

Laparoscopic treatment of metabolic syndrome in patients with type 2 diabetes mellitus

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Abstract

Background Metabolic syndrome refers to risk factors for cardiovascular disease. Hyperglycemia is a critical component contributing to the predictive power of the syndrome. This study aimed to evaluate the results from the laparoscopic interposition of an ileum segment into the proximal jejunum for the treatment of metabolic syndrome in patients with type 2 diabetes mellitus and a body mass index (BMI) lower than 35.

Methods Laparoscopic procedures were performed for 60 patients (24 women and 36 men) with a mean age of 51.7 ± 6.4 years (range, 27–66 years) and a mean BMI of 30.1 ± 2.7 (range, 23.6–34.4). All the patients had a diagnosis of type 2 diabetes mellitus (T2DM) given at least 3 years previously and evidence of stable treatment using

oral hypoglycemic agents, insulin, or both for at least 12 months. The mean duration of type 2 diabetes mellitus was 9.6 ± 4.6 years (range, 3–22 years). Metabolic syndrome was diagnosed for all 60 patients. Arterial hypertension was diagnosed for 70% of the patients (mean number of drugs, 1.6) and hypertriglyceridemia for 70%. High-density lipoprotein was altered in 51.7% of the patients and the abdominal circumference in 68.3%. Two techniques were performed: ileal interposition (II) into the proximal jejunum and sleeve gastrectomy (II-SG) or ileal interposition associated with a diverted sleeve gastrectomy (II-DSG).

Results The II-SG procedure was performed for 32 patients and the II-DSG procedure for 28 patients. The mean postoperative follow-up period was 7.4 months (range, 3–19 months). The mean BMI was 23.8 ± 4.1 kg/m², and 52 patients (86.7%) achieved adequate glycemic control. Hypertriglyceridemia was normalized for 81.7% of the patients. An high-density lipoprotein level higher than 40 for the men and higher than 50 for the women was achieved by 90.3% of the patients. The abdominal circumference reached was less than 102 cm for the men and 88 cm for the women. Arterial hypertension was controlled in 90.5% of the patients. For the control of metabolic syndrome, II-DSG was the more effective procedure.

Conclusions Laparoscopic II-SG and II-DSG seem to be promising procedures for the control of the metabolic syndrome and type 2 diabetes mellitus. A longer follow-up period is needed.

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Metabolic syndrome has been well recognized in the medical literature since Reaven's [1] report that several risk factors for cardiovascular disease commonly cluster together. Patients with metabolic syndrome and type 2 diabetes mellitus (T2DM) have the highest prevalence of coronary heart disease (CHD), and those who have diabetes without metabolic syndrome have no greater prevalence of CHD than those with neither [2].

A number of organizations have developed different definitions for metabolic syndrome [3–6], but those of the World Health Organization (WHO) and the Third Report of the National Cholesterol Education Program's (NCEP) Adult Treatment Panel (ATPIII) have been the most frequently used. Despite the different criteria used for defining metabolic syndrome, with different cut points, probably affecting the sensitivity and specificity of the diagnosis, Ford and Giles [7] showed in an adult US population that metabolic syndrome was identified in the same proportion by the WHO and ATPIII criteria. However, approximately 15% to 20% of the individuals were classified as having the syndrome by one set of criteria but not the other.

Abdominal obesity is considered mainly responsible for the rising prevalence of metabolic syndrome. Obesity and T2DM are diseases of epidemic proportions, and the association between them is well established.

It is postulated that the pathologic sequence of events leading to T2DM is characterized by failure of beta cells to secrete adequate amounts of insulin to compensate for insulin resistance in peripheral tissues and by increased endogenous glucose production [8]. Insulin resistance, or hyperinsulinemia, is key in the pathogenesis of metabolic syndrome, with the term "insulin resistance syndrome" also commonly used. The dissociation of obesity and insulin resistance in patients with the metabolic syndrome is difficult.

Weight loss is beneficial for patients with obesity, T2DM, and metabolic syndrome. However, long-term realistic weight loss by nonsurgical methods has a variable impact on glycemic control, and only a proportion of T2DM patients have a worthwhile response [9].

