, GB and gastroplasty, allows substantial weight reduction and remarkable improvement of glucose metabolism and glucose tolerance in severely obese subjects [40–47]. As a consequence, hyperinsulinism, which is a common finding in massive obesity, is markedly reduced after improvement of metabolism associated with weight loss.

Our group carefully evaluated insulin secretion, clearance and action before and after gastroplasty in severely obese non-diabetic subjects [48]. Eight severely obese non-diabetic women (BMI averaging 37.7 kg/m<sup>2</sup>) were studied before and 14 ± 2 months after successful gastroplasty and recovery of ideal body weight (BMI 23.7 kg/m<sup>2</sup>) and compared with age-matched lean control women [49]. Serial measurements of plasma glucose, insulin and C-peptide during an intravenous glucose tolerance test allowed calculation of the insulin secretion rate, the insulin metabolic clearance rate and the coefficients of insulin sensitivity and of glucose effectiveness using the minimal model approach. Obese subjects before gastroplasty were characterized by higher insulin secretion, lower insulin clearance and lower insulin sensitivity compared with controls. Interestingly, a complete normalization of all these abnormalities was observed after recovery of ideal body weight following gastroplasty in the postobese subjects [49].

Such favourable metabolic effects may explain why marked weight loss associated with bariatric surgery could prevent the development of overt diabetes in severely obese subjects. Indeed, the conversion rate from impaired glucose tolerance to Type 2 diabetes was estimated to be 4.72 cases per 100 person-years in obese subjects, but was drastically decreased to 0.15 cases per 100 person-years in subjects who succeeded in obtaining important and sustained weight reduction after bariatric surgery, corresponding to a more than 30-fold reduction in the risk of diabetes [50]. Similarly, the preliminary results of the prospective, controlled Swedish Obese Subjects (SOS) study demonstrated in a large cohort of obese patients that bariatric surgery resulted in a

marked reduction of the 2-year incidence of hyperglycaemia (0.3 vs 6.8% in obese subjects treated by conservative methods) [51].

### Bariatric surgery: an overview of its efficacy in Type 2 diabetes

#### *Effects on body weight*

Bariatric surgery has been shown to be the most effective therapeutic approach for extreme obesity [18]. Weight loss is rapid, as most weight excess is lost during the first 6–12 months after surgery, and sustained during a follow-up of several years [35–37]. Average weight reduction is similar with the two surgical procedures VRG and ASGB, but somewhat greater with GB because of additional malabsorption [34–37]. Several studies have been performed in obese individuals with Type 2 diabetes, and the results were similar to those obtained in non-diabetic subjects (*Table I*). Available studies comprised small ( $n = 9$ ) to large ( $n = 154$ ) series of subjects who, in most cases, were submitted to VRG or GB. Mean initial body weight averaged 118–157 kg, and mean weight loss averaged 28–45 kg, 6–108 months after surgery. Such a weight reduction is much more impressive than that obtained by the more classical medical approaches (see above).

#### *Effects on glucose control*

Several studies have reported that bariatric surgery is able to reduce hyperglycaemia in most severely obese patients with Type 2 diabetes (*Table I*). Remarkable improvements in glucose control have been demonstrated after GB or VRG in patients with both mild [56] and severe [38, 53, 59] diabetes. In the series of Pories et al. [38, 59], HbA<sub>1c</sub> levels dramatically decreased from 11.8 to 6.5%. Both fasting plasma glucose and insulin levels decreased in all studies (*Table I*).

It is noteworthy that bariatric surgery allows the suppression or, at least, drastic reduction of antidiabetic drugs (*Table II*). In several studies [52, 55, 64], insulin therapy may be withdrawn in all subjects, while in others [53, 62, 63] it may be stopped in 65–75% of patients initially treated with insulin. Similarly, drastic weight reduction associated with bariatric surgery allowed the interruption of sulphonylurea therapy in the vast majority of the diabetic patients. In those patients still receiving hypoglycaemic drugs after surgery, the pharmacological dosage was significantly reduced. In this respect, the results were particularly impressive in the large series reported by Scopinaro et al. [64] in which

