



# Correlation Between Post Over Preoperative Surrogate Insulin Resistance Indexes' Ratios and Reversal of Metabolic Syndrome After Roux-en-Y Gastric Bypass

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Published online: 17 April 2014  
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**Abstract** Metabolic syndrome (MetS) is strongly linked to insulin resistance and has a high resolution rate after bariatric surgery. This study aims to determine whether post over preoperative ratios of surrogate insulin resistance markers (HOMA, TyG, and TG/HDL-c) are associated to postsurgical MetS reversal. This is a retrospective cohort study which involved 96 subjects with MetS who underwent Roux-en-Y gastric bypass (RYGB). Post over preoperative ratios of TyG and TG/HDL-c indexes were statistically associated to MetS resolution. The use of these ratios as a way to assess postsurgical insulin sensitivity response appears to be a simple and useful tool in clinical practice.

**Keywords** Metabolic syndrome X · Insulin resistance · Gastric bypass · Diabetes mellitus · Bariatric surgery

## Background

Metabolic syndrome (MetS) is defined as a combination of clustering factors that increase the risk of type 2 diabetes mellitus (T2DM) and cardiovascular disease. It appears to be caused by a complex array of interconnected mechanisms, and insulin resistance (IR) seems to be its key point [1, 2]. Direct estimation of individual IR demands diagnostic tests which have considerably high costs and low availability for use in large scale. Hence, surrogate tests for determining IR and cardiometabolic risk have become common and easily applied

tools and tend to get an ever crescent usefulness on clinical practice, and especially for epidemiologic purposes [3]. Homeostasis model assessment (HOMA), triglyceride/high-density lipoprotein ratio (TG/HDL-c), and the products of triglycerides and fasting glucose index (TyG) are the most commonly used of these tests and have been previously validated [3, 4].

As bariatric surgeries have become the standard treatment option for morbid obesity, many studies have shown an important impact of these procedures on IR, thus leading to reversal of metabolic comorbidities or preventing their onset [5]. This effect occurs early after the intervention, and its exact pathophysiology is not completely known, but it is strongly linked to changes on gastrointestinal hormones called incretins and fat tissue-active peptides called adipokines, rather than weight loss itself [6]. It has been also shown that some subjects tend to have considerably less metabolic improvement after surgery than the majority of the individuals, due to not completely understood mechanisms that may involve insufficient incretin response, persistent adiposopathy, and chronic inflammation [7, 8].

## Aim

The aim of this study is to determine whether the ratio between post and preoperative values of surrogate IR indexes (HOMA, TG/HDL-c, and TyG) are linked to reversal of MetS after RYGB.

## Materials and Methods

This study involved a retrospective cohort which included obese subjects that filled the International Diabetes Federation (IDF) criteria for MetS [9] who underwent open

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RYGB at Hospital de Clínicas—UNICAMP between 2000 and 2010. This study was approved by the local Research Ethics Committee. Surgery was indicated based on the National Institutes of Health Consensus Statement criteria [10]. The estimation of sample size was performed using single proportion formula with 95 % confidence interval. Precision was set at 10 %, and the calculated sample size was 84.

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

From 672 subjects who underwent RYGB, 96 who filled criteria for MetS as specified by IDF and had been followed for at least 12 months were included. Main characteristics regarding demographics were assessed. Biochemical characteristics evaluated included the fasting glucose (FG), fasting insulin (FI), HDL-c, triglycerides, homeostasis model assessment—insulin resistance (HOMA-IR), triglyceride/high-density lipoprotein ratio (TG/HDL-c), and the product of triglycerides and fasting glucose index (TyG). HOMA-IR, TG/HDL-c, and TyG were calculated according the previous descriptions [11–13]. Postsurgical ratios of HOMA, TG/HDL-c, and TyG were calculated through division of post over preoperative values as it is presented below:

$$\text{Index ratio} = [\text{postoperative index value}] / [\text{preoperative index value}]$$

Comparisons were made between the periods immediately before and at least 1 year after surgery, in order to measure the association between the surrogate IR markers' respective ratios and ultimate reversal of MetS, whose resolution was achieved through not filling the IDF criteria. Preoperative measurements were taken immediately before surgery, and postoperative measurements were taken from the last annotation on the patients' medical records.

