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Resolution of Diabetes Mellitus and Metabolic Syndrome following Roux-en-Y Gastric Bypass and a Variant of Biliopancreatic Diversion in Patients with Morbid Obesity

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Background: Obesity is associated with increased prevalence of type 2 diabetes mellitus (DM2) and metabolic syndrome and increased morbidity and mortality. Bariatric surgery results in significant and long-term weight loss. Two of the most effective and popular bariatric procedures are Roux-en-Y gastric bypass (RYGBP) and biliopancreatic diversion (BPD). The objective of this study was to investigate the effects of RYGBP and BPD-RYGBP, a variant of BPD with a lower rate of metabolic deficiencies than BPD, on DM2 and the major components of metabolic syndrome in patients with morbid obesity and DM2.

Methods: The prospective database of our unit, from June 1994 until May 2006, was analyzed and 137 patients with DM2 were found. 26 underwent RYGBP (BMI 46.1±2.9 kg/m^2) and 111 BPD-RYGBP (BMI 59.7±10.6 kg/m^2). 7 of the patients were on insulin (4.90%) and 37 on oral hypoglycemic agents (25.87%). Pre- and postoperative medications, and clinical and biochemical parameters were considered in the analysis. The mean follow-up was 26.39 ± 21.17 months.

Results: Excess weight loss was ~70% after either procedure. DM2 resolved in 89% and 99% of the cases following RYGBP and BPD-RYGBP, respectively. 2 years after BPD-RYGBP all the patients had blood glucose <110 mg/dl, 95% had normal cholesterol, 92% normal triglycerides and 82% normal blood pressure. The respective values following RYGBP were 66%, 33%, 78% and 44%. Uric acid decreased significantly only after BPD-RYGBP. Liver enzymes improved in both groups.

Conclusions: RYGBP and BPD-RYGBP are safe and lead to normalization of blood glucose, lipids, uric acid, liver enzymes and arterial pressure in the majority of patients, although this variant of BPD was more effective than RYGBP. We suggest that further studies should also investigate its usefulness in patients with milder degrees of obesity, DM2 and metabolic syndrome.

Key words: Morbid obesity, bariatric surgery, diabetes, metabolic syndrome, gastric bypass, biliopancreatic diversion

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Introduction

Obesity is a disease of epidemic proportions worldwide and is closely linked to the development of diabetes mellitus type 2 (DM2).[1,2] Obesity predisposes to DM2 and glucose intolerance, hypertension, dyslipidemia, sleep apnea and other co-morbidities.[1] These abnormalities usually cluster in the same individual as components of the insulin resistance syndrome or metabolic syndrome.[3] Metabolic syndrome increases the risk for the development of DM and cardiovascular disease, conditions predisposing to increased mortality.[4] The association of obesity with increased morbidity and mortality makes weight loss mandatory.

Long-term weight loss following life-style intervention or medical therapy has proven to be disappointing.[5,6] It is well known that only surgery for obesity has shown remarkable results in helping patients achieve significant weight loss in the long-term.[7] In addition, it is associated with improvement of co-morbid conditions including DM2, hypertension, hypoventilation syndrome and sleep apnea, hypercholesterolemia, hypertriglyceridemia, polycystic ovary syndrome and non-alcoholic steatohepatitis.[8]

Roux-en-Y gastric bypass (RYGBP) and biliopancreatic diversion (BPD) are considered the most effective bariatric surgical procedures in terms of weight loss and the resolution of DM2 in morbidly obese patients.[8-10] Both procedures result in normal plasma glucose and insulin concentrations and restoration of normal β-cell response to hyperglycemia.[11,12] The aim of this study was to investigate the effect of RYGBP and BPD-RYGBP (a variant of BPD) on DM2 and the major components of metabolic syndrome in morbidly obese diabetic patients.

