

# Changes in clinical and laboratory parameters in obese patients with type 2 diabetes mellitus submitted to Roux-en-y gastrojejunal bypass without ring

## *Alterações dos parâmetros clínicos e laboratoriais em pacientes obesos com diabetes melito tipo 2 submetidos à derivação gastrojejunal em y de Roux sem anel*

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### A B S T R A C T

**Objective:** To assess the changes in body weight and body mass index in grade 2 and 3 obese patients with type 2 diabetes mellitus, pre and postoperatively; 2) to assess the changes in pre and postoperative laboratory parameters for fasting blood glucose, postprandial glucose, glycated hemoglobin, and insulin. **Methods:** A prospective study was undertaken with 40 selected patients with grade 2 and 3 obesity and type 2 diabetes mellitus, all with indication for surgical treatment of obesity. All patients underwent Roux-en-Y gastric bypass without ring. The clinical parameters weight and body mass index were analyzed, as well as the laboratory parameters fasting blood glucose, postprandial glucose, glycated hemoglobin, and insulin. Those parameters were analyzed in the preoperative period and at 60 postoperative days. The statistical analysis was conducted using Student's t test and the Kolmogorov-Smirnov test. **Results:** Mean preoperative weight was 107.3 kg, declining to 89.5 kg postoperatively. Mean initial body mass index was 39.5 kg/m<sup>2</sup>, and 32.9 kg/m<sup>2</sup> at 60 postoperative days. Preoperative fasting blood glucose was 132 mg/dL, which was reduced to 40.4 mg/dL, on average, postoperatively. Postprandial blood glucose was 172 mg/dL in the preoperative period, and 111.6 mg/dL in the postoperative measurement. Initial glycated hemoglobin was 7%, declining to 5.7% postoperatively. Preoperative and postoperative insulin levels were 29.6 µIU/mL and 13.9 µIU/mL, respectively. The level of significance was p<0.001 for all variables. **Conclusion:** A statistically significant reduction in body weight and body mass index was found between the preoperative and postoperative periods and also in the reduction in fasting blood glucose, postprandial glucose, glycated hemoglobin and insulin between the pre and postoperative periods.

**Key words:** Patients. Obesity. Diabetes mellitus, type 2. Gastric bypass. Bariatric surgery.

### INTRODUCTION

Obesity is the accumulation of fat tissue due to genetic or endocrine-metabolic diseases or by nutritional changes<sup>1</sup>.

The association between obesity and type 2 diabetes mellitus (DM2) is well defined. The fat located in the abdomen can raise in ten times the risk of DM2 development. To each increase of 10% on body weight, there is an increase of 2 mg/dL in blood glucose<sup>2</sup>. Ninety percent of DM2 patients are above weight or are considered obese<sup>3</sup>.

The prevalence of DM2 has grown in large proportions. It is estimated that about 150 million people world suffer from DM2 worldwide, with expected increase to about 300 million in 2025<sup>4</sup>.

The bases to treat it consist in the maintenance of normal levels of glucose and insulin. That control is considered the better approach to prevent acute and chronic complications of the disease. Appropriate values of glucose are not achieved in majority of patients only with drug treatment. They are normally above weight and resistant to dietary control<sup>5</sup>.

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The unsatisfactory responses with drug treatment led to development of new therapeutic modalities, increasing the interest in bariatric surgery, which produces remission of the disease, recovering the function of pancreatic beta cells <sup>6</sup>.

Although having the loss of weight as initial goal, with time an important improvement or even definitive control of DM2 was observed after Roux-en-Y gastrojejunal bypass; the same said Pories *et al.* <sup>7</sup>, reporting remission of the disease in 82.9% of patients after this procedure. There are also reports of other types of operations resulting in DM2 clinical improvement after weight loss <sup>8</sup>.

The mechanisms accountable for weight loss and control of the disease include not only the restrictive and disabsorptive effects, but also hormonal changes responsible for the control of appetite and speed of food intestinal transit <sup>9</sup>.

The Roux-en-Y gastrojejunal bypass is an operation that produces hunger control through incretine control, with loss of weight and improvement of comorbidities, mainly DM2. There is an intense reduction in intake accompanied by paradoxical reduction of appetite due to reduction of the hormone ghrelin with the gastric exclusion <sup>10</sup>. The reversal of DM2 involves also the recovery of first phase of secretion of insulin that follows the increase of glucagon-like peptide 1 (GLP-1), an incretinic action, which is increased in jejunoileal bypass <sup>11,12</sup>. This procedure is considered the gold standard to morbidly obese patients with DM2 <sup>13</sup>.

The goals of this study are to assess the changes of weight and body mass index (BMI) in patients with obesity degree II and III with type 2 diabetes mellitus in the pre and postoperative periods, and to analyze the changes in the following laboratory parameters: fasting glucose, postprandial glucose, glycated hemoglobin and insulin.

