DIABETES TECHNOLOGY & THERAPEUTICS
Volume 16, Number 4, 2014
© Mary Ann Liebert, Inc.
DOI: 10.1089/dia.2013.0249

DTT
Diabetes Technology & Therapeutics

ORIGINAL ARTICLE

Impact of Roux-en-Y Gastric Bypass on Metabolic Syndrome and Insulin Resistance Parameters

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Abstract

Background: Metabolic syndrome (MetS) is a complex association of clustering metabolic factors that increase risk of type 2 diabetes mellitus (T2DM) and cardiovascular disease. Surgical treatment has become an important tool to achieve its control. The aim of this study was to evaluate the impact of Roux-en-Y gastric bypass (RYGB) on MetS and its individual components, clinical characteristics, and biochemical features.

Subjects and Methods: The study is a retrospective cohort of 96 subjects with MetS who underwent RYGB and were evaluated at baseline and after surgery. Clinical and biochemical features were analyzed.

Results: After surgery, significant rates of resolution for MetS (88.5%), T2DM (90.6%), hypertension (85.6%), and dyslipidemias (54.2%) were found. Significant decreases in levels of fasting glucose, fasting insulin, hemoglobin A1c, low-density lipoprotein, and triglycerides and an increase in high-density lipoprotein level were also shown. The decrease in insulin resistance evaluated by homeostasis model assessment (HOMA-IR) was consistent. MetS resolution was associated with postoperative glycemic control, decreases in levels of fasting glucose, hemoglobin A1c, HOMA-IR, and triglycerides and in antihypertensive usage, and percentage weight loss.

Conclusions: This study found high rates of resolution for MetS, T2DM, hypertension, and dyslipidemias after RYGB in obese patients. This finding was consistent with current literature. Hence RYGB should be largely indicated for this group of subjects as it is a safe and powerful tool to achieve MetS control.

Introduction

Metabolic syndrome (MetS) is defined by a cluster of interconnected metabolic factors that increase the risk of coronary heart disease and type 2 diabetes mellitus (T2DM).[1,2] The prevalence of MetS as defined by the Adult Treatment Panel III (ATP III) in the United States increased from 23.7% according to the National Health and Nutrition Examination Survey (NHANES) in 1976–1980 to 34.5% in the 1999–2002 NHANES.[3] The metabolic factors involved include glycemic metabolism abnormalities, hypertension, atherogenic dyslipidemia, and central obesity.[2]

The underlying causes of MetS appear to be genetic and environmental: overweight, obesity, and sedentary lifestyle, which bring about insulin resistance (IR), hyperinsulinemia, endothelial dysfunction, and inflammation.[3–6] There are also abnormalities of adipocyte function, accompanied by inappropriate secretion of multiple hormones and cytokines, along with abnormal accumulation of fat in tissues like muscle and liver.[3,4]

Friedman et al.[7] reported amelioration of T2DM after gastrectomy in 1955. In 1995 Pories et al.[8] observed high prevalence of remission of T2DM after several bariatric procedures. A meta-analysis by Buchwald et al.[9] showed complete remission of T2DM in 85% of patients after gastric bypass and also greater resolution after malabsorptive procedures. The causes of improvement of MetS factors after bariatric surgery are complex and related to changes in the enteroinsular axe mediated by gastrointestinal hormones called incretins.[10–12]

This study aims to determine the impact of Roux-en-Y gastric bypass (RYGB) on MetS and its clustering factors in obese patients. Moreover, it also aims to determine which biochemical and clinical factors are associated with resolution of MetS and its individual components after RYGB.

Subjects and Methods

This study is descriptive and longitudinal and designed as a retrospective cohort. It included obese subjects who met the MetS diagnostic criteria according to the ATP III[13] and the

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International Diabetes Federation (IDF)[14] who underwent open RYGB at the Hospital de Clínicas, UNICAMP between 2000 and 2010. This study was submitted to and approved by the local Research Ethics Committee. Surgery was indicated based on the National Institutes of Health Consensus Statement criteria.[15] The estimation of sample size was performed using the single proportion formula with a 95% confidence interval.[16] Precision was set at 10%, and the calculated sample size was 84.

Exclusion criteria for this study were as follows: individuals who had undergone other bariatric procedures after RYGB, subjects whose postoperative follow-up time was less than 12 months, and those belonging to vulnerable groups (mentally ill, institutionalized, or under 18 years of age).

From 672 subjects who underwent RYGB, 96 who fulfilled the criteria for MetS as specified by the IDF and the ATP III and had been followed up for at least 12 months were included. Main characteristics regarding demographics, presence of components of MetS, and preoperative pharmacological treatments were assessed. Biochemical characteristics evaluated included fasting glucose, fasting insulin, hemoglobin A1c (HbA1c), glycemic control according to the American Diabetes Association,[17] homeostasis model assessment (HOMA) of IR (HOMA-IR), total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and triglycerides.