**Table I:** Effects of bariatric surgery on glycaemic control in obese patients with Type 2 diabetes [16,17].

Reference	Type of surgery	Subjects (n)	Study period (months)	Body weight (kg)		Glycaemia (mmol/l)		Insulinaemia (µmol/l)		HbA <sub>1c</sub> (%)	
				Before	Loss	Before	After	Before	After	Before	After
Ackerman [52]	JIBP	24	19	152	?	10.2	5.6	—	—	—	—
Herbst et al. [53]	GB	23	20	120	31	17.8	6.4	—	—	11.8	7.9
Kellum et al. [54]	GB	9	6	139	?	6.9	4.6	273	52	—	—
Deitel et al. [55]	VG	27	12–24	94–174	24–76	12.1–17.6	4.8–6.5	—	—	—	—
Pories et al. [38]	GB	52	12	120	37	11.8	6.5	321	96	10.8	6.4
Tourniaire et al. [56]	VG	36 <sup>a</sup>	6	±118	28	6.4	5.5	193	108	5.8	5.3
MacDonald et al. [57]	GB	154	108	157	45	10.4	<7.8	—	—	—	—
Scheen et al. [58]	VG	24	28	119	28	8.6	5.8	—	—	8.3	5.6

JIBP, jejunio-ileal bypass; GB, gastric bypass; VG, vertical gastroplasty.

<sup>a</sup>Including patients with impaired glucose tolerance.

biliopancreatic bypass resulted in the suppression of any antidiabetic drug in every diabetic patient. As suggested by the results reported in Table II, the outcome might be more favourable after bypass surgical techniques than after simple gastroplasty, because of the great weight loss usually reported with these more aggressive techniques.

Our group studied 24 severely obese patients with overt diabetes mellitus in whom gastroplasty was performed, resulting in a marked weight reduction of about 30 kg [16, 20, 58]. Despite the fact that body weight was not normalized (reduction of BMI from 44.8 ± 1.6 to 33.3 ± 1.2 kg/m<sup>2</sup>, 28 ± 4 months after gastroplasty), a remarkable improvement in glucose control was

**Table II:** Effects of bariatric surgery on antidiabetic treatment modalities in obese patients with Type 2 diabetes [16,17].

Reference	Type of surgery	Subjects (n)	Study period (months)	Weight loss (kg)	Treatment before surgery (n)		Treatment after surgery (n)	
					Sulphonylurea	Insulin	Sulphonylurea	Insulin
Ackerman [52]	JIBP	24	19	?	6	6	0	0
Herbst et al. [53]	GB	23	20	31	0	23	?	7
Gleysteen et al. [60]	GB	9	12	±45	9	0	0	0
Pories et al. [61]	GB	88	±18	±55	13	20	1	2
Deitel et al. [55]	VG	27	12–24	24–76	5	4	0	0
Jensen et al. [62]	VG	83	±60	±30	23	26	5	9
Smith et al. [63]	GB	135	3–84	20–45	64	46	18	11
Scopinaro et al. [64]	BPD	388	>12	?	108	32	0	0
MacDonald et al. [57]	GB	154	108	45	22	28	?	13
Scheen et al. [58]	VG	24	28	28	5	7	1	4

JIBP, jejunio-ileal bypass; GB, gastric bypass; VG, vertical gastroplasty; BPD, bilio-pancreatic bypass.

observed which persisted more than 2 years after surgery. Fasting blood glucose levels decreased from 8.6 to 5.8 mmol/l and HbA<sub>1c</sub> levels diminished from 8.3 to 5.6%. This metabolic improvement was observed despite a marked diminution of the antidiabetic treatment. Indeed, the number of patients treated by insulin, sulphonylureas and metformin decreased after gastroplasty and weight loss (from 7 to 4, from 5 to 1 and from 17 to 5, respectively), and the corresponding dosages had to be markedly decreased in the remaining treated patients.

#### *Effects on associated risk factors*

Weight loss is usually accompanied by a remarkable correction of disorders associated with obesity [12, 65], and beneficial effects on cardiovascular risk factors have already been reported after a modest weight reduction [25–27]. In a large cohort of 505 obese patients followed for 21 ± 15 months after gastroplasty, a clear-cut improvement was observed after a weight reduction of about 30 kg, with significant reductions in serum glucose, insulin, triglycerides, total cholesterol, uric acid and plasma fibrinogen levels, and a significant increase in serum HDL cholesterol concentration [66]. Both the severity and the prevalence of all of these biological abnormalities were significantly reduced after drastic weight loss. Furthermore, as the metabolic abnormalities of obese subjects were significantly associated with liver steatosis, the prevalence and the severity of the latter have also been shown to be remarkably reduced after weight reduction following bariatric surgery [67].

