

Liver markers, prevalence of the metabolic syndrome abnormalities and effect of Roux-en-Y gastric bypass in morbidly obese subjects

Marcadores hepáticos, prevalência de alterações da síndrome metabólica e efeito do *bypass* gástrico com reconstrução em Y-de-Roux em pacientes obesos mórbidos

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ABSTRACT

Objectives: To evaluate the relations between liver markers (GGT, ALT and AST) and the metabolic syndrome (and its components) in morbidly obese subjects, and to determine the response of these metabolic factors and hepatic enzymes after weight loss induced by Roux-en-Y gastric bypass. **Methods:** This study was carried out at a university hospital, in Santo André (SP), Brazil. We evaluated 140 morbidly obese subjects aged from 18 to 60 years submitted to a Roux-en-Y gastric bypass, who were followed for a mean period of 8 months. Patients with a history of heavy drinking, type 1 diabetes, and/or liver disease were excluded. **Results:** Liver markers, most notably GGT, were strongly associated with metabolic abnormalities, mainly hyperglycemia. The prevalence of type 2 diabetes significantly increased with increasing levels of GGT (highest versus lowest quartile GGT: odds ratio 3.89 [95%CI: 1.07-14.17]). Liver markers significantly decreased 8 months after the Roux-en-Y gastric bypass and the reduction of GGT levels were associated with the reduction of glucose levels (Pearson $r = 0.286$; $p = 0.001$). **Conclusions:** Elevated levels of liver markers, principally GGT, in morbidly obese subjects are associated with metabolic abnormalities. In addition to the well-known benefits of bariatric surgery, Roux-en-Y gastric bypass, reduced the levels of liver markers to the normal range.

Keywords: Obesity, morbid; Biological markers; Metabolic syndrome; Anastomosis, Roux-en-Y

RESUMO

Objetivos: Avaliar as relações entre os marcadores hepáticos (GGT, ALT e TGO) e a síndrome metabólica (e seus componentes) em indivíduos com obesidade mórbida, e determinar a resposta desses fatores metabólicos e enzimas hepáticas após a perda de peso induzida pelo *bypass* gástrico em Y-de-Roux. **Métodos:** Estudo

realizado em um hospital universitário, localizado em Santo André (SP). Foram avaliados 140 indivíduos com obesidade mórbida, entre 18 e 60 anos de idade, submetidos ao *bypass* gástrico em Y-de-Roux, acompanhados por um período médio de 8 meses. Pacientes com história de alcoolismo pesado, diabetes tipo 1 e/ou doença hepática foram excluídos. **Resultados:** Os marcadores hepáticos, principalmente GGT, foram fortemente associados a alterações metabólicas, principalmente hiperglicemia. A prevalência de diabetes tipo 2 aumentou significativamente com a elevação dos níveis de GGT [quartil superior versus inferior: *odds ratio* 3,89 (IC95%: 1,07-14,17)]. Os marcadores hepáticos diminuíram significativamente 8 meses após o *bypass* em Y-de-Roux e a redução dos níveis de GGT estava associada à redução dos níveis de glicose (Pearson $r = 0,286$; $p = 0,001$). **Conclusões:** Níveis elevados de marcadores hepáticos, principalmente GGT, em pacientes com obesidade mórbida, estavam associados a alterações metabólicas. Além dos já conhecidos benefícios da cirurgia bariátrica, o *bypass* gástrico em Y-de-Roux reduziu os níveis dos marcadores hepáticos a valores normais.

Descritores: Obesidade mórbida; Marcadores biológicos; Síndrome metabólica; Anastomose em-Y de Roux

INTRODUCTION

Metabolic syndrome (MS), characterized by a core set of disorders, including abdominal obesity, dyslipidemia, hypertension, and hyperglycemia, has been shown to be an important predictor of type 2 *diabetes mellitus* (DM2) and of cardiovascular disease⁽¹⁾. Recent research has provided evidence that a wider constellation of disorders may be part of the MS cluster. These proposed nontraditional components of MS include

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microalbuminuria, subclinical inflammation, and nonalcoholic fatty liver disease (NAFLD)^(2,3).