Patients and Methods

From June 1994, when the Morbid Obesity Unit in our Department was established, until May 2006, 745 patients with clinically severe obesity underwent various bariatric surgical procedures. Data for patients with DM2 were collected and analyzed from the prospective database of the Morbid Obesity Unit. Diabetes was diagnosed when fasting serum glucose concentration was >125 mg/dl on two occasions or the 2-hour glucose concentration was >200 mg/dl after a 75 g oral glucose tolerance test (OGTT). The search revealed 143 patients with DM2 in total and 137 with DM2 (18.39% of the operated patients) who underwent RYGBP[13,14] and BPD with RYGBP (BPD-RYGBP), a variant of BPD previously described in detail.[15] Seven of the patients were treated with insulin (5.11%), 36 with oral hypoglycemic agents (26.28%) and 94 (68.61%) with diet. The mean age of the whole group, consisting of 31 males and 106 females, was 41.38 ± 8.18 years, with a mean preoperative BMI of 56.34 ± 10.86 kg/m^2. Mean preoperative fasting serum glucose concentration of the whole group was 153.60 ± 50.22 mg/dl.

Patients were considered as hypertensive when systolic blood pressure was ≥140 mmHg and/or diastolic ≥90 mmHg or were on anti-hypertensive therapy. The hypertension was considered resolved when both systolic and diastolic pressures, without medication, were steadily below 140 and 90 mmHg, respectively.

Normal upper values for total cholesterol, LDL-cholesterol and triglycerides were considered 200 mg/dl, 160 mg/dl and 150 mg/dl respectively. Normal lower values for HDL cholesterol were considered 40 mg/dl for men and 50 mg/dl for women.

All the patients underwent surgery for obesity. Twenty-six patients (18.98%) with BMI<50 kg/m^2 underwent RYGBP and 111 (81.02%) with BMI ≥50 kg/m^2 underwent BPD-RYGBP, a variant of BPD. The main characteristics of RYGBP were: a 15 ± 5 ml gastric pouch, a biliopancreatic limb of 60 cm, an alimentary limb of 100 cm and a common limb consisting of the remainder of the small intestine (Figure 1A). The main characteristics of BPD-RYGBP were: a 15 ± 5 ml gastric pouch, a biliopancreatic limb of 150-200 cm depending on the full length of the small intestine, a common limb of 100 cm, and an alimentary limb consisting of the remainder of the small intestine (Figure 1B).

All patients underwent complete evaluation during follow-up including: medications, nutritional behavior, anthropometric and clinical parameters and blood sampling for glucose, triglycerides, cholesterol and other laboratory tests at 1, 6, and 12 months postoperatively and every year thereafter. Weight loss eval-

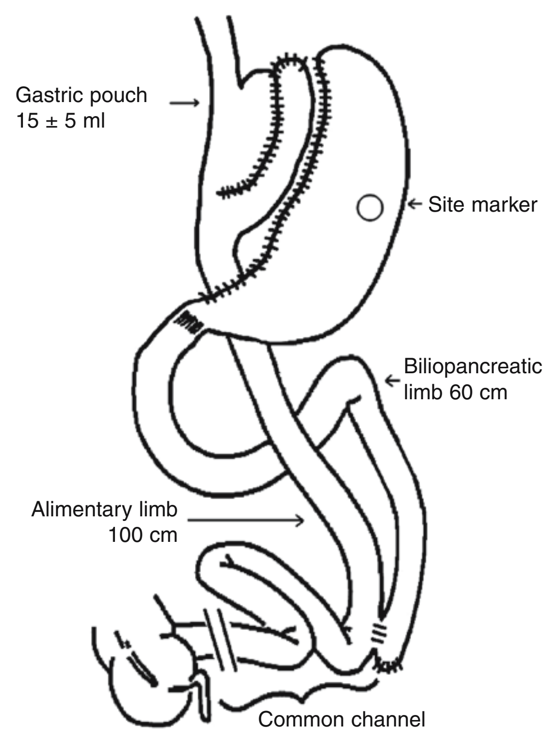

Figure 1A. Schematic representation of Roux-en-Y gastric bypass.