Comparisons were made between the periods immediately before and at least 1 year after surgery, in order to measure the impact of the procedure on resolution of MetS, T2DM, hypertension, and dyslipidemia, as well as comparing clinical and biochemical parameters.

MetS resolution was achieved through not meeting the ATP III and IDF criteria. T2DM resolution was achieved according to the American Diabetes Association criteria (fasting glucose <100 mg/dL and HbA1c $\leq 6.5\%$).[17] Hypertension resolution was achieved through three nonconsecutive measures below 130/85 mm Hg. Dyslipidemia resolution was achieved when high-density lipoprotein cholesterol was above 40 mg/dL in men or 50 mg/dL in women, low-density lipoprotein cholesterol was below 160 mg/dL, and triglycerides were below 150 mg/dL.

Statistical analysis

The baseline characteristics of patients are described and then compared with those in the postoperative period. Data were examined for normality according to the Pearson's χ^2 test. For univariate analysis of categorical variables, χ^2 and Fisher's exact tests were carried out. The Wilcoxon test was used for comparisons of continuous or ordinal measures between the two periods of evaluation for related samples. The McNemar test was used for comparison of proportions between the two periods. To identify possible factors associated with the studied outcomes, multiple logistic regression analysis was used. The significance level adopted was 5% (value of $P<0.05$). Analysis was performed with SAS software for Windows version 9.2 (SAS Institute, Cary, NC).

Results

Of the 96 patients selected for study, 74 (77%) were female, and 22 (23%) were male. The mean age at surgery was 46 (range, 22–64) years. The mean postoperative and follow-up interval was 34 (range, 12–120) months. Main subject characteristics at baseline are summarized in Table 1.

Mean hospital stay was 4.3 ± 0.3 days. Overall surgical morbidity was 11.4%, and the main complications were wound infection (4.2%) and atelectasis (3.1%). There was no mortality.

Patients experienced a significant mean body mass index decrease from 44.3 ± 8.7 kg/m^2 to 31.5 ± 7.7 kg/m^2 ($P<0.001$). Mean weight loss was 29.9 ± 9.1 kg ($P<0.0001$). Mean waist circumference was 128 ± 13.9 cm preoperatively and 98 ± 14.3 cm postoperatively ($P<0.001$). Percentage of excess weight loss after surgery was $71.8\pm27.4\%$. Preoperatively, 90 (94%) patients had hypertension; after surgery, 13 (13.5%) still had hypertension. Thus the hypertension resolution rate was 85.6% ($P<0.0001$). Among patients who did not achieve hypertension resolution, a significant reduction in number of antihypertensive classes used, from 2.3 before to 1.3 after surgery ($P=0.001$), was observed. The factors statistically associated with hypertension resolution were HOMA-IR ($P=0.0482$), postoperative body mass index ($P=0.0017$), preoperative fasting insulin ($P=0.0385$), number of preoperative antihypertensive classes ($P=0.0072$), number of postoperative antihypertensive classes ($P=0.0002$), and percentage weight loss ($P=0.0011$).

Preoperatively, 83 (86.5%) patients had any type of dyslipidemia; after surgery, 38 (39.6%) still had any dyslipidemia. Thus the dyslipidemia resolution rate was 54.2% ($P<0.0001$). After a multivariate analysis no independent variable was associated with dyslipidemia resolution in this sample. Before surgery, no male subject had high-density lipoprotein cholesterol above 40 mg/dL, and no female had it above 50 mg/dL; after surgery, 67 (69.8%) had it above these parameters ($P<0.0001$). Before surgery, 46 (47.9%) had triglycerides above 150 mg/dL, and after surgery, nine (9.4%) did so ($P<0.0001$).

Before surgery, all patients had T2DM; postoperatively, nine (9.4%) still had T2DM. Thus the resolution rate of T2DM was 90.6% ($P<0.0001$). The factors statistically associated with T2DM resolution were postoperative usage of

Table 1. Subjects' Characteristics at Baseline

Characteristic	*Value*
Gender	
Male	23%
Female	77%
Age (years)	46 ± 10.8
BMI (kg/m^2)[a]	44.3 ± 8.74 (35–80.8)
Weight (kg)[a]	102.2 ± 18.1 (72–180)
Postoperative follow-up (months)	34.2 ± 25.1
MetS components	
T2DM	100%
Hypertension	93.8%
Dyslipidemia	86.5%
Pharmacological treatments	
Insulin	22.9%
Oral hypoglycemic	98.7%
Antilipid	72.9%
Antihypertensive	93.8%

[a]Mean ± SD (range) values.

BMI, body mass index; MetS, metabolic syndrome; T2DM, type 2 diabetes mellitus.

