Metabolic Intestinal Bypass Surgery for Type 2 Diabetes in Patients with a BMI < 35 kg/m²: Comparative Analysis of 16 Patients Undergoing either BPD, BPD-DS, or RYGB

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Keywords

Metabolic surgery · Intestinal bypass surgery · Type 2 diabetes · BMI < 35 · Low BMI

Summary

Background: Metabolic surgery for type 2 diabetes mellitus in patients with low body mass index (BMI) is a novel concept. Early studies show the surgery to be safe and effective but are inconclusive regarding the most effective procedure. **Methods:** Metabolic intestinal bypass surgery was performed in n = 16 patients with type 2 diabetes and a BMI < 35 kg/m² (mean age 56 years, range 36–68; 8 females; mean BMI 32 kg/m², range 26–34.5). Biliopancreatic diversion with duodenal switch (BPD-DS), biliopancreatic diversion according to Scopinaro (BPD), and Roux-en-Y gastric bypass (RYGB) were performed in 7, 5, and 4 diabetic patients, respectively. Mean preoperative duration of medical antidiabetic therapy was 16 years (range 4–40). Thirteen patients used insulin on average for 6 years (range 1–12), the mean insulin requirement was 92 IU per day (range 30–140). The analysis was accomplished retrospectively from data prospectively collected in our data base. **Results:** At discharge from hospital, only 3 of the 13 patients who used insulin preoperatively required small amounts of insulin (mean 21 IU per day, range 15–30) to keep fasting and postprandial plasma glucose levels below 200 mg/dl. After 1 year, none of the patients used insulin or oral antidiabetic drugs. The HbA_{1c} level decreased for the total patient population from 8.6% (range 5.8–12.1) preoperatively to 6.0% (range 4.3–7.8), 5.7% (range 4.1–7.6), and 5.6% (range 4.1–7.8) after 3, 6, and 12 months, respectively. The HbA_{1c} levels at 1 year were significantly lower after

BPD-DS and BPD than after RYGB (5.2%, range 4.1–6.4 versus 6.7%, range 5.8–7.8, p < 0.01, ΔHbA_{1c} 1.4%, 95% confidence interval 0.5–2.4). **Conclusion:** Metabolic intestinal bypass surgery for type 2 diabetes in low BMI patients is effective, with HbA_{1c} levels at 1 year after the operation being significantly lower after BPD-DS or BPD than after RYGB.

Introduction

Type 2 diabetes mellitus has traditionally been viewed as a chronic metabolic disease with a relentless progressive course leading to microvascular and macrovascular complications [1, 2]. The rate and severity of complications are not only influenced by the duration of the diabetes but also by the control of the metabolic state of the disease [3]. Since the development of complications of type 2 diabetes mellitus is associated with reduction of life time [4] and reduction of quality of life [5, 6], the major aim of therapy is to prevent or delay complications mainly by aggressive treatment of hyperglycemia and related metabolic diseases [7]. Keystones of therapy are education for lifestyle, diet and exercise, oral antidiabetic agents, recently parenteral incretin analogs and insulin therapy along with medical treatment of associated comorbidities.

Intestinal surgery bypassing the duodenum and the first part of the jejunum causes rapid normalization or improvement of glucose metabolism in patients with type 2 diabetes mellitus [8]. Complete remission of type 2 diabetes mellitus is a characteristic of all surgical [9, 10] and endoluminal [11] procedures that exclude the duodenum and the proximal jeju-

num from food passage. Diabetes usually resolves within days after the bypassing procedure, long before a significant weight loss has occurred [12, 13]. In fact, insulin sensitivity improves within a few days after Roux-en-Y gastric bypass (RYGB) [14], biliopancreatic diversion according to Scopinaro (BPD) [15], and biliopancreatic diversion with duodenal switch (BPD-DS) [16]. These findings of rapid postoperative remission of type 2 diabetes are in sharp contrast to purely restrictive procedures which appear to improve diabetes simply by promoting weight loss [17] and do not improve insulin sensitivity early after surgery [18]. Remission of diabetes with maintaining euglycemia without antidiabetic medication has been demonstrated to be sustainable after intestinal bypass surgery for at least 10–15 years [12, 19, 20].