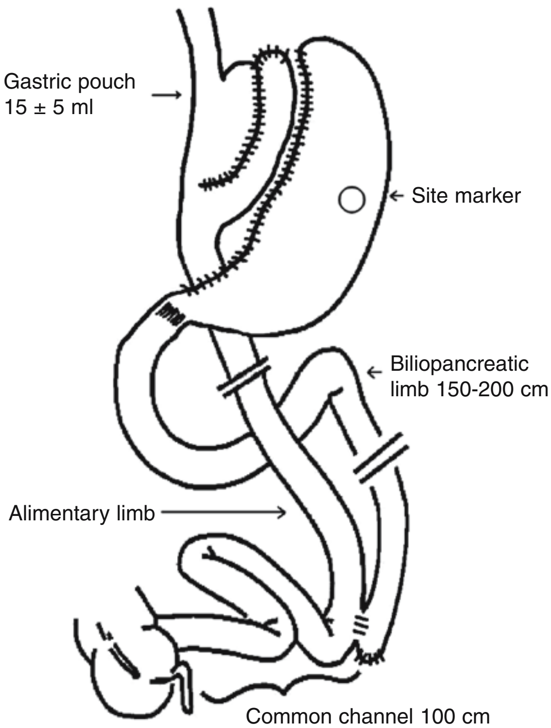

Figure 1B. Schematic representation of Biliopancreatic diversion with Roux-en-Y gastric bypass.

uation was based on postoperative BMI and percent of excess weight loss (%EWL). Ideal body weight was determined according to the Metropolitan Life Insurance Company 1983 height/weight tables.

Statistical Analysis

Data are expressed as mean ± standard deviation, unless otherwise stated. Comparisons between groups were performed using the Student's *t*-test and ANOVA for normally distributed variables. The Mann-Whitney and Kruskal-Wallis tests were used when distribution of the variables was not normal and the Fisher exact test for categorical variables. All reported *P*-values were two-sided and were considered significant at a level of $P \leq 0.05$.

Results

The mean follow-up was 26.39 ± 21.17 months for the whole group, 29.76 ± 25.05 months for the RYGBP group and 25.31 ± 19.34 months for the BPD-RYGBP group. Three patients (2.19%) were lost to long-term follow-up. Results to 60 months postoperatively are presented. Successful long-term follow-up was close to 80%. One patient from the BPD-RYGBP group died during the first 30 postoperative days (0.73%), due to intestinal necrosis and subsequent septic shock. Two patients died during the late postoperative period after BPD-RYGBP (1.46%). The first patient, with a medical history of scleroderma and hypertension, died during the first postoperative year due to cardiac arrest. The second patient died 6 months postoperatively due to aortic aneurysm rupture. The aneurysm was known preoperatively and was scheduled for repair after adequate weight loss had occurred.

Weight Loss

The patients, as a whole group, had 70% EWL during the first year and maintained the weight loss for the whole study period. BMI decreased from 56.34 ± 10.86 to 33.15 ± 6.63 kg/m^2 ($P<0.0001$). The BPD-RYGBP group of patients had a higher BMI preoperatively ($P<0.0001$) and a much greater reduction of BMI postoperatively than the RYGBP group (Tables 1 and 2).

Diabetes Mellitus

DM2 was cured in 133 / 137 patients (97.08%) and ameliorated in four patients (2.92%) who were on insulin treatment before the operation. DM2 resolved in 88.5% of RYGBP and 99.1% of BPD-RYGBP patients. DM2 resolution was faster after BPD and its prevalence was significantly lower after the first year following BPD. Three of the seven insulin-treated patients stopped any medication and are euglycemic until now, following BPD-RYGBP. Their BMI decreased from 60 and 65 kg/m^2 to 33.9 and 41.4 kg/m^2 respectively, 12 months postoperatively and they discontinued any medication for DM2. The third patient's BMI declined to 26 kg/m^2 and he stopped any medication from the second postoperative year and is still euglycemic 36 months postoperatively.