Bariatric surgery, especially gastric bypass [10] and malabsorptive surgeries [11], are effective in achieving long-term control of obesity and in controlling T2DM. De Paula et al. [12] performed a technique termed "neuroendocrine break" characterized by a sleeve gastrectomy associated with an ileal interposition. They reported complete resolution of T2DM for morbidly obese patients. The mechanisms in relation to the ileal interposition and sleeve gastrectomy involved providing early exposure of ingested nutrients to the interposed ileum aimed at determining an early rise in glucagon like peptide 1 (GLP-1) and consequently influencing the defective early-phase insulin secretion. The aim is to induce an adjustable and long-

lasting weight loss, to restrict the caloric intake, and to diminish or abolish excessive stimulation of the duodenum.

This study aimed to evaluate the results for laparoscopic interposition of an ileum segment to the proximal jejunum associated with either sleeve gastrectomy or diverted sleeve gastrectomy used to treat the components of metabolic syndrome experienced by T2DM patients with a body mass index (BMI) lower than 35.

Materials and methods

Until September 2006, 60 patients with metabolic syndrome and T2DM were submitted to laparoscopic ileal interposition (II) associated with either a sleeve gastrectomy (II-SG) or ileal interposition related to a diverted sleeve gastrectomy (II-DSG). The 60 patients comprised 36 men (60%) and 24 women (40%) with a mean age of 51.7 ± 6.4 years (range, 27–66 years). The demographic data from each operation are summarized in Table 1. All the patients had a BMI lower than 35 kg/m^2 . The preoperative BMI ranged from 23.6 to 34.4 (mean, $30.1 \pm 2.7 \text{ kg/m}^2$).

A number of risk factors and other variables related to metabolic syndrome were assessed at baseline. The components of metabolic syndrome were defined according to the Third Report of the National Cholesterol Education Program's Adult Treatment Panel (ATPIII). The presence of T2DM did not exclude the diagnosis of metabolic syndrome [13]. The cut points for the five components included a waist circumference of 102 cm for men and 88 cm for women, a triglyceride level of 150 mg/dl or higher, a high-density lipoprotein (HDL) cholesterol level lower than 40 mg/dl for the men and lower than 50 mg/dl for the women, a blood pressure of 130/85 mmHg or higher, and a fasting glucose level of 100 mg/dl or higher. Patients were classified as having metabolic syndrome if they fulfilled three or more of these listed criteria thresholds.

All the patients had received the diagnosis of T2DM at least 3 years previously. The mean duration of T2DM was 9.6 ± 4.6 years (range, 3–22 years). Associated criteria included documentation of glycated hemoglobin (HbA1c) exceeding 7.5% for at least 3 months; stable weight, defined as no significant change ($>3\%$) over the 3 months before enrollment; and evidence of stable treatment with oral hypoglycemic therapy, insulin, or both for at least 12 months.

No special criteria were used to determine the two different configurations of the procedures, although it was assumed that the diverted version would be more effective in controlling T2DM. The exclusion criteria specified elderly patients (age, >66 years), previous major upper abdominal surgery, pregnancy, malignant or debilitating

Table 1 Demographic data

	Total	II-SG	II-DSG	<i>p</i> -Value
Patients	60	32	28	
Mean age (years)	51.7 ± 6.4	53.0 ± 6.8	49.6 ± 7.2	0.327
Range	27–66	27–66	33–63	
Males	36	20	15	0.182
Females	24	12	13	
Mean BMI	30.1 ± 2.7	31.4 ± 3.6	28.4 ± 3.1	0.102
Range	23.6–34.4	23.8–34.4	23.6–34.1	
Mean T2DM duration	9.6 ± 4.6	8.3 ± 4.5	11.4 ± 4.21	0.021
Range	3–22	3–22	4–22	
Oral hypoglycemic agent (%)	53.2	64.3	36.8	0.174
Insulin (%)	12.8	10.7	15.8	
Both (%)	34.0	25.0	47.4	

II-SG, ileal interposition sleeve gastrectomy; II-DSG, ileal interposition diverted sleeve gastrectomy; BMI, body mass index; T2DM, type 2 diabetes mellitus

disease, severe pulmonary or cardiac disease, severe renal disease (glomerular filtration rate lower than 30 ml/min), use of appetite suppressant medication, eating disorder such as bulimia or binge-eating, and obesity due to any other endocrine disorder.

Specific preoperative clinical assessment included family history of cardiovascular or coronary heart disease (11.7%), family history of T2DM (75%), associated CHD (15%), cigarette smoking (10%), waist circumference, and blood pressure via casual blood pressure measurement. Specific preoperative tests included fasting lipid profile, tests for microalbuminuria and serum creatinine, and estimates of glomerular filtration rate, C-reactive protein (CRP) levels, nonesterified fatty acids, adiponectin, resistin, interleukin-6, leptin, glucagon-like peptide-1 (GLP-1), glucose-dependent insulinotropic peptide (GIP), peptide YY and anti-GAD test.