Table 2. Clinical and Biochemical Features Before and After Surgery

	Baseline	*Postsurgical*	P *value*
BMI (kg/m^2)	44.3	31.5	< 0.0001
Waist circumference (cm)	128.5	97.9	< 0.0001
Weight (kg)	102.2	72.4	< 0.0001
Fasting glucose (mg/dL)	117	85	< 0.0001
Fasting insulin (μIU/dL)	14.61	7.97	< 0.0001
HbA1c (%)	7.03	5.55	< 0.0001
Total cholesterol (mg/dL)	195	167	< 0.0001
LDL-C (mg/dL)	125	95	< 0.0001
HDL-C (mg/dL)	36	52	< 0.0001
Triglycerides (mg/dL)	171	95	< 0.0001
HOMA-IR	4.45	1.93	< 0.0001

BMI, body mass index; HbA1c, hemoglobin A1c; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, insulin resistance evaluated by homeostasis model assessment; LDL-C, low-density lipoprotein cholesterol.

oral hypoglycemic agents ($P < 0.0001$), postoperative glycemic control ($P < 0.0001$), postoperative fasting glucose ($P = 0.0075$), postoperative HbA1c ($P = 0.0003$), diabetes duration ($P = 0.0321$), preoperative insulin usage ($P = 0.0148$), and postoperative HOMA-IR ($P = 0.0069$).

Postoperatively, 11 (11.5%) still fulfilled both diagnostic criteria of MetS (IDF and ATP III). The MetS resolution rate was 88.5% ($P < 0.0001$). The factors statistically associated with MetS resolution were postoperative usage of oral hypoglycemic agents ($P = 0.0025$), postoperative glycemic control ($P = 0.0004$), postoperative fasting glucose ($P = 0.0074$), postoperative HbA1c ($P = 0.0022$), postoperative HOMA-IR ($P = 0.0210$), preoperative number of antihypertensive classes ($P = 0.0062$), postoperative number of antihypertensive classes ($P = 0.0005$), postoperative triglycerides ($P = 0.0008$), and postoperative percentage weight loss ($P = 0.0073$). Preoperatively, 36 patients (37.5%) had inadequate glycemic control before surgery; postoperatively, six (6.2%) still had inadequate control ($P < 0.0001$).

Mean HOMA-IR before surgery was 4.45, and postoperatively it decreased to 1.93 ($P < 0.0001$). The Brazilian Metabolic Syndrome study group determined the cutoff values for HOMA-IR as 2.7 and for the presence of MetS as 2.3.[18]

Main clinical and biochemical features before and after surgery are shown in Table 2.

Discussion

Evidence is solid about the greater effectiveness of bariatric surgery compared with intensive clinical treatment of MetS and its clustering factors, with improvement of biochemical and clinical features.[19–22] RYGB leads to improvement of MetS through a series of partially elucidated mechanisms. These mechanisms include decrease of food intake, which leads to lower glycemic load, weight loss, which increases insulin sensitivity, and increase of incretin action, mainly through higher levels of glucagon-like peptide 1 due to duodenal exclusion (foregut hypothesis) or early arrival of the food bolus to the ileum (hindgut hypothesis). The overall incretin action leads to an increase of insulin sensitivity and pancreatic endocrine function.[12] The global impact of surgery on long-term mortality reduction has already been observed for obese patients, with a 40% reduction of all-causes mortality, 56% of coronary heart disease, 92% of diabetes complications, and 60% of any type of cancer.[23] The present study showed elevated postoperative resolution of MetS (88.5%) and also on individual components when evaluated separately: hypertension (85.6%), dyslipidemias (54.2%), and T2DM (90.6%). Buchwald et al.[9] observed in a meta-analysis high resolution of comorbidities related to MetS; however, that study did not evaluate the syndrome as a whole. These researchers reported resolutions after RYGB of 83.7% for diabetes, 67.5% for hypertension, and 99.1% for dyslipidemias (considering only total cholesterol and triglycerides).[9] Batsis et al.[24] in a longitudinal populational study considering the IDF criteria for MetS showed an overall resolution of 68% compared with 10% for the control group subjected to exclusive clinical therapy over 12 months. In a longitudinal evaluation of a database containing 23,106 patients considered with MetS by presenting T2DM, hypertension, and dyslipidemia at the same time, Inabnet et al.[25] found related resolution rates of 44.8% for hypertension, 62.2% for T2DM, and 44.9% for dyslipidemias. Thus the resolution rates for MetS observed in this study were comparable to those observed in other populational series.

Among the factors related to MetS resolution, this study showed clear evidence that clinical control is strongly associated with postoperative glycemic homeostasis parameters (fasting glucose and HbA1c) and also with surrogate IR evaluation through HOMA. This study also showed association of percentage weight loss with MetS resolution, reinforcing the importance of changes in enteroinsular and adipoinsular axes on early control of MetS and suggesting weight loss as a late mechanism of maintaining the long-term benefits previously achieved.

The significant impact of RYGB on MetS and its clustering components in obese subjects reinforces the concept that there is a clear benefit of RYGB for this group of subjects. Therefore, because MetS has a rising importance as a public health issue, RYGB should be largely indicated as a safe therapeutic tool for obese patients with MetS or evidence of IR, leading to lower cardiovascular morbimortality.

Author Disclosure Statement

No competing financial interests exist.

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