Four of the seven insulin-treated patients showed amelioration in the severity of DM2. Three of them underwent RYGBP and one BPD-RYGBP. One patient is on oral hypoglycemic agents and the other

Table 1. RYGBP: Anthropometric and biochemical parameters at baseline and during follow-up

Time (months)	Preop	1	12	24	36	48	60	P*
Successful follow-up		100%	80%	81.8%	90.9%	90.9%	81.8%	
Patients	26	18	12	9	10	10	9	
BMI (kg/m^2)	46.1±2.9	42.8±6.6	30.7±6.2	30.1±5.2	31.0±4.9	31.3±4.7	32.6±5.6	<0.0001
%EWL		22.7±7.5	69.6±17.6	68.5±18.8	64.7±18.3	63.3±17.0	57.4±21.2	<0.0001
Glucose (mg/dl)	173±67	112±32	92±34	107±46	109±41	111±54	111±33	<0.0001
Cholesterol (mg/dl)	239±60	168±44	190±44	207±45	168±53	198±48	196±65	0.0002
LDL-C (mg/dl)	148±54	105±41	124±45	127±33	91±37	114±38	118±48	0.0471
HDL–C (mg/dl)	43.2±.9.0	32.7±6.0	48.4±9.2	54.9±8.8	49.9±19.2	51.7±12.7	56.3±14.8	<0.0001
Triglycerides (mg/dl)	191±78	151±46	104±46	131±114	97±50	124±99	109±72	<0.0001
Uric acid (mg/dl)	5.30±1.50	6.27±1.20	5.00±2.24	-	5.00±2.97	5.16±2.38	4.52±1.48	0.3744
AST (IU/L)	30.4±15.1	41.7±13.6	22.3±8.7	-	26.4±11.1	22.9±12.5	24.3±5.8	0.004
ALT (IU/L)	43.8±25.3	62.0±36.9	26.0±10.5	-	26.4±12.8	23.8±10.0	22.3±11.6	0.0011
γ-GT (IU/L)	45.1±32.1	54.0±43.4	19.3±13.2	-	20.2±13.3	29.9±37.5	17.4±7.7	0.0168

*The significance attributed to the difference of preoperative to postoperative values.

Table 2. BPD-RYGBP: Anthropometric and biochemical parameters at baseline and during follow-up

Time (months)	Preop	1	12	24	36	48	60	P*
Successful follow-up		100%	93.67%	78%	85.29%	77.78%	75%	
Patients	111	96	74	39	29	21	12	
BMI (kg/m^2)	59.7±10.6	51.0±9.7	34.3±6.9	30.8±5.6	32.7±6.2	33.9±6.9	39.9±7.2	<0.0001
%EWL		21.5±10.1	70.0±18.6	73.6±16.6	67.2±18.3	70.3±28.0	49.3±18.8	<0.0001
Glucose (mg/dl)	151±42	114±34	85±15	85±9	88±12	91±15	95±18	<0.0001
Cholesterol (mg/dl)	209±37	147±28	135±27	144±28	154±35	157±26	150±27	<0.0001
LDL (mg/dl)	135±37	86±24	78±24	81±21	91±27	93±25	81±19	<0.0001
HDL (mg/dl)	42.6±12.9	31.6±6.9	41.8±10.3	47.3±12.0	46.3±11.1	47.1±10.9	44.5±7.7	<0.0001
Triglycerides (mg/dl)	169.±74	158±51	89±27	82±29	97±59	96±34	122±64	<0.0001
Uric acid (mg/dl)	5.91±1.73	7.44±2.43	3.93±0.98	3.79±1.03	3.53±1.23	3.82±0.97	4.06±0.99	<0.0001
AST (IU/L)	25.9±12.4	42.0±17.6	28.3±21.3	33.4±40.1	25.8±8.5	27.5±8.0	21.6±5.8	<0.0001
ALT (IU/L)	34.5±21.4	59.1±47.8	28.3±24.4	32.1±31.4	24.4±10.7	30.5±14.2	23.1±9.4	<0.0001
γ–GT (IU/L)	39.9±28.2	46.0±39.8	26.7±21.7	22.7±22.4	13.7±4.1	14.2±5.9	16.7±7.6	<0.0001