Subjects with NAFLD, which is the most common cause of chronically elevated transaminase levels⁽⁴⁾, have been reported to have high prevalence rates of MS and associated disorders⁽⁵⁾. Alanine aminotransferase (ALT) is the most specific marker of hepatic dysfunction resulting from the insulin resistance syndrome. Gamma-glutamyltransferase (GGT) is considered a sensitive indicator of liver damage, but is not specific⁽⁶⁾.

A number of cross-sectional studies showed relation between GGT and ALT and the MS and insulin resistance, suggesting that GGT/ALT may serve as a marker for insulin resistance^(7,8). Furthermore, liver markers have been shown to be associated with MS variables in large representative samples of the general population^(4,9).

OBJECTIVES

To examine the cross-sectional relationships between liver markers (GGT, ALT and AST) and the MS (and its components) in morbidly obese subjects; to determine the response of these metabolic factors and hepatic enzymes after weight loss induced by Roux-en-Y gastric bypass (RYGBP); and to evaluate whether liver markers provide useful supplementary markers identifying subjects at a high risk of DM2 and in particular whether they provide further prognostic information in patients with MS.

METHODS

Institution

This study was carried out at a University Hospital, in Santo André (SP), Brazil.

Study population

A total of 140 morbidly obese patients were considered eligible to participate in this study according to the inclusion criteria: body mass index (BMI) ≥ 40 kg/m², age between 18 and 60 years, and no history of liver disease. Patients with a history of heavy drinking (three or more drinks per day) or with type 1 *diabetes mellitus* (DM1) were excluded. Most patients (68.5%) were women and the mean BMI was 46.1 ± 5.4 kg/m² (40.0 - 65.6 kg/m²).

Study protocol and follow-up

Pre and postoperative (at 8 months after bariatric surgery) blood samples were taken after a minimum

fasting period of 8 hours. BMI is defined as the individual's body weight divided by the square of his/her height. To define MS, we used the International Diabetes Federation (IDF) criteria: waist circumference ≥ 94 cm in men, ≥ 80 cm in women or BMI ≥ 30 kg/m²; triglycerides levels ≥ 150 mg/dL (1.7 mmol/L) and/or specific treatment; HDL-C levels < 40 mg/dL (1 mmol/L) in men, < 50 mg/dL (1.3 mmol/L) in women and/or specific treatment; fasting glucose ≥ 100 mg/dL (5.6 mmol/L) and/or DM2 patient; systolic blood pressure ≥ 130 mmHg, diastolic blood pressure ≥ 85 mmHg and/or specific treatment. The individual must present at least three of the five risk factors to be diagnosed with MS.

The obese patients underwent laparoscopic RYGBP and after 8 months all tests were repeated. RYGBP is a mixed technique that is more restrictive and less malabsorptive. Its main characteristics are the formation of gastric "pouch" (15 ± 5 mL), an alimentary loop of 100 cm, a biliopancreatic loop of 60 cm, and a common loop.

Statistical methods

Data were first tested for normal distribution with the Kolmogorov-Smirnoff test. For cross-section comparisons, concentration of liver markers between those with and without baseline MS and its components were compared using ANCOVA adjusted for age, sex, and ethnicity. The patients were divided into four equal quartiles on the basis of ALT, AST, AST-to-ALT ratio, and GGT distributions, and linear regression analysis was used to test for trends across the four groups fitting quantitative variables for the four groups.

For prospective analyses, baseline means (with standard deviation – SD) were calculated for subjects by follow-up with *t* tests, Wilcoxon tests, or χ^2 tests. The association between liver markers with anthropometric and metabolic variables was evaluated using Pearson's correlation analysis controlled for age, ethnicity, and sex. Multivariate logistic regression models were used to assess associations of liver markers with the risk of prevalent MS and with its improvement after weight loss, taking into account potential confounders. Each liver marker was modeled as either a continuous variable (with risk expressed per SD increase in the natural log of the marker) or as a categorical variable, comparing risk among those in the fourth quartile *versus* those in the first quartile. Two models were constructed for each liver marker: in model A, adjustments were made only for age; and in model B, for age, sex and ethnicity. It has been pointed out that the AST-to-ALT ratio may be informative in differentiating alcoholic *versus* nonalcoholic liver disease (subjects with NAFLD having a ratio below 1), and thus this ratio

was considered an additional exposure variable⁽¹⁰⁾. We evaluated the degree to which liver markers predicted improvement of MS after RYGBP using logistic regression.