All samples were assayed in duplicate through enzyme-linked immunoassay (ELISA) tests after the following sequence. Blood samples were collected into chilled tubes containing ethylenediaminetetraacetic acid (EDTA) and aprotinin, then kept on ice until centrifugation at 4°C. Plasma was separated and stored at –20°C until analysis through ELISA commercial kit tests (Linco Research, St Louis, MO, USA), performed within 30–60 min. This method with the respective kit was used for adiponectin, resistin, interleukin-6, leptin, GLP-1, GIP, and peptide YY. Other tests included Doppler study of the carotid arteries, retinopathy screening, and detailed cardiac evaluation. Biochemical markers of T2DM were obtained including fasting plasma glucose, postprandial plasma glucose, HbA1c, fasting plasma insulin, homeostasis model assessment of insulin resistance (HOMA-IR), and C-peptide. Plasma glucose concentrations were measured by a glucose oxidase method using a glucose analyzer (Yellow Springs Instrument Model YSI 2300 STAT plus analyzer; YSI, Inc., Yellow Springs, OH, USA). Plasma

insulin and C-peptide concentrations were measured by auto-DELPHIA automatic fluoroimmunoassay (Wallac, Inc., Turku, Finland).

The preoperative preparation for surgery included clear liquids for 48 h before the operation in association with regular insulin according to capillary glucose. Preoperative bowel cleansing, perioperative antibiotics, and low-molecular-weight heparin were administered.

Technique

Two different techniques were performed: ileal interposition associated with sleeve gastrectomy (II-SG) and ileal interposition associated with diverted sleeve gastrectomy (II-DSG). A standard five- or six-port laparoscopic technique was used after establishment of pneumoperitoneum.

The first technique, II-SG, started with division of the jejunum 30 cm from the ligament of Treitz using a linear stapler. An ileal segment of 150 cm was created 50 cm proximal to the ileocecal valve, interposed peristaltically into the proximal jejunum. All three anastomoses were performed functionally side by side using 60-mm linear staplers, with care taken to close mesenteric defects using interrupted 3–0 polypropylene sutures. For standardization purposes, intestinal measurements were performed with traction along the antimesenteric border using a 10-cm marked atraumatic grasper. The sleeve gastrectomy was performed after devascularization of the greater curvature using the ultrasonic scalpel, beginning in the distal portion of the antrum (5 cm proximal to the pylorus). A 38-Fr Fouchet orogastric calibration tube was placed by the anesthesiologist along the lesser curvature toward the pylorus. The gastric resection was performed starting at the antrum and proceeding up to the angle of His using a linear 45- or 60-mm stapler. A 3–0 polypropylene running

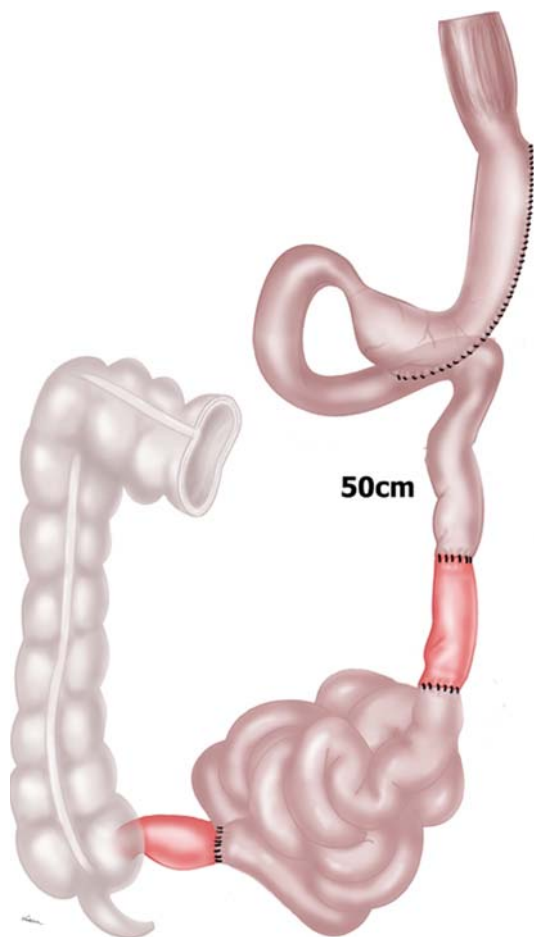


Fig. 1 Ileal interposition associated to a sleeve gastrectomy (II-SG)

invaginating suture covered the staple line. The gastric tube measured approximately 1.4 cm (Fig. 1).