*The significance attributed to the difference of preoperative to postoperative values

three require reduced dosage of insulin. All four partial responders had known DM2 for >5 years and required preoperatively >40 units of insulin daily. Their mean age was 52.25 ± 4.65 years, significantly higher than the mean age of the whole group (*P*=0.01).

Glucose Levels

Fasting serum glucose levels decreased significantly in all patients during the whole follow-up period (*P*<0.0001). Glucose levels following either procedure decreased significantly from the first postoperative month (Tables 1 and 2). Glucose declined to lower levels in the BPD-RYGBP than in the RYGBP group after the first year, although the difference was not statistically significant. As shown in Table 3, the percentage of patients with serum glucose ≥125 mg/dl at 12 and 24 months postoperatively was lower after BPD-RYGBP compared to RYGBP (*P*=0.03 and *P*=0.01, respectively). The same was observed when the cutoff glucose value was set at 110 mg/dl (*P*=0.05 and *P*=0.01, respectively).

Hypertension

Sixty-four of the patients (46.72%) were hypertensive and 37 / 64 (57.81%) were treated preoperatively with anti-hypertensive medication. Systolic and diastolic blood pressure decreased significantly in the whole cohort of hypertensive patients with DM2 postoperatively ($P<0.0001$). Systolic blood pressure decreased progressively from 153.30 ± 20.87 mmHg to 128.30 ± 18.48 mmHg at 60 months postoperatively. In the same manner, diastolic pressure decreased from 94.09 ± 16.43 mmHg to 78.00 ± 15.21 mmHg. Blood pressure decreased significantly following either procedure, but the prevalence of hypertension was significantly lower in the BPD-RYGBP group compared to RYGBP at the second (Pearson χ^2=5.51, P=0.019) and at the third (Pearson χ^2=6.71, P=0.01) year of follow-up (Table 3).

Dyslipidemia

Preoperatively, 82 of the patients (59.85%) suffered from hypercholesterolemia and 74 (54.01%) from hypertriglyceridemia (Table 3). Postoperatively, total and LDL cholesterol, as well as triglyceride levels, decreased significantly ($P<0.0001$) and HDL values increased significantly ($P<0.0001$) for the whole study group.

Preoperative total cholesterol mean value was lower in the BPD-RYGBP group than in the RYGBP group (P=0.003). Postoperative total cholesterol values were also lower after BPD-RYGBP at 12, 24 and 48 months ($P<0.0001$, P=0.0007 and P=0.02, respectively) (Tables 1 and 2). The postoperative prevalence of hypercholesterolemia was lower after BPD-RYGBP compared to RYGBP, at 1, 12, 24 and 48 months (P=0.0017, P=0.0001, P=0.0031 and P=0.02, respectively).

Preoperative LDL cholesterol concentration was not different between the two groups but decreased to significantly lower levels after BPD-RYGBP compared to RYGBP, $P<0.001$ at 12 and 24 months (Tables 1 and 2). Postoperative HDL increase was similar after either procedure.