All statistical analyses were made with the statistical software package *Statistical Package for the Social Science* (SPSS), version 16.0 (Chicago, IL) and MedCalc software. Statistical significance was considered at $p < 0.05$.

RESULTS

Table 1 shows the baseline characteristics by quartiles of the GGT, ALT, and AST distributions. With the exception of the white cell count, all the metabolic risk factors significantly increased with increasing GGT levels, whereas HDL levels decreased with it. The prevalence of diabetes and hypertension also increased with increasing levels of GGT. ALT was

significantly associated with glucose levels and with diabetes prevalence, but showed a significant inverse relationship with the white cell count. AST was associated only with glucose levels. The prevalence of MS did not correlate with increasing levels of GGT, ALT, or AST. However, GGT and AST increased significantly with the increasing number of metabolic abnormalities ($p = 0.003$ and $p = 0.048$, respectively). Mean GGT values for those with 1, 2, 3, 4, and 5 abnormalities were 31.8, 33.7, 38.0, 64.0, and 51.8 units/L, respectively, and for AST the corresponding means were 23.9, 27.4, 27.4, 29.6, and 32.4 units/L, respectively (Table 2).

MS disorders, when assessed individually, were characterized by significant differences only in GGT, before bariatric surgery (Table 2). After surgery no liver marker differed in subjects with MS or metabolic disorders assessed individually. Some situations approached significance, however, due to the median

Table 1. GGT, AST, ALT and metabolic and cardiovascular risk factors

GGT (IU/L)	Quartiles				p value
	≤ 27	28 – 35.9	36 – 42.9	≥ 43	
Age (years)	35.4 ± 10.2	37.2 ± 9.9	37.3 ± 10.0	39.3 ± 10.1	0.120
BMI (kg/m ²)	44.3 ± 4.5	43.0 ± 3.1	43.7 ± 3.7	45.3 ± 5.6	0.287
Diabetes mellitus (%)	8.3	15.6	11.1	33.3	0.012
Hypertension (%)	36.1	37.5	41.7	72.2	0.002
Metabolic markers					
HDL (mg/dL)	49.1 ± 11.8	49.8 ± 10.2	46.0 ± 9.8	44.6 ± 11.4	0.037
Triglycerides (mg/dL)	139.8 ± 73.1	137.4 ± 74.2	166.1 ± 95.2	180.3 ± 95.5	0.021
Glucose (mg/dL)	91.5 ± 17.6	95.8 ± 21.9	98.6 ± 21.2	109.6 ± 30.0	0.001
White cell count (10 ⁹ /L)	7.7 ± 1.8	7.6 ± 2.0	6.9 ± 1.4	7.2 ± 2.2	0.143
Metabolic syndrome (%)	66.7	53.1	50.0	47.2	0.098
ALT (IU/L)	≤ 22	23 – 29.9	30 – 39.6	≥ 39.7	
Age (years)	35.5 ± 10.3	38.3 ± 9.5	36.9 ± 9.9	38.7 ± 10.4	0.265
BMI (kg/m ²)	43.3 ± 3.4	44.1 ± 3.5	43.9 ± 4.0	45.2 ± 6.1	0.104
Diabetes mellitus (%)	10.8	9.1	22.9	25.7	0.041
Hypertension (%)	43.2	51.5	37.1	57.1	0.463
Metabolic markers					
HDL (mg/dL)	47.3 ± 11.5	46.8 ± 9.6	49.5 ± 12.2	45.7 ± 10.3	0.793
Triglycerides (mg/dL)	136.1 ± 66.0	163.0 ± 80.7	154.6 ± 101.2	173.5 ± 93.8	0.105
Glucose (mg/dL)	91.8 ± 18.4	97.4 ± 25.8	100.5 ± 22.9	106.4 ± 26.8	0.009
White cell count (10 ⁹ /L)	8.1 ± 1.8	7.2 ± 2.0	7.3 ± 1.6	6.8 ± 2.0	0.008
Metabolic syndrome (%)	64.9	57.6	40.0	54.3	0.184
AST (IU/L)	≤ 20	21 – 24.9	25 – 33.9	≥ 34	
Age (years)	36.5 ± 8.8	37.1 ± 10.5	36.3 ± 10.8	39.2 ± 9.8	0.336
BMI (kg/m ²)	43.8 ± 4.4	43.6 ± 3.6	43.9 ± 3.4	45.2 ± 5.8	0.163
Diabetes mellitus (%)	13.3	8.6	20.5	25.0	0.096
Hypertension (%)	53.3	34.3	46.2	55.6	0.557
Metabolic markers					
HDL (mg/dL)	47.8 ± 12.8	48.1 ± 10.7	47.9 ± 10.8	45.5 ± 9.8	0.406
Triglycerides (mg/dL)	143.0 ± 85.3	165.3 ± 81.5	142.7 ± 76.9	173.9 ± 100.2	0.313
Glucose (mg/dL)	97.1 ± 20.0	93.2 ± 18.0	95.7 ± 21.7	109.5 ± 30.8	0.023
White cell count (10 ⁹ /L)	8.0 ± 1.7	7.3 ± 1.7	7.1 ± 2.0	7.1 ± 2.0	0.068
Metabolic syndrome (%)	60.0	60.0	48.7	50.0	0.281