The second technique, II-DSG, was an ileal interposition associated with a diverted sleeve gastrectomy, performed as mentioned earlier. Next, the devascularization along the greater curvature of the stomach continued to the duodenum, 3–4 cm beyond the pylorus. The duodenum was transected using a 60-mm linear stapler. A 3–0 polypropylene running invaginating suture covered the duodenal staple line. The gastric pouch and proximal duodenum then were transposed to the lower abdomen through the mesocolon. An ileal segment of 150 cm was created 50 cm proximal to the ileocecal valve, interposed and anastomosed peristaltically to the proximal duodenum. A point in the jejunum 50 cm from the ligament of Treitz was measured and anastomosed to the distal part of the interposed ileum. The anastomoses were performed functionally using 60-mm linear staplers, with care taken to close mesenteric defects using interrupted 3–0 polypropylene sutures. The duodenum–ileal anastomosis was performed using hand-sewing techniques with interrupted sutures (Fig. 2). The trocar openings were closed.

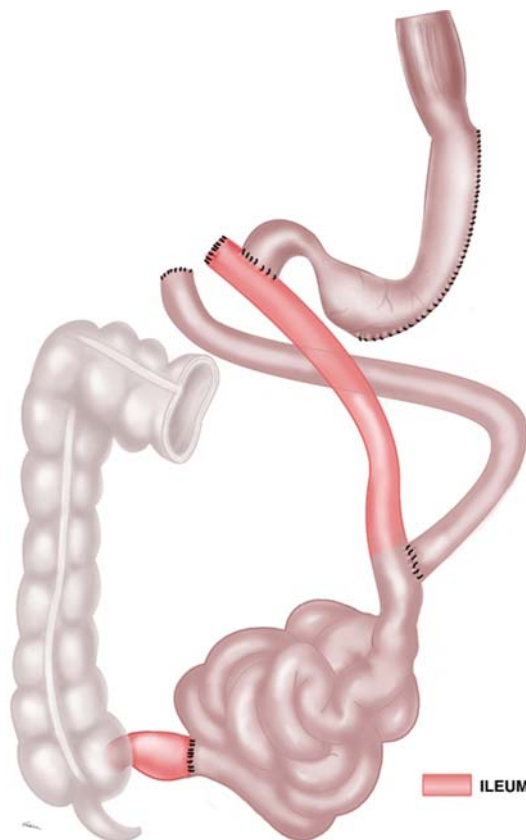


Fig. 2 Ileal interposition associated to a diverted sleeve gastrectomy (II-DSG)

Outcomes measures were collected prospectively. The main parameters evaluated included components of metabolic syndrome, fasting and postprandial glucose, HbA1c, diabetes, and antihypertensive medication usage (agents, doses, frequency), weight loss (expressed as BMI and percentage of weight loss), resolution or improvement of associated diseases and complications, reoperation rate, and morbidity–mortality of the procedure. Patient and laboratory evaluations were scheduled to be performed every 3 months until 18 months after the operation. The ethics committee of the hospital approved the study, and all subjects gave their written informed consent.

Statistical analysis

Statistical analysis was performed using Fisher's exact test and Student's *t*-test according to the data. A significance level of 0.05 ($\alpha = 5\%$) was adopted, and levels lower than this were considered significant.

Results

Laparoscopic II-SG was performed for 32 patients and II-DSG for 28 patients. There was no conversion to open

surgery. Associated procedures included four cholecystectomies (6.7%) with cholangiography and two hiatal hernia repairs (3.3%). The mean operative time was 160 min (range, 130–210 min) for II-SG and 185 min (range, 160–255 min) for II-DSG. The overall mean operative time was 190 min, and the median hospital stay was 3.9 days (range 2–49 days).

The intraoperative complications (5%) included resection of an ischemic segment (8 cm) of the transposed ileum ($n = 1$), cardiac arrhythmia ($n = 1$), and hypertensive crisis ($n = 1$). There was no mortality. Seven patients (11.7%) experienced major postoperative complications including severe cardiac arrhythmia ($n = 2$), urinary tract infection ($n = 2$), gastrointestinal bleeding ($n = 1$), massive subcutaneous hematoma ($n = 1$), and intraabdominal abscess ($n = 1$). This last patient needed to undergo reoperation (1.7%).