Triglycerides decreased markedly after both procedures, but no statistical difference was observed between the two procedures. Although the prevalence of hypertriglyceridemia was in general lower

Table 3. Prevalence of DM and other co-morbidities in obese diabetic patients undergoing RYGBP vs BPD-RYGBP

	Diabetes[1]		Glucose >110 mg/dl		Cholesterol >200 mg/dl		Triglycerides >150 mg/dl		Hypertension[2]	
Time (months)	RYGBP n (%)	BPD n (%)	RYGBP n (%)	BPD n (%)	RYGBP n (%)	BPD n (%)	RYGBP n (%)	BPD n (%)	RYGBP n (%)	BPD n (%)
Preop	26/26 (100)	111/111 (100)	26/26 (100)	111/111 (100)	20/26 (76.9)	62/111 (55.9)	18/26 (69.2)	56/111 (50.5)	13/26 (50)	51/111 (46)
1	7/18 (38.9)	21/96 (21.9)	12/18 (66.7)	41/96 (42.7)	6/18 (33.3)	3/96 (3.1)	11/18 (61.1)	53/96 (55.2)	6/18 (33.3)	33/96 (34.4)
12	3/12 (25)	2/74 (2.7)	3/12 (25)	3/74 (4.1)	5/12 (41.7)	0/74 (0.0)	2/12 (16.7)	4/74 (5.4)	3/12 (25)	14/74 (18.9)
24	3/9 (33.3)	0/39 (0.0)	3/9 (33.3)	0/39 (0.0)	6/9 (66.7)	2/39 (5.1)	2/9 (22.2)	3/39 (7.7)	5/9 (55.6)	7/39 (17.9)
36	1/10 (10)	2/29 (6.9)	1/10 (10)	3/29 (10.3)	4/10 (40)	4/29 (13.8)	2/10 (20)	2/29 (6.9)	6/10 (60)	5/29 (17.2)
48	2/10 (20)	0/21 (0.0)	2/10 (20)	5/21 (23.8)	7/10 (70)	2/21 (9.5)	3/10 (30)	2/21 (9.5)	5/10 (50)	5/21 (23.8)
60	3/9 (33.3)	1/12 (8.3)	3/9 (33.3)	2/12 (16.6)	6/9 (66.7)	1/12 (8.3)	1/9 (11.1)	3/12 (25)	3/9 (33.3)	3/9 (33.3)

Definitions: [1]Fasting glucose ≥125 mg/dl or >200 mg/dl at 2 hours post 75 g oral glucose; [2]Systolic blood pressure ≥140 mmHg and/or diastolic of at least 90 mmHg or under anti-hypertensive medication.

following BPD-RYGBP, the difference was not significant. Two RYGBP patients were excluded from the triglycerides' analysis due to very high preoperative values (852 and 1226 mg/dl), although they decreased to near normal levels postoperatively.

Uric Acid

There was a transient increase in uric acid levels at the first postoperative month and a gradual decrease thereafter to significantly lower levels compared to baseline in the whole cohort of patients ($P<0.0001$). The reduction in uric acid was significant only after BPD-RYGBP (Table 2).

Liver Enzymes

AST, ALT and γ-GT concentrations increased during the first month and declined subsequently to levels significantly lower than the baseline in the whole population of patients ($P<0.0001$) and to a similar degree after either bariatric procedure (Tables 1 and 2).

Discussion

In the present study, both bariatric procedures proved effective in terms of weight loss and DM2 resolution. The patients of the BPD-RYGBP group had higher BMI preoperatively but they also exhibited a greater reduction in BMI after the operation. %EWL was 68% and 69% after RYGBP and 70% and 73% after BPD-RYGBP at 12 and 24 months respectively. Buchwald et al[8] in a recent meta-analysis of 136 studies including 22094 morbidly obese patients, reported a mean %EWL of 61.6% (56.7%-66.5%) for RYGBP and 70.1% (66.3%-73.9%) for BPD.

DM2, in the present study, resolved in 97% of cases and improved in the few unresolved cases. The antidiabetic effect of both procedures became obvious from the first postoperative month, although weight loss was not remarkable at this time-point. Again, the variant of BPD was more effective than RYGBP in diabetes and impaired fasting glucose resolution (Table 3). DM2 resolved in the present study in 88.5% of cases after RYGBP and 99.1% after BPD-RYGBP, and this is in agreement with previous reports. Scopinaro et al[12] reported DM2 resolution in 97% of cases after BPD. In the meta-analysis by Buchwald et al,[8] resolution of DM2 ranged from 47.9% after gastric banding to 83.7% after RYGBP and 98.9% after BPD.