p value: trend across groups (linear regression); BMI: body mass index.

Table 2. Concentrations of liver markers in morbidly obese subjects with and without IDF-defined metabolic syndrome and its components at baseline and after 8 months of Roux-en-Y gastric bypass

Liver markers	Yes/No	AST (IU/L)	ALT (IU/L)	GGT (IU/L)	AST-to-ALT ratio (IU/L)
Before Roux-en-Y gastric bypass					
IDF metabolic syndrome	No	28.1 ± 10.6	33.6 ± 11.6	41.0 ± 22.1	0.86 ± 0.22
	Yes	27.5 ± 12.4	34.3 ± 21.2	41.2 ± 35.2	0.90 ± 0.33
Fasting hyperglycemia	No	27.0 ± 11.8	32.5 ± 18.6	35.8 ± 19.1	0.91 ± 0.30
	Yes	29.3 ± 11.2	36.6 ± 14.9	50.6 ± 41.6*	0.84 ± 0.24
Elevated triglyceride	No	27.0 ± 12.3	31.8 ± 18.2	38.9 ± 35.0	0.92 ± 0.31
	Yes	28.6 ± 10.9	36.1 ± 16.5	43.3 ± 23.8	0.85 ± 0.25
Reduced HDL	No	27.3 ± 9.2	34.6 ± 15.1	37.2 ± 21.3	0.87 ± 0.33
	Yes	28.2 ± 13.2	33.5 ± 19.0	44.0 ± 34.6*	0.89 ± 0.24
Hypertension	No	27.4 ± 12.0	33.1 ± 18.9	35.3 ± 17.6	0.89 ± 0.25
	Yes	28.3 ± 11.2	34.9 ± 15.7	47.7 ± 38.5*	0.87 ± 0.31
After Roux-en-Y gastric bypass					
IDF metabolic syndrome	No	21.2 ± 8.4	21.6 ± 12.0	21.5 ± 16.2	1.08 ± 0.42
	Yes	26.8 ± 9.9	24.4 ± 12.7	35.3 ± 25.4	1.29 ± 0.67
Fasting hyperglycemia	No	21.8 ± 8.8	22.0 ± 12.0	22.5 ± 17.8	1.09 ± 0.42
	Yes	22.8 ± 8.0	21.6 ± 13.9	37.6 ± 18.6	1.51 ± 1.11
Elevated triglyceride	No	21.7 ± 8.5	21.9 ± 11.8	23.0 ± 17.3	1.09 ± 0.45
	Yes	25.6 ± 12.6	23.6 ± 17.0	24.8 ± 29.6	1.33 ± 0.63
Reduced HDL	No	21.3 ± 7.6	23.9 ± 15.4	22.1 ± 15.3	0.99 ± 0.29
	Yes	22.2 ± 9.2	20.9 ± 9.8	23.6 ± 19.2	1.17 ± 0.52
Hypertension	No	21.6 ± 8.9	22.0 ± 12.5	21.9 ± 17.8	1.08 ± 0.44
	Yes	23.7 ± 7.4	21.7 ± 9.33	29.4 ± 18.1	1.23 ± 0.58