The most frequent early complaints were related to nausea, anorexia, early satiety, heartburn, and discomfort in the lower abdomen. These symptoms progressively improved late in the follow-up period, with heartburn and food intolerance as the most important symptoms. Four patients had late hospitalizations including one case of persistent nausea and vomiting, which resolved spontaneously, two urinary tract infections treated with appropriate antibiotics, and one suspected intestinal obstruction, which resolved spontaneously.

The 60 patients were followed for a mean of 7.4 months (range, 3–19 months). Both operations adequately treated the components of the metabolic syndrome, although the diverted version was considered to be more effective in treating the different components of the metabolic syndrome. Metabolic syndrome was no longer characterized in 95% of the patients. The waist circumference exceeded 102 cm for the men and 88 cm for the women in 68.3% of the patients during the preoperative period.

Postoperatively, all the patients achieved parameters below the reference points. Triglycerides decreased from a mean of 259.5 ± 204.1 mg/dl in the preoperative period to 97 ± 40.3 mg/dl postoperatively ($p < 0.001$). Hypertriglyceridemia, diagnosed for 70% of the patients before surgery, was normalized for 81.7% of the patients after the operations, with the diverted version, II-DSG (89.3%), more effective than II-SG (74.2%). The HDL level increased from a mean of 38.8 ± 9.2 mg/dl to 51.3 ± 8.6 mg/dl ($p = 0.011$). It was altered in 51.7% of the patients and normalized in 90.3%. Total cholesterol decreased from a mean of 215.1 ± 49.9 mg/dl to 160.6 ± 28.1 mg/dl ($p < 0.001$), and low-density lipoprotein (LDL) decreased from a mean of 132.5 ± 50.7 mg/dl to 90.6 ± 22.5 mg/dl ($p = 0.012$).

Preoperatively, 70% of the patients had hypertension, as determined by casual blood pressure measurement. All the patients were using antihypertensive medications (mean

number of drugs, 1.6). The blood pressure normalized ($\leq 130/\leq 85$ mmHg) without medication for 90.5% of the patients according to casual blood pressure measurement. Fasting plasma glucose decreased from 209.8 ± 65.3 mg/dl to 106.3 ± 21.3 mg/dl ($p < 0.001$) and postprandial plasma glucose from 269.2 ± 100.4 mg/dl to 140.7 ± 59.6 mg/dl ($p < 0.001$). Hyperinsulinemia was diagnosed for 31.7% of the patients. Fasting plasma insulin decreased from 17.7 ± 16.6 mU/ml to 4.9 ± 3.5 mU/ml ($p = 0.129$). The homeostasis model assessment of insulin resistance decreased from preoperative levels of 8.7 ± 9.8 to 1.4 ± 1.1 ($p = 0.200$). According to these criteria of insulin resistance, 50.8% of the patients had parameters above 3.6. C-peptide decreased from 4.1 ± 2.04 ng/ml to 2.5 ± 0.9 ng/ml ($p = 0.111$). The data are summarized in Table 2.

Mean HbA1c decreased from $9 \pm 1.7\%$ to $5.8 \pm 0.8\%$ ($p < 0.001$). Overall, an HbA1c level lower than 7% was achieved by 86.7% of the patients without antidiabetic medication. A HbA1c lower than 6% was reached by 69.7% of the patients. Glycemic control (HbA1c between 6 and 7%) was achieved by 17% of the patients and improvement by 13.3% of the patients (Table 3). Both the II-SG and II-DSG were effective ($p < 0.001$), although patients treated with II-DSG had a longer period of disease (mean, 11.4 ± 4.21 to 8.3 ± 4.5 years; $p = 0.021$). They also resulted in a higher percentage of patients using insulin (63.2–35.7%). Remission (HbA1c < 6%) was more frequent among patients with less than 5 years of T2DM and those receiving oral agents preoperatively.

Preoperatively, oral hypoglycemic agents were used by 53.2% of the patients (mean number of drugs, 1.5), with 12.8% requiring insulin therapy (regular and NPH) and 34% receiving both insulin and oral agents. Nearly 87% of the patients permanently discontinued preoperative oral hypoglycemic agents, insulin, or both. The incretin hormones and peptide YY were assayed both before and after surgery at a mean of 13 months (range, 6–19 months). Fasting GLP-1 increased from a mean of 359–1035.9 pMol/L ($p < 0.001$) (Fig. 3). The highest level achieved was at 30 min after a special diet of 420 calories: 29.3 pmol/l before surgery to 89.6 pmol/l after surgery. Fasting GIP increased from a mean of 32.1–59.7 pmol/l ($p < 0.001$) (Fig. 4), and fasting peptide YY increased from a mean of 1.98–6.26 pmol/l ($p < 0.001$) (Fig. 5).