An interesting finding of the present study that has also been described by others,[16] concerns the history of unresolved cases of DM2. The patients usually had DM2 for >5 years, they needed higher doses of insulin, and they were older than the rest of the patients. It is reasonable to conclude that the resolution of DM2 is influenced by the duration and the severity of the disease. It is known that patients with DM2 have increased islet β-cell apoptosis, attributed among others to the chronic presence of insulin resistance and hyperglycemia, increased levels of TNFα and other cytokines, increased levels of free fatty acids and increased oxidative stress.[17] The increased rate of β-cell apoptosis leads with time to deterioration of DM2 due to progressive decrease of β-cell mass. In severe and long-lasting cases of DM2, it is more likely that the number of the β-cells that have survived is very low at the time of bariatric surgery and cannot compensate even after the restoration of normal insulin sensitivity.

The mechanisms of diabetes resolution after bariatric surgery are not completely understood. Obvious mechanisms are the marked reduction of calorie intake, weight loss and reduction of fat mass that lead to marked improvement in insulin sensitivity. Resolution of diabetes after pure restrictive bariatric procedures is based on this mechanism,[18,19] the same as very low-calorie diets.[5,20] RYGBP and BPD result in greater weight loss and resolution of DM2 in a higher percentage of patients.[8] The greater antidiabetic effect of RYGBP and BPD relative to restrictive procedures, can be due to the greater effects on body weight loss and fat mass reduction but also to the greater reduction in the plasma levels of free fatty acids (FFAs). Insulin sensitivity following BPD improves starting in the first postoperative months before remarkable weight loss has occurred, and this has been explained by the marked reduction of intra-myocellular lipid in skeletal muscle following this type of bariatric procedure that markedly decreases intestinal fat absorption.[21] In the present study, the variant of BPD proved superior to RYGBP in diabetes resolution from the first month, and this may be attributed to the greater weight loss and fat malabsorption after BPD.[22]

In addition to the above mechanisms, changes in GI hormones have been proposed to contribute to the restoration of euglycemia after RYGBP.[23,24] Bypass of the duodenum and proximal jejunum and rapid passage of food from the stomach the distal ileum augment the secretion of GLP-1.[25] GLP-1 potently increases insulin secretion and possibly insulin sensitivity.[26] Moreover, at least in rodents, GLP-1 triggers β-cell neogenesis and proliferation, while inhibiting apoptosis.[27] We have shown that BPD-RYGBP, performed in morbidly obese patients with DM2 of mild to moderate severity, leads to euglycemia and normal insulin sensitivity, but most importantly, it restores a normal β-cell acute insulin response (AIR) to glucose and a normal relationship of AIR to insulin sensitivity.[11] It is likely that changes in the enteropancreatic axis induced by this variant of BPD have contributed to the restoration of a normal AIR.

In the long-term, BPD reduces the increased β-cell apoptosis that is promoted by insulin resistance and hyperglycemia, the increased levels of FFAs and cytokines, and the increased oxidative stress. Recently, several cases of β-cell hypertrophy and hyperplasia with hyperinsulinemic hypoglycemia were published following RYGBP and BPD, suggesting that increased β-cell neogenesis and proliferation due to increased levels of GLP-1 and other β-cell trophic factors occur after operations of this type.[28]

Another finding of this study was the marked improvement in the major components of the metabolic syndrome after either operation. The improvement in hypertension was stable for the whole study period. In the SOS study, the therapeutic effect of vertical banded gastroplasty and Roux-en-Y gastric bypass on hypertension lost its significance after 10 years postoperatively.[10] On the contrary, after BPD, the percent of patients with normal arterial pressure increased from 50% at 1 year to 74% at 10 years, despite aging and body weight stability.[12] We also observed better results after our variant of BPD than after RYGBP, but no permanent conclusions can be made until longer follow-up. The therapeutic effect of BPD on hypertension has been attributed to the excellent weight loss and long-term weight maintenance and also to the complete and sustained disappearance of insulin resistance, with its key role in the metabolic syndrome.[12,29]