## METHODS

The present study was conducted at the Service of Bariatric and Metabolic Surgery and at the Medical Center of the Evangelical University Hospital of Curitiba, PR, Brazil. It was approved by the Ethics Committee of the Evangelical Society.

The sample was prospective and composed of 40 patients with age ranging from 18 to 65 years in both genders (mean age 41 years), all with obesity degree II and III (BMI above 35 kg/m<sup>2</sup>).

The inclusion criteria were: weight variation less than 10% in the last three months; all patients with indication for surgical treatment of obesity and with DM2 with less of 10 years of evolution; in use of oral hypoglycemic and/or insulin (in case of insulin use the period should not exceed five years) with serum level of peptide C more of that 1 ng/mL.

We excluded patients with history of liver disease, as cirrhosis or chronicle active hepatitis; with alteration in renal function (creatinine more than 1.4 mg/dl in women and more that 1.5 mg/dl in men); with alteration in liver function (alanine aminotransferase and/or aspartate aminotransferase three times above normal value); pregnancy; recent report of neoplasia (less than five years); use of corticoid for more than 14 consecutive days in the last three months; laboratory findings of tendency to failure of insulin production (peptide C less that 1 ng/mL); presence of Anti-GAD and/or anti-insulin and/or anti-islet antibodies; alcoholism; drug addiction; autoimmune disease; HIV positivity; and uncompensated or not likely of be controlled psychiatric patients.

Preoperatively, patients selected to the study had blood drawn for the following tests: fasting glucose, glycated hemoglobin, postprandial glucose and insulin. The values of weight and BMI were also measured.

The same tests and measured the values of weight and BMI were performed after 60 days postoperatively.

The operative procedure consisted in accessing the peritoneal cavity by laparoscopy with section of the stomach by linear stapling to form a gastric reservoir at the cardia with capacity of about 20 ml, constituting the postoperative functional stomach. The remainder of stomach was permanently excluded from the food transit, as well as the duodenum and the proximal 80 cm of te jejunum. The gastric reservoir was anastomosed to an isolated jejunal segment in a Roux en-Y fashion, its emptying limited to an orifice of 1.3 cm in diameter. The secretions from the excluded stomach and duodenum were directed to the jejunum by an anastomosis 100 cm distal from the duodenojejunal angle <sup>14</sup> (Figure 1).

For the evaluation of the effects of operation on the quantitative variables, we used the Student's t test for paired samples. The condition of normality of variables was evaluated by the Kolmogorov-Smirnov's test. Values of  $p < 0.05$  indicated statistical significance. Data were analyzed with the software Statistica v.8.0.

## RESULTS

### Weight

Weight decreased significantly in the period of analysis ( $p < 0.001$ ). Weight loss was in average 17.8 Kg between the preoperative period and 60 days after the procedure. The average preoperative weight was 107.3 kg.

### BMI

BMI presented with a statistically significant decrease ( $p < 0.001$ ). Between the preoperative and postoperative periods, the average decrease was 6.6 Kg/m<sup>2</sup>. The average preoperative BMI was 39.5 Kg/m<sup>2</sup>, and 32.9 Kg/m<sup>2</sup> postoperative.

### Fasting glucose

The average preoperative glucose fasting was 132 mg/dl, and within 60 days of the postoperative period it was 91.6 mg/dl. Between preoperative and 60 days of postoperative time the average fall of fasting glucose was 40.4 m /dl, with a significant statistic decrease between the analyzed periods ( $p < 0.001$ ) (Figure 2).

### Postprandial glucose

The analysis of postprandial glucose levels indicated that there were significant differences between the values of the preoperative period and 60 days postoperatively ( $p < 0.001$ ). The average postprandial glucose in the preoperative time was 172 mg/dl, declining to 111.6 mg/dl 60 days after surgery. The average decrease in postprandial glucose was 60.5 mg/dl (Figure 3).

### Glycated hemoglobin

When analyzing this variable, we found that, between the pre and postoperative periods, there was a statistically significant decrease in glycated hemoglobin levels ( $p < 0.001$ ). The average preoperative was 7%, and postoperatively, 5.7%, falling 1.3% (Figure 4).

### Insulin

The preoperative insulin was 29.6 iIU/ml in average. On the postoperative time it was 13.9 iIU/ml. The difference between pre and postoperative measurements was of 15.7 iIU /ml, with statistical significance ( $p < 0.001$ ) (Figure 5).