Adjusted for age, sex and ethnicity. $p < 0.05$. IDF: International Diabetes Federation.

number of patients and the restrictive effect of the model (sex, age, and ethnicity), significance was not reached.

Associations of liver markers with anthropometric and metabolic variables in morbidly obese patients before and after RYGBP are analyzed. Before surgery AST, ALT, and GGT levels showed positive correlations with fasting glucose, GGT showed an inverse correlation with HDL, ALT showed an inverse correlation with the white cell count, and the AST-to-ALT ratio showed a positive correlation with the white cell count. The magnitude of these associations was strongest for GGT, especially for fasting glucose and HDL. After surgery, only age correlated with liver markers.

Prevalence rates and odds ratio of DM2 by the four groups of ALT, GGT, and AST, using those in the lowest quartile as the reference group, are analyzed. Only GGT values, when adjusted for age, were significantly predictive of DM2. We further examined the relation, adjusting for sex, ethnicity, and age. Such adjustment, as shown in table 2 column B, reduced the risk to levels below statistical significance. On a receiver operating characteristic curve (ROC curve), GGT showed the larger area when compared with AST and ALT (0.670, 0.627, and 0.639, respectively) (Figure 1).

In the analysis of liver markers and prediction of individual MS components, only GGT values were

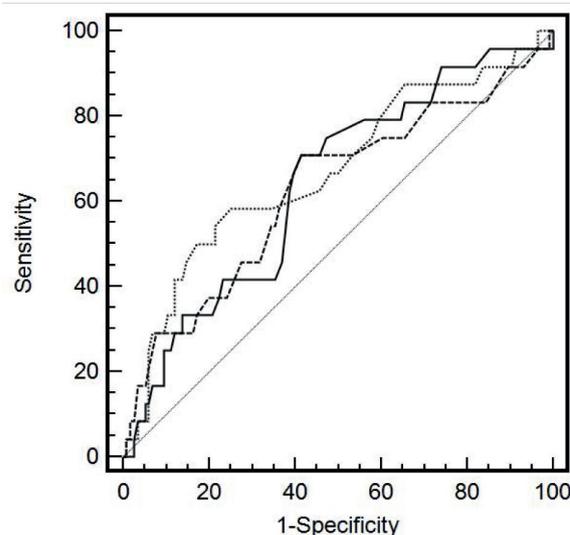


Figure 1. Receiver-operating characteristic curve (ROC) for type 2 diabetes diagnosis. AUC for AST (0.627 [0.541 - 0.707]), ALT (0.639 [0.554 - 0.718]) and GGT (0.670 [0.585 - 0.747]). Comparisons of AUC: AST versus ALT ($p = 0.629$), AST versus GGT ($p = 0.879$) and ALT versus GGT ($p = 0.798$). GGT (— · —), ALT (—) and AST (---)

significantly associated with prevalent hypertension. These associations were significant regardless of whether the exposures were modeled as continuous (risk per SD increase: 1.23 [1.02 – 1.33]) or categorical variables (quartile 4 versus quartile 1: 3.95 [1.33 – 11.69]).

Eight months after surgery, all liver markers (with the exception of bilirubin) showed a significant decrease, as shown in table 3. The drop was more accentuated in GGT, followed by ALT. The AST-to-ALT ratio showed an inverse ratio before surgery (0.88 versus 1.11). After surgery, the Δ BMI correlated with Δ MSFactors (Pearson $r = 0.195$; $p = 0.021$) and the Δ GGT correlated with Δ Glucose (Pearson $r = 0.286$; $p = 0.001$).