The mean percentage of weight loss was $23 \pm 7\%$ of the initial weight (range, 9–34.1%). Mean BMI decreased from 30.1 ± 3.3 kg/m² in the preoperative period to 23.8 ± 4.1 kg/m² (range, 19.4–30.6 kg/m²) (Fig. 6). Adipose-related tissue markers were assayed and are summarized in Table 4. Nonesterified free fatty acids decreased from a mean of 1.12 mmol/l (range, 0.4–1.41 mmol/l) to 0.72 mmol/l (range, 0.27–1.07 mmol/l) ($p = 0.002$). Adiponectin increased from a mean of 4.69 to 13.31 ng/ml ($p < 0.001$).

Table 2 Pre- and postoperative blood work

	Preoperative	Postoperative	<i>p</i> -value
Triglycerides (mg/dl)	259.5 ± 204.1	97.0 ± 40.3	<0.001
HDL (mg/dl)	38.8 ± 9.2	51.3 ± 8.6	0.011
Total cholesterol (mg/dl)	215.1 ± 49.9	160.6 ± 28.1	<0.001
LDL (mg/dl)	132.5 ± 50.7	90.6 ± 22.5	0.012
Fasting plasma glucose (mg/dl)	209.8 ± 65.3	106.3 ± 21.3	<0.001
Postprandial plasma glucose (mg/dl)	269.2 ± 100.4	140.7 ± 59.6	<0.001
Fasting plasma insulin (mU/ml)	17.7 ± 16.6	4.9 ± 3.5	0.129
Homa IR	8.7 ± 9.8	1.4 ± 1.1	0.200
C-peptide (ng/ml)	4.1 ± 2.04	2.5 ± 0.9	0.111

HDL, high-density lipoprotein;
LDL, low-density lipoprotein;
IR, insulin resistance

Table 3 Type 2 diabetes mellitus resolution according to different procedures

Hyperglycemia	Remission A1c < 6	Control A1c 6–7	Improvement A1c > 7	<i>p</i> -value
Total (%)	69.7	17.0	13.3	<0.001
	4.7 ± 2.0	6.5 ± 0.27	7.4 ± 0.25	0.001
Ileal interposition	70.0	14.3	15.7	<0.001
Sleeve gastrectomy (%)	4.2 ± 2.45	6.5 ± 0.35	7.5 ± 0.30	0.026
Ileal interposition/diverted sleeve gastrectomy (%)	68.4	21.1	10.5	<0.001
	5.4 ± 0.37	6.4 ± 0.19	7.3 ± 0.07	<0.001

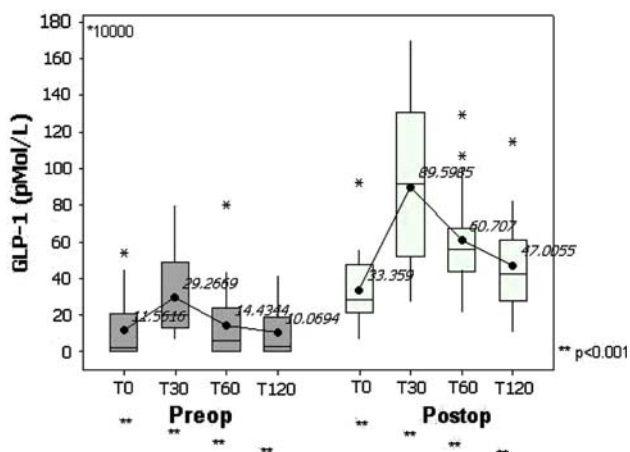
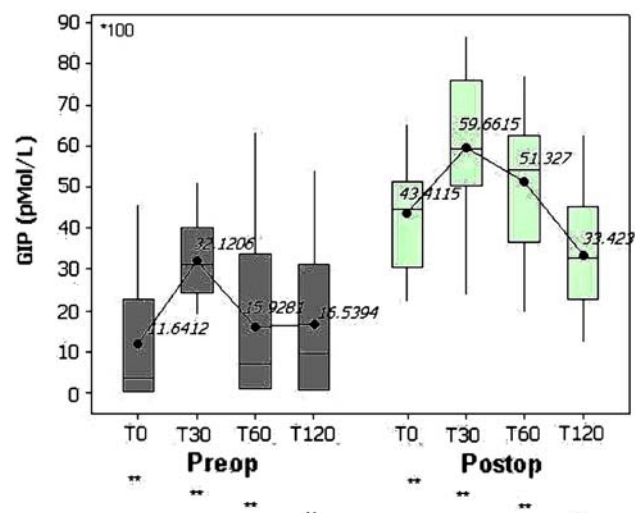
A1c, glycated hemoglobin