Currently, bariatric surgery is considered appropriate for individuals with type 2 diabetes and a body mass index (BMI) > 35 kg/m² [7, 21]. Therefore, most of our knowledge regarding remission of diabetes after intestinal bypass surgery derives from studies on morbidly obese patients. However, a few studies have been published in patients with type 2 diabetes and a BMI < 35 kg/m². A recent review by Fried et al. [22] detected 18 studies including a total of 343 patients dealing with metabolic surgery for diabetes in patients with a BMI < 35 kg/m². After exclusion of publications on restrictive procedures and ileal interposition, only 11 papers were left on intestinal bypass surgery containing 189 patients with a BMI < 35 kg/m². The authors state that the best available evidence to date is that metabolic surgery for resolution of type 2 diabetes in the non-morbidly obese is safe and effective [22].

For the last 5 years, we have been routinely performing 3 different intestinal bypass procedures (BPD-DS, BPD, RYGB) in our institution to treat type 2 diabetes mellitus. In 2009, the American Diabetes Association revised their recommendations and included for the first time bariatric surgery as a therapeutic option in patients with type 2 diabetes, especially if the diabetes is difficult to control with lifestyle and pharmacologic therapy [7]. Thus, poorly controlled diabetes has evolved to a self-contained indication. About 80% of our patients are treated with insulin. Since our main indication is diabetes, some of our diabetic patients did not fulfill the criteria of morbid obesity. The aim of the present study is to analyze our preliminary data on intestinal bypass surgery in patients with type 2 diabetes and a low BMI (< 35 kg/m²).

Patients and Methods

The patient population consisted of 16 consecutively operated patients with type 2 diabetes mellitus and a BMI < 35 kg/m². Principally, 3 types of metabolic intestinal bypass surgery were offered to the patients: BPD-DS (always done in a conventional open way), BPD according to Scopinaro (usually performed laparoscopically, 4 in 5 cases), and RYGB (always laparoscopically). All 3 operations are well established bariatric surgical procedures with excellent remission rates of type 2 diabetes. Decision making as to which operation should be performed was mainly based on

the following criteria: first, the different remission rates of the 3 procedures in patients with a BMI > 35 kg/m² according to the literature [9] and own experience; second, the duration of diabetes and insulin usage since a strong correlation of duration and severity of diabetes to remission rate has been demonstrated for the RYGB procedure [23]; third, different mortality rates [24]; fourth, different adverse effects following the 3 procedures (malnutrition, protein deficiency, malodorous stools, frequent stools, dumping, risk of weight regain); fifth, necessity to use anticoagulant or aspirin for macrovascular disease with the surgeon's suggestion to perform a BPD or BPD-DS in these cases for easy feasibility of gastroscopic intervention at bleeding, sixth a patient's urgent interest in laparoscopic surgery; sixth, the patient's preference. The decision for surgery was made in collaboration with a multidisciplinary team. All patients were well informed about the risks and benefits of the procedures, and about the necessity of lifelong surveillance and dietary supplementation with vitamins, micronutrients, calcium, on occasion iron, and proteins. They usually participated in a support group before surgery. The present study analyses data collected prospectively in our database.

Surgical Technique

BPD-DS consisted of an open approach. A gastric sleeve resection was performed along a 44 French bougie. Motility of the antrum was preserved by starting the resection 6–8 cm above the pylorus. The duodenum was transected approximately 4–5 cm distally to the pylorus and anastomosed to the ileum. The small bowel was usually transected 250 cm proximal to the ileocolic valve, but at 300 cm if the length of the total small bowel exceeded 600 cm. A common channel of 100 cm was created. Cholecystectomy and appendectomy were routinely performed simultaneously. In 1 patient, a gastric band was removed simultaneously; in another patient, a sleeve had been performed 2 years before; in both cases the diabetes persisted and was poorly controlled. BPD according to Scopinaro consisted of a creation of a large proximal gastric pouch of about 300 ml and resection of the remnant of the stomach. The ileum was transected at 300 cm proximal to the ileocolic valve, the gastroileostomy was performed in a retrocolic way, a common channel of 80 cm was constructed. Cholecystectomy and appendectomy were also performed simultaneously. BPD was performed laparoscopically in 4 of 5 cases. In 1 patient, a gastric band was removed simultaneously. RYGB was always performed by laparoscopy with creation of a small pouch, a 150 cm Roux limb, and a 50–60 cm biliopancreatic limb. The Roux limb was brought up to the gastric pouch by an antecolic antegastric route.

Follow-Up

With the exception of 1 BPD-DS patient who was lost to follow-up (moved abroad), all patients were re-examined 3, 6, and 12 months after surgery.