## DISCUSSION

The Roux-en-Y gastrojejunal bypass is the most performed operation for morbid obesity in the World, representing 65% of all procedures. Beyond the mechanical restrictive and disabsorptive effects, it promotes decrease

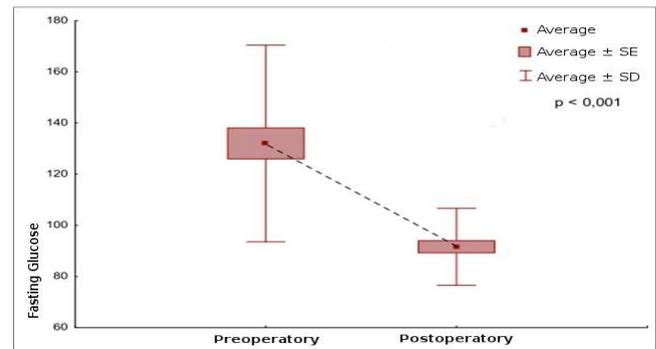


Figure 2 – Fasting glucose in the periods evaluated. SE: Standard Error; SD: Standard Deviation.

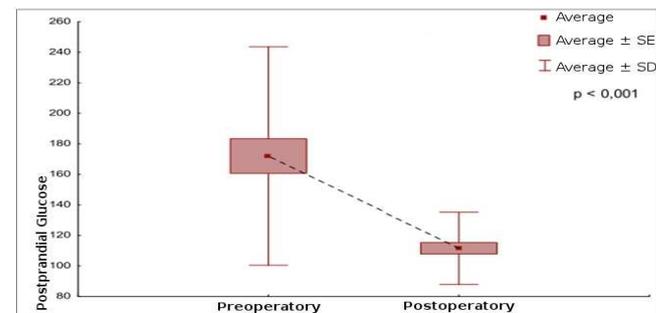


Figure 3 - Postprandial glucose in the periods evaluated. SE: Standard Error; SD: Standard Deviation.

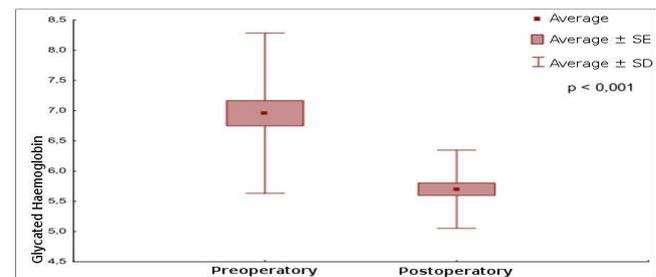


Figure 4 - Glycated hemoglobin in the periods evaluated. SE: Standard Error; SD: Standard Deviation.

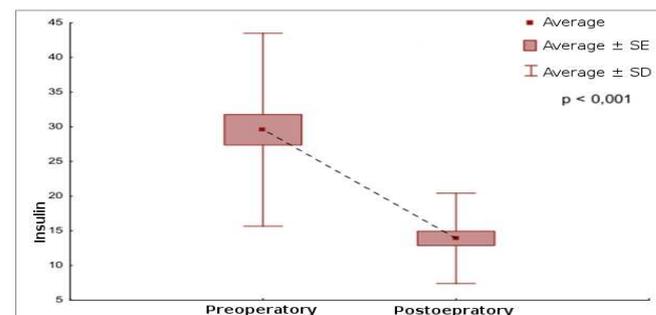


Figure 5 - Insulin in the periods evaluated. SE: Standard Error; SD: Standard Deviation.

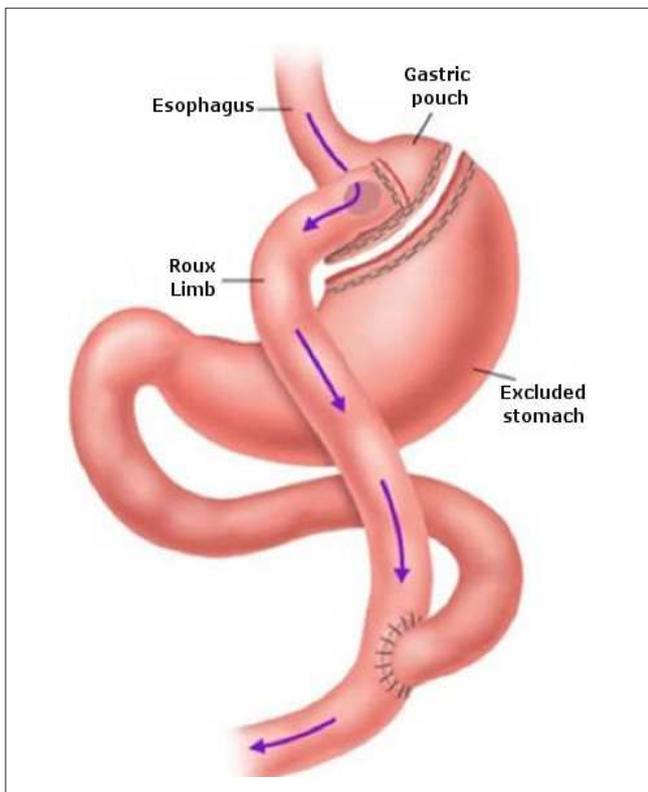


Figure 1 - Roux-en-Y gastrojejunal bypass.