Resistin decreased from a mean of 11.3 ng/ml to 2.4 ng/ml ($p = 0.001$), leptin from a mean of 9.44 to 4.31 ng/ml ($p < 0.001$), and interleukin-6 from a mean of 0.025 to 0.023 ng/ml, ($p = 0.644$). The level of CRP decreased from a mean of 0.622 ng/ml preoperatively to 0.398 ng/ml postoperatively ($p = 0.226$).

Preoperative microalbuminuria was diagnosed for 45% of the patients and macroalbuminuria for 8.3%. A glomerular filtration rate of 60–89 ml/min was found for 23.3% of the patients. Postoperatively, renal function showed a substantial improvement. Eight patients (13.3%) still had microalbuminuria, and macroalbuminuria was no

longer diagnosed. All patients with a glomerular filtration rate of 60–89 normalized their filtration rate (>90 ml/min).

Retinopathy was found in 20 patients (33.3%) preoperatively. Six patients (30%) showed objective improvement in retinopathy. Symptomatic improvement was observed for all the patients. Carotid artery results were abnormal for 45% of the patients, ranging from intimal–medial thickness to partial stenosis, up to 40% of the arterial lumen. Postoperative routine evaluation at 6 months demonstrated only minor improvement.

**Fig. 3** Pre- and postoperative glucagon-like peptide-1 (GLP-1) ($p < 0.001$)**Fig. 4** Pre- and postoperative glucose-dependent insulinotropic peptide (GIP) ($p < 0.001$)

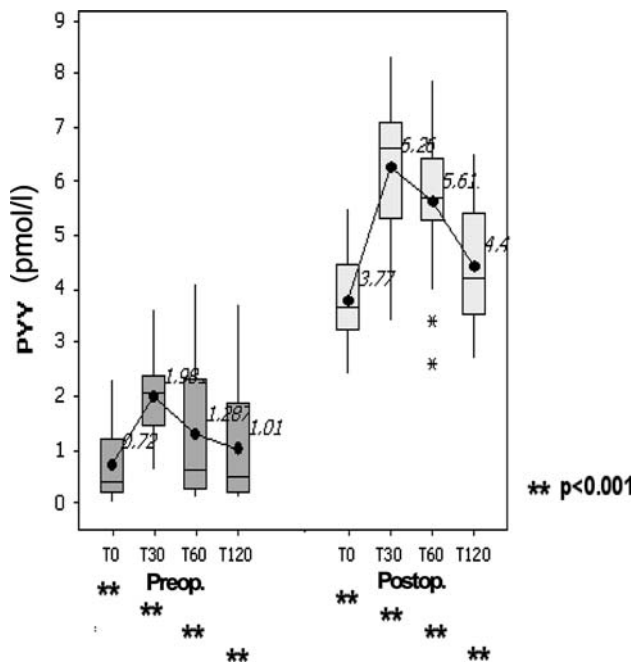


Fig. 5 Pre- and postoperative peptide YY ($p < 0.001$)

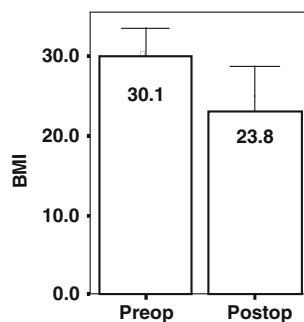


Fig. 6 Pre- and postoperative body mass index (BMI) ($p < 0.001$)

Table 4 Adipose tissue markers

	Mean Preop	Mean Postop	p -Value	SD
Nonesterified free fatty acids (mmol/l)	1.12	0.72	<0.001	1.35
Adiponectin (ng/ml)	4.69	13.31	<0.001	1.10
Resistin (ng/ml)	11.3	2.4	<0.001	2.11
Leptin (ng/ml)	9.44	4.31	<0.001	1.66
IL-6 (ng/ml)	0.025	0.023	0.644	0.001
RCP (ng/ml)	0.622	0.98	0.226	0.15

Preop, preoperative; Postop, postoperative; SD, standard deviation; IL, interleukin; RCP, reactive C-protein

Discussion

This report examined the resolution of the metabolic syndrome according to the NCEP criteria for patients with

T2DM and a BMI of 23.6–34.4 after laparoscopic ileal interposition associated with a sleeve or diverted sleeve gastrectomy. Overall, the metabolic syndrome could no longer be characterized for 95% of the patients. The impact of these operations on the individual components of metabolic syndrome was variable. Scopinaro et al. [14] recently demonstrated the efficacy of the biliopancreatic diversion for T2DM and metabolic syndrome in a group of seven patients followed up for a mean of 13 years.