Statistics

The data are presented as mean values, usually also the range is shown. Significant differences between groups were calculated using the Student's unpaired t-test. Results were considered statistically significant if the p value was < 0.05.

Results

The total patient population (n = 16) was divided into 3 groups according to the type of intestinal bypass procedure performed. The baseline characteristics of the 3 groups and of the total population are shown in table 1. Patients undergoing a RYGB procedure were significantly younger than patients with BPD-DS but not than patients with BPD or a combination of the patients with BPD-DS and BPD. No difference

Table 1. Baseline characteristics of the patient population

	BPD-DS (n = 7)	BPD (n = 5)	RYGB (n = 4)	Total (n = 16)
Mean age, years (min–max)	61 ^a (54–68)	52 ^{b, c} (36–62)	50 (37–63)	56 (36–68)
Gender (female/male), n	4/3	3/2	1/3	8/8
Mean BMI, kg/m ² (min–max)	32 (26–34.5)	32 (31–34)	32 (31–34)	32 (26–34.5)
n = Number of patients.				
^a p < 0.05 compared to RYGB.				
^b n.s. compared to BPD-DS.				
^c n.s. compared to RYGB.				

Table 2. Diabetes characteristics before surgery

	BPD-DS (n = 7)	BPD (n = 5)	RYGB (n = 4)	Total (n = 16)
Mean duration of medical treatment of type 2 diabetes, years (min–max)	19 ^a (4–40)	17 ^a (10–25)	10 (6–18)	16 (4–40)
Treatment modality preoperatively (OAD/insulin), n	2/5	0/5	1/4	3/13
Mean treatment with insulin, years* (min–max)	6 ^a (3–12)	7 ^a (4–11)	3 (1–6)	6 (1–12)
Mean daily amount of insulin, IU* (min–max)	108 ^b (75–140)	96 ^a (30–130)	58 (35–80)	92 (30–140)
Mean HbA _{1c} , % (min–max)	9.3 ^a (7.3–12.1)	8.2 ^a (6.3–10.8)	7.8 (5.8–10.6)	8.6 (5.8–12.1)
n = Number of patients; OAD = oral antidiabetic drugs.				
*Relates to n = 13 patients.				
^a n.s. compared to RYGB.				
^b p < 0.05 compared to RYGB.				

was found in preoperative BMI values; 14 patients had BMI values between 30 and 34.5 kg/m² and 2 patients had a BMI value < 30 kg/m².

Diabetes characteristics of the patients are recorded in table 2. Although the mean duration of medical treatment of the diabetes and the mean duration of insulin treatment seem to be shorter in the RYGB group than in the BPD-DS and the BPD group, no significant difference could be detected. The lack of significance is probably due to wide variations in the groups and the small number of patients. However, the daily amount of insulin was significantly higher in the BPD-DS group than in the RYGB group, and also the BPD-DS and BPD patients combined used significantly more insulin per day than the RYGB patients. No significant differences could be seen in the preoperative values of HbA_{1c} levels of the 3 groups.

The BMI values after 1 year dropped for each single patient, no patient was obese after 1 year. No excessive weight loss occurred. After 1 year, the mean BMI values and the minimum and maximum values of BMI were 23 (19–28), 27 (24–30), and 27 (26–28) kg/m² for the BPD-DS group, BPD group and RYGB group, respectively. The differences between the groups did not reach significance.

At discharge from hospital, only 3 patients required small amounts of insulin (mean 21 IU per day, range 15–30), all other patients were off any antidiabetic medications.

The HbA_{1c} levels decreased from 9.3, 8.2, and 7.8% preoperatively in the BPD-DS, the BPD, and the RYGB group (see table 1) to 5.2% (range 4.1–6.4), 5.3% (range 4.2–6.3), and 6.7% (range 5.8–7.8), respectively, after 1 year. The difference be-

tween the BPD-DS group and the RYGB group as well as the BPD group and the RYGB group was statistically significant (p < 0.05). Since the HbA_{1c} levels after 1 year were similar in the BPD-DS and the BPD group, these groups were combined and compared to the RYGB group. Despite the small number of patients, the difference was highly significant (p < 0.01). The development of HbA_{1c} after surgery is shown in figure 1.