in postprandial levels of ghrelin, an important orexigenic hormone. Other intestinal hormones, as the peptide YY and GLP-1, have anorectic function and are increased after operation<sup>15</sup>. It acts initially as a restrictive procedure, leading to early satiety. The exclusion of part of the stomach-duodenum-jejunum segment leads to lower levels of postprandial ghrelin, decreasing the appetite even more. The more precocious presence of food on the terminal ileum leads to more production of PYY and GLP-1, decreasing the intake and optimizing the glucose-insulin metabolism. This is an important anti-diabetogenic effect of this operation<sup>16,17</sup>.

The resolution of diabetes happens early, even before great weight loss. Such fact can be explained by the early endocrine effect produced by the procedure<sup>13,18</sup>.

Corroborating with other papers, the patients submitted to this bypass without ring had significant reduction of clinical and laboratory parameters 60 days after the procedure, displaying normalization of the variables studied<sup>7,15,19-24</sup>.

As for age and gender, the results agreed with other studies on prevalence of obesity and DM2 in world population<sup>15,25,26</sup>, 62.5% being women. The age in average was 41 years, ranging from 24 to 62.

The preoperative BMI in this study was 39.5 Kg/m<sup>2</sup>, with decrease of 6.6 Kg/m<sup>2</sup> in 60 days; this weight loss was similar to the literature's<sup>15,23,26-28</sup>.

Preoperative glucose average was 132 mg/dl, decreasing to 91.6 mg/dl in two months postoperatively. A similar thing happened to glycated hemoglobin, which was 7.0% on the preoperative time, and in 60 days, 5%. These findings were also reported by other authors<sup>13,22,23,29-32</sup>.

Marina and Trence<sup>33</sup> published preliminary results suggesting that fasting glucose and glycated hemoglobin were not sufficient criteria to determine the remission of DM2 after surgery. The authors suggest that continuous glycemic monitoring and postprandial glucose measurements are necessary to evaluate the glycemic profile specifically in the observation of the effects of Roux-en-Y gastric bypass in patients with DM2.

In this study, besides fasting glucose and glycated hemoglobin, the values of postprandial glucose also normalized. The average preoperative postprandial glucose was of 172 mg/dl, decreasing in average 60.5 mg/dl, reaching values of 111.6 mg/dl within 60 days after surgery.

In conclusion, a statistically significant reduction in body weight and body mass index was found between the preoperative and postoperative periods and also in the reduction of fasting blood glucose, postprandial glucose, glycated hemoglobin and insulin between the pre and postoperative periods.

## R E S U M O

**Objetivos:** Verificar as alterações do peso e índice de massa corporal em pacientes obesos grau II e III com diabetes melito tipo 2 nos períodos pré e pós-operatório e as alterações dos parâmetros laboratoriais de glicemia de jejum, glicemia pós-prandial, hemoglobina glicada, insulina nos períodos pré e pós-operatório. **Métodos:** Realizou-se estudo prospectivo selecionando 40 pacientes com obesidade grau II e III, submetidos à derivação gastrojejunal em Y-de-Roux sem anel. Analisou-se no pré e pós-operatório de 60 dias o peso, índice de massa corporal, glicemia de jejum, glicemia pós-prandial, hemoglobina glicada e insulina. **Resultados:** O peso médio pré-operatório foi de 107,3Kg diminuindo para 89,5Kg no pós-operatório. O índice de massa corporal médio inicial foi de 39,5Kg/m<sup>2</sup> e 32,9Kg/m<sup>2</sup> com 60 dias de pós-operatório. A glicemia de jejum no pré-operatório foi de 132 mg/dl e no pós-operatório diminuiu 40,4 mg/dl em média. A glicemia pós-prandial foi de 172 mg/dl no pré-operatório e 111,6 mg/dl no controle pós-operatório. A hemoglobina glicada inicial foi de 7% declinando para 5,7% no pós-operatório. A insulina pré-operatória foi 29,6 uIU/ml e a pós-operatória 13,9 uIU/ml. Todas as variáveis apresentaram significância estatística com p<0,001. **Conclusão:** Houve significante diminuição de peso e no índice de massa corporal entre os períodos pré e pós-operatórios e diminuição também significante dos parâmetros laboratoriais de glicemia de jejum, glicemia pós-prandial, hemoglobina glicada, insulina entre os mesmos períodos.

**Descritores:** Pacientes. Obesidade. Diabetes mellitus tipo 2. Derivação gástrica. Cirurgia Bariátrica.

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