Dyslipidemia improved markedly after both procedures, and again the therapeutic effects of BPD-RYGBP were noticeably better. BPD-RYGBP, as a variant of BPD, causes greater fat malabsorption so that hypercholesterolemia and hypertriglyceridemia are cured almost always after this procedure.[12,22] BPD decreases dietary cholesterol absorption along with partial disruption of enterohepatic bile salt circulation. Decreased bile salt reabsorption increases hepatic synthesis of bile salts at the expense of cholesterol synthesis.[30] The hallmark of dyslipidemia in patients with DM2 and/or metabolic syndrome is the high levels of triglycerides in the presence of low levels of HDL cholesterol. Hepatic insulin resistance leads to increased liver production of triglyceride-rich VLDL particles, which in the circulation exchange triglycerides for cholesterol esters with the LDL and HDL particles, leading to triglyceride enrichment of LDL and HDL particles.[31] The triglyceride-rich LDL and HDL particles are good substrates for hepatic lipase, which is commonly increased in DM2 and metabolic syndrome. The hydrolysis of LDL and HDL particles converts them to small dense LDL and HDL. Small dense LDL particles are very atherogenic, and small dense HDL particles are catabolized faster leading to low levels of HDL cholesterol.[31] Complete normalization of insulin sensitivity after RYGBP and BPD decreases triglyceride levels and increases the HDL cholesterol levels.

The temporary increase in uric acid levels at the first postoperative month in this study could be due to the increased catabolism in the early postoperative period due to restricted calorie intake. In the long term, uric acid was reduced significantly only after the variant of BPD, an effect that was constant during the whole study period. This effect of BPD-RYGBP on uric acid metabolism was another advantage of this procedure over RYGBP. It has been reported that patients with metabolic syndrome have increased serum uric acid levels due to decreased urinary uric acid excretion.[32] We postulate that the resolution of metabolic syndrome and the restoration of normal insulin sensitivity after BPD probably increase urinary uric acid excretion back to normal.

Nonalcoholic fatty liver disease occurs in 30% to 100% of morbidly obese adults. Weight loss has been demonstrated as a therapeutic tool for this clinical entity, via improved insulin sensitivity.[33,34] This study confirms previous clinical observations, providing a decline in liver enzyme values postoperatively. As previously reported, this decline in liver enzymes reflects a real improvement of nonalcoholic fatty liver disease, as has been confirmed by postoperative liver biopsies.[35]

Mortality was low in our series; none of the 26 patients has died following RYGBP. One patient of 111 who underwent BPD-RYGBP died during the first postoperative month and two additional patients died from severe coexisting health problems 6 and 12 months after the operation. The mortality in our series after BPD-RYGBP was similar to general BPD series,[36] significantly lower than that reported following BPD in patients with DM2[12] and much lower than that reported in non-operated patients with DM.[37]

In the present study, the effects of two popular bariatric operations on diabetes resolution and improvement of the major components of the metabolic syndrome were investigated. Although the study was not prospective, our database is prospective. BPD-RYGBP had low mortality and was more effective in terms of weight loss, diabetes resolution and restoration of normal arterial pressure, normal levels of lipids and uric acid. Because BPD-RYGBP is not followed more frequently by metabolic deficiencies than RYGBP, as we have previously reported,[38,39] this variant of BPD may be suggested as an effective and safe procedure for the treatment of DM2 and metabolic syndrome in morbidly obese patients. Bariatric operations are currently performed only in patients with BMI >40 kg/m^2 or with BMI >35 kg/m^2 with co-morbid conditions such as type 2 diabetes. Prospective studies are needed to investigate the effects of this variant of BPD on diabetic patients with metabolic syndrome and lower BMI.

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