Discussion

In our study, 16 patients with type 2 diabetes and a BMI < 35 kg/m² underwent 1 of 3 well established metabolic intestinal bypass procedures to treat a long-standing type 2 diabetes: BPD-DS, BPD, or RYGB. There are 3 major findings. First, all 3 types of intestinal bypass surgery proved to be very effective in the amelioration of type 2 diabetes. At discharge from hospital, only 3 patients were dependent on antidiabetic medication to keep plasma glucose levels below 200 mg/dl, and the mean HbA_{1c} level decreased from a preoperative level of 8.6% to 6.0% within 3 months after surgery. One year after surgery, none of the patients used any antidiabetic drugs or insulin. Given the fact that in our patient population the mean duration of medically treated diabetes was 16 years, 80% of the patients required insulin for an average of 6 years and used more than 90 IU a day, and the glucose metabolism was insufficiently controlled in most of the patients as indicated by a mean HbA_{1c} level of 8.6% preoperatively, the results of all 3 intestinal bypass procedures are intriguing. As has been comprehensively docu-

Fig. 1. Development of HbA_{1c} from baseline levels preoperatively to postoperative values 3, 6, and 12 months after surgery. The grey columns represent the mean HbA_{1c} levels of the total population (n = 16). Also shown are the minimum and maximum values of the total population (left bars). The bars with the filled circles represent mean and range values of the patients with BPD-DS and BPD combined (n = 12, ●), the bars with the open circles represent the patients with RYGB (n = 4, ○). Mean values of these 2 patient populations are denoted preoperatively and after 12 months. Significance between the 2 populations is shown at the top (n.s. = not significant).

mented in morbidly obese patients [9], it is evident that intestinal bypass surgery also offers the chance of a complete remission of diabetes in the non-morbidly obese patient population. Second, 1 year after surgery, the HbA_{1c} level was significantly lower in the BPD-DS and BPD group than in the RYGB group. There is high evidence that 2 factors are decisive for the chance of resolution of type 2 diabetes after gastrointestinal bypass surgery: first, the type of surgical procedure [9] and second, the duration and severity of the disease [23]. Both the duration of medically treated diabetes as well as the duration of insulin treatment tended to be shorter in the RYGB group, and also the daily amount of insulin in the insulin-requiring patients was lower for the RYGB patients than for the BPD-DS/BPD patients. Since this study has a retrospective design, the finding of shorter duration and less severe diabetes in the RYGB group reflects our attitude to prefer and to suggest to our patients a BPD-DS or a BPD rather than a RYGB the more long-standing and difficult to control the diabetes is. Despite the fact that the diabetes tended to be of shorter duration and of less severity in the RYGB group, the better outcome in glucose metabolism of the BPD-DS/BPD group is noteworthy. Unfortunately, only few studies have been published to date showing the results of metabolic intestinal surgery in patients with low BMI [22]. There are only 2 studies on RYGB comprising 37 [25] and 15 [26] patients, 3 studies on BPD including 7 [27], 5 [28], and 30 [29] patients, and 1 study on BPD-DS without gastric sleeve resection including 10 patients [30]. The other studies on metabolic intestinal bypass surgery in low BMI diabetic patients deal with novel antidiabetic procedures including duodenal-jejunal bypass and mini-gastric bypass [22]. Five of the 6 studies performing established metabolic intestinal bypass procedures showed a 100% abandonment of diabetes medication. However, no comparative studies on different operative procedures

have been published yet. Thus, there are no data in the literature to support or challenge our findings of a higher efficacy of the biliopancreatic diversion regarding complete remission of diabetes in the low BMI patients. However, our observation is well in line with the well-known higher efficacy of BPD and BPD-DS compared to RYGB for resolution of type 2 diabetes in the morbidly obese patient population. It is of utmost interest whether these initial results on HbA_{1c} translate into a better medium- and long-term outcome. Third, we could not detect a difference in efficacy of BPD and BPD-DS. Except for the study of Noya [30] who performed a BPD-DS without gastric sleeve resection, our present study is to our knowledge the first study on BPD-DS in patients with low BMI, and it shows the same high efficacy to treat type 2 diabetes in patients with low BMI as the standard BPD according to Scopinaro. Based on our extensive experience with BPD-DS in patients with diabetes mellitus, especially insulin-dependent type 2 diabetes, and a BMI > 35 kg/m² [13], we were not reluctant to offer this kind of surgery also to diabetic patients with a BMI < 35 kg/m².

Conclusion

Our data support the statement of Rubino et al. [31] that metabolic gastrointestinal bypass surgery offers a novel endpoint to the armamentarium of diabetes care: complete disease remission, and BPD/BPD-DS seem to be the most effective surgical tool to achieve this goal also in the low BMI patient population.

Disclosure Statement

The authors declare no conflict of interest.

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