In obese patients with Type 2 diabetes, in addition to the improvement in glycaemic control, gastroplasty-induced weight loss resulted in a major reduction of other risk factors such as arterial hypertension and dyslipidaemia, as observed in non-diabetic individuals [60, 66]. In a series of 24 obese diabetic patients submitted to bariatric surgery (resulting in a 28.1 ± 2.7 kg weight loss after 28 ± 4 months), systolic (from 167 ± 4 to 137 ± 4 mmHg,  $p < 0.001$ ) and diastolic (from 98 ± 3 to 78 ± 3 mmHg,  $p < 0.002$ ) arterial blood pressure decreased after weight loss and antihypertensive drugs could be reduced in 7 out of 12 treated patients. Similarly, serum total cholesterol tended to decrease from 6.04 ± 0.38 to 5.68 ± 0.31 mmol/l (ns), HDL cholesterol increased from 0.94 ± 0.10 to 1.48 ± 0.23 mmol/l ( $p < 0.05$ ) and triglyceride levels decreased from 2.69 ± 0.39 to 1.45 ± 0.23 mmol/l ( $p < 0.01$ ) [16, 20, 58]. Thus, the overall risk profile of

severely obese diabetic patients is markedly improved after successful bariatric surgery.

#### *Effects on morbidity and mortality*

The ultimate objective of bariatric surgery is not to reduce risk factors, but to improve the prognosis and the quality of life of the obese patient. No prospective study has demonstrated that bariatric surgery prolongs life-expectancy when compared with medical supervision, especially in the population with Type 2 diabetes. Nevertheless, a recent study compared the outcome of 154 obese diabetic subjects submitted to GB with that of 78 obese subjects who were not submitted to surgery (controls) [57]. After a mean follow-up of 6.2 years and 9 years, respectively, the mortality rate in the control group was 28%, compared with 9% in the surgical group (including perioperative deaths) ( $p < 0.0003$ ). For every year of follow-up, patients in the control group had a 4.5% risk of dying *vs* a 1.0% risk for those in the surgical group ( $p < 0.0001$ ). This improvement in the mortality rate in the surgical group was primarily due to a decrease in the number of cardiovascular deaths. Such favourable results, which are in agreement with the remarkable reduction of risk factors, need to be confirmed in large prospective studies such as the ongoing SOS study [68].

### **Bariatric surgery: a brief overview of its safety**

Operative mortality is currently below 0.5% in centres specializing in antiobesity surgery [35–37], and is likely to decrease further because of the development of less invasive surgical techniques. The most common side effect of GB is the ‘dumping syndrome’, while the most prevalent side effects of gastric restriction (VRG or ASGB) are intolerance of solid food, vomiting and reflux oesophagitis. In a series of 1000 gastroplasties, gastrointestinal complications requiring surgical revision were rare in the early phase (<2% during the first year) but relatively common in the long term (up to 20–25%) [35]. In the above-mentioned series of 24 obese diabetic individuals [16, 20, 58], four patients had to undergo surgery again 2–3 years after their initial VRG, essentially because of staple line disruption or outlet stenosis. It is noteworthy, however, that the occurrence of such mechanical complications has been reduced over recent years, probably due to improvement in surgical techniques. Finally, the complications of bariatric surgery may be reduced by a good

selection and follow-up of obese patients by a well-trained, multidisciplinary team [69].

## Conclusions

Weight loss is a major target in treating obese patients with Type 2 diabetes. Consequently, aggressive weight reduction programmes may be used in selected patients refractory to conventional diet and drug treatment. Bariatric surgery is probably the only approach able to markedly reduce and sometimes completely correct severe weight excess in the long term. Successful gastroplasty not only fully reverses the abnormalities of insulin secretion, clearance and action on glucose metabolism present in severely obese non-diabetic patients, but also reduces associated cardiovascular risk factors. Most importantly, gastric reduction surgery allows significant improvement of glycaemic control and alleviation (and even interruption) of antidiabetic therapy in most obese patients with Type 2 diabetes, as well as correction of dyslipidaemia and arterial hypertension. Thus, bariatric surgery may be helpful in well-selected severely obese diabetic patients, provided that it is performed by a skilled multidisciplinary team. However, long-term prospective studies, such as the ongoing SOS study, still should more precisely determine the long-term benefits of bariatric surgery and the real place of the surgical approach in the overall management of obese diabetic patients.

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