After the operations, central obesity was completely resolved, with all the patients achieving parameters of waist circumference below the reference points. This was demonstrated by an adjusted weight loss, with 5% of the patients achieving a BMI lower than 20.

Hypertriglyceridemia was normalized for 81.7% of the patients, with the diverted version (II-DSG), proving to be more effective than II-SG. We hypothesize that diverting the duodenum may alter the GIP-resistant state of these T2DM/metabolic syndrome patients. Zhou et al. [15] demonstrated that GIP plays a crucial role in the switch from fat oxidation to fat accumulation under diminished insulin action and inhibition of GIP, signaling ameliorated insulin resistance. A significant rise in HDL was observed after both operations. Onat et al. [16] demonstrated that metabolic syndrome was a major determinant of CHD risk in a population with low levels of HDL. Laws and Reaven [17] also showed that high triglycerides and low HDL cholesterol are strong indicators of insulin resistance. Lipid management aimed at lowering LDL cholesterol, raising HDL cholesterol, and lowering triglycerides reduced macrovascular disease and mortality in patients with T2DM, particularly in those who had experienced prior cardiovascular events [18], a condition present in 15% of these patients.

Targeted levels of blood pressure ($\leq 130/\leq 85$ mmHg) without medication were achieved by 90.5% of the patients according to a casual blood pressure measurement. Hypertension is a major risk factor for cardiovascular disease and microvascular complications such as retinopathy and nephropathy, and the benefits of lowering blood pressure have been demonstrated by randomized trials [19].

The aforementioned procedures were designed specifically for the treatment of diabetes. Most of the patients (86.7%) achieved adequate glycemic control (HbA1c <7%) at a mean follow-up period of 7.4 months. A normalization HbA1c of less than 6% was reached by 69.7% of the patients. A significant reduction in the use of antidiabetic medications also was observed. Hyperinsulinemia was ameliorated in all the patients. Insulin resistance characterized by Homa insulin resistance also was significantly influenced. Stern et al. [20] mentioned that 93% of diabetic patients were insulin resistant. Ferrannini and Balkau [21] demonstrated that the relationship between insulin resistance and

hyperinsulinemia is complex. Both parameters can partially identify different groups of patients with metabolic syndrome [22]. In nonobese subjects with impaired glucose tolerance and T2DM, an early defective insulin secretion after an oral glucose is a key factor. This defective beta cell function is associated with and may be caused by a reduced early GLP-1 response [23].

After both operations, a substantial rise in preoperative levels of GLP-1, GIP, and peptide YY was demonstrated. The main characteristic of these operations is early exposure of ingested nutrients to the interposed ileum, allowing an early rise in GLP-1 that consequently corrects the first-phase defective insulin secretion.

Other relevant independent factors for the metabolic syndrome were improved. Levels of CRP decreased after both operations. Ridker et al. [24] demonstrated that measurement of CRP adds clinically important prognostic information to the metabolic syndrome. Pearson et al. [25] concluded that it is reasonable to measure CRP as an adjunct to the major risk factors for CHD. Other fat cell-related markers such as interleukin-6, resistin, leptin, and nonesterified fatty acids decreased after the operations. Adiponectin increased significantly in relation to preoperative levels. Hypoadiponectinemia is more closely related to the degree of insulin resistance and hyperinsulinemia than to the degree of adiposity and glucose intolerance [26]. The association of low adiponectin levels with obesity, insulin resistance, CHD, and dyslipidemia indicates that this protein may be an important marker of the metabolic syndrome [27]. The incidence of microalbuminuria decreased after the operations. Microalbuminuria is a well-established marker of increased cardiovascular disease risk [28].

The laparoscopic approach was the preferred access, and there was no need for conversion. A major morbidity rate of 11.7% seems reasonable for such a high-risk group of patients.

In conclusion, laparoscopic ileal interposition with either a sleeve or diverted sleeve gastrectomy proved to be adequate treatment for the components of the metabolic syndrome and some other important independent factors.

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