Table 3. Liver markers before and eight months after Roux-en-Y gastric bypass

Markers	Before RYGB	After RYGB	p value*
ALT (IU/L)	33.99 \pm 17.47	22.00 \pm 12.09	< 0.0001
AST (IU/L)	27.85 \pm 11.65	21.92 \pm 8.75	< 0.0001
GGT (IU/L)	41.15 \pm 29.9	23.10 \pm 17.99	< 0.0001
AST-to-ALT ratio	0.88 \pm 0.28	1.11 \pm 0.46	< 0.0001
Bilirubin (mg/dL)	0.61 \pm 0.52	0.62 \pm 0.41	0.870

* Paired-samples t Test.

RYGBP: Roux-en-Y gastric bypass.

Table 4 and figure 2 show sensitivity and specificity for selected threshold values of ALT, GGT, and AST predicting improvement of the MS 8 months after the RYGBP in morbidly obese subjects. The receiver operating characteristic analyses suggested AST, ALT, and GGT cut-off values of 23, 33, and 31 IU/L with corresponding sensitivities of 51.4, 64.2, and 44.2%. The area under the curve for the three markers was similar.

Table 4. Sensitivity and specificity for selected thresholds of GGT, ALT and AST for predicting metabolic syndrome improvement

Markers	Sensitivity (95%CI)	Specificity (95%CI)	AUC (95%CI)*
GGT (IU/L)			0.56 (0.47 - 0.64)
Threshold 27	31.4 (20.9 - 43.6)	80.0 (68.7 - 88.6)	
Threshold 35	50.0 (37.8 - 62.2)	52.8 (40.6 - 64.9)	
Threshold 43	77.1 (65.6 - 86.3)	28.5 (18.4 - 40.6)	
Threshold 54	84.2 (73.6 - 91.9)	18.5 (10.3 - 29.7)	
Threshold 31 [†]	44.2 (32.4 - 56.7)	70.0 (57.9 - 80.4)	
ALT (IU/L)			0.57 (0.48 - 0.65)
Threshold 22	32.8 (22.1 - 45.1)	80.0 (68.7 - 88.6)	
Threshold 30	58.5 (46.2 - 70.2)	58.5 (46.2 - 70.2)	
Threshold 40	75.7 (64.0 - 85.2)	21.4 (12.5 - 32.9)	
Threshold 52	87.1 (77.0 - 93.9)	8.5 (3.2 - 17.7)	
Threshold 33 [†]	64.2 (51.9 - 75.4)	52.8 (40.6 - 64.9)	
AST (IU/L)			0.55 (0.46 - 0.63)
Threshold 20	31.4 (20.9 - 43.6)	78.5 (67.1 - 87.5)	
Threshold 25	55.7 (43.3 - 67.6)	54.2 (41.9 - 66.3)	
Threshold 35	78.5 (67.1 - 87.5)	18.5 (10.3 - 29.7)	
Threshold 40	90.0 (80.5 - 95.9)	12.8 (6.1 - 23.0)	
Threshold 23 [†]	51.4 (39.2 - 63.6)	64.2 (51.9 - 75.4)	

* Area under the curve derived from receiver-operating characteristic analyses.

[†] Threshold maximizing the sum of sensitivity and specificity.

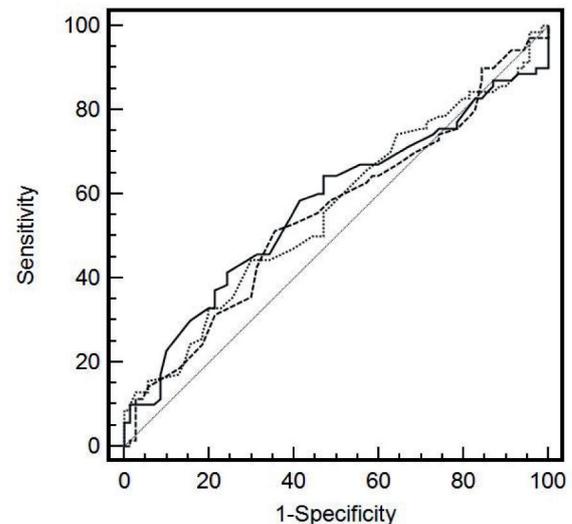


Figure 2. Receiver-operating characteristic curve (ROC) for metabolic syndrome improvement after Roux-en-Y gastric bypass. Comparisons of AUC: AST versus ALT ($p = 0.826$), AST versus GGT ($p = 0.531$) and ALT versus GGT ($p = 0.658$). GGT (---), ALT (___) and AST (---)

DISCUSSION

In the present study we documented, among morbidly obese subjects, significant cross-sectional associations of liver markers, primarily GGT, with metabolic abnormalities, most notably fasting hyperglycemia. Furthermore, at baseline, GGT and ALT levels increased significantly with the increase in number of metabolic abnormalities. Also, we demonstrated that concentrations of GGT were associated with an almost fourfold increase in DM2 prevalence and threefold increase in hypertension prevalence after adjustment for age. In contrast, significant associations with ALT/AST and metabolic abnormalities were not seen in the multivariate analysis. Finally, liver markers significantly decreased 8 months after the RYGBP, and the reduction of GGT levels was associated with the reduction of glucose levels.

In earlier results, our group showed the beneficial effects of RYGBP in MS^(11,12) and renal function of morbidly obese subjects⁽¹³⁾. However, as demonstrated by prior studies, we showed that RYGBP can reduce liver markers to normal levels⁽¹⁴⁻¹⁶⁾. Obesity is a major risk factor for the development of fatty liver disease, and several studies have associated elevated liver enzymes, obesity, and DM2⁽¹⁷⁾. A growing body of evidence also supports the notion that NAFLD is a feature of the MS and that the elevations of liver markers found in this situation, particularly of ALT, are prospectively associated with incident DM2, an important sequel of the MS^(9,18-21).

There are a number of possible mechanisms to explain the associations of liver markers with MS and its factors. First, these markers are known to be significantly correlated with increased hepatic fat content, a disorder

that has detrimental effects on components of the MS⁽²²⁾. It has been demonstrated that hepatic fat content, directly measured using proton spectroscopy, is associated with several features of insulin resistance independent of body weight. In particular, hepatic fat was associated with defects in the suppression by insulin of endogenous glucose production⁽²³⁾, which is noteworthy in the context of our results showing that all liver markers were related to fasting hyperglycemia. It is also possible that these associations reflect more generalized insulin resistance.

Fat accumulation in the liver can stimulate cytokine production, and it was found that inflammatory cytokines, such as tumor necrosis factor- α (TNF- α) and interleukin-6 (IL-6) can influence fatty acid metabolism in the liver and predispose to the formation of fatty liver⁽²⁴⁾. Thus, another possible mechanism is that elevated liver enzymes may reflect inflammation, which in turn impairs insulin signaling in both the liver and other organs. Inflammation has been associated with the development of diabetes⁽²⁵⁾. It has also been suggested that GGT might be an early marker of oxidative stress^(26,27). Inflammation is one manifestation of oxidative stress, and the pathways that generate the mediators of inflammation, such as adhesion molecules and interleukins, are all induced by oxidative stress⁽²⁸⁾. This may explain the association between inflammation, which might reveal nonalcoholic steatohepatitis, and GGT.

The contribution of the present study is the demonstration that liver markers, mainly GGT, are significantly associated with metabolic abnormalities and that GGT also correlates with DM2 and hypertension prevalence in a well-characterized multiethnic cohort of morbidly obese subjects. The weight loss induced by RYGBP can reduce liver markers to levels in the normal range and this decline, in GGT, is associated with an improvement in glucose metabolism. The main limitation of our study is the number of patients, which hinders the finding of a statistically significant result in a very restricted logistic regression model.

CONCLUSIONS

Elevated levels of liver markers, principally GGT, in morbidly obese subjects are associated with metabolic abnormalities. In addition to the well-known benefits of bariatric surgery, Roux-en-Y gastric bypass, reduced the levels of liver markers to the normal range.

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