## Statistical Analysis

The baseline characteristics of patients are described and then compared with postoperative period. Data were examined for

**Table 1** Subject characteristics at baseline

Gender	Male—23 % Female—77 %
Age	46±10.8 years
Body mass index (BMI)	44.3±8.74 (35–80.8) kg/m <sup>2</sup>
Weight (kg)	102.2±18.1 (72–180) kg
Postoperative follow-up	34.2±25.1 months

**Table 2** Mean surrogate insulin resistance indexes before and after surgery

Index	Preoperative	Postoperative	<i>p</i> value
HOMA-IR	4.45	1.93	<0.0001
TyG	4.87	4.46	<0.0001
TG/HDL-c	5.06	1.92	<0.0001

normality according to Pearson's chi-squared test. Wilcoxon test was used for comparisons of continuous measures between the two periods of evaluation for related samples. Mann-Whitney test was used to compare continuous measures between independent groups. The significance level adopted was 5 % (*p* value <0.05). For execution of analysis, Statistic Analysis System (SAS) software for Windows version 9.2 was used.

## Results

Of 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 time 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. The 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 BMI decrease from 44.3±8.7 kg/m<sup>2</sup> to 31.5±7.7 kg/m<sup>2</sup> (*p*<0.001). Mean weight loss was 29.9±9.1 kg (*p*<0.0001).

Postoperatively, 11 (11.5 %) still filled IDF criteria for MetS, leading to a resolution rate of 88.5 % (*p*<0.0001). HOMA-IR, TyG, and TG/HDL-c values before and after surgery are shown in Table 2.

It was observed there was a statistically significant association of MetS resolution with post over preoperative ratios of TyG (*p*=0.0195) and TG/HDL-c (*p*=0.0116). Conversely, there was no significant association of HOMA-IR ratio with MetS resolution (*p*=0.1456). Table 3 summarizes the mean ratios within the groups of subjects that presented reversal or not.

**Table 3** Mean post over preoperative surrogate insulin resistance indexes' ratio and reversal of MetS

Index ratio	Reversal	Non-reversal	<i>p</i> value
HOMA-IR	0.48	2.49	0.1456
TyG	0.91	0.98	0.0195
TG/HDL-c	0.45	0.77	0.0116

## Discussion

Surrogate IR indexes are simple tools to evaluate insulin sensitivity through non-invasive and practical ways. HOMA-IR is the most frequently used nowadays and is a reliable method to assess liver insulin sensitivity. Both TyG and TG/HDL-c were described more recently and have the advantage of using biochemical variables more routinely measured [14–16].

Reversal of MetS after RYGB is a well-known occurrence [5, 17, 18]. It is not completely understood; however, it is linked to great improvement on IR brought by incretin and adipokine response as well as decrease in inflammatory activity [6]. Although the resolution rates previously described are considered high, there is a reasonable number of patients who do not present reversal or even experience worsening of IR on late postoperative periods. Furthermore, the pathophysiologic pathways by which these patients develop persistent or refractory postsurgical IR are even more obscure [7, 8].

This study suggests a novel approach to evaluate IR evolution after RYGB by assessing indirectly the insulin sensitivity response through calculation of ratios of surrogate IR markers. Comparison of the major clinical feature related to IR (MetS) with ratios of both TyG and TG/HDL-c indexes revealed statistical significance, which represents that the routine use of these markers and, especially after bariatric surgery, of the post over preoperative ratio may bring a simple way to assess postsurgical insulin sensitivity response. It is possible that HOMA index ratio may also present significance within larger samples. Hence, these simple calculations are able to evolve into an easy and practical form to identify which group of subjects may develop poor IR decrease after surgery. Regular usage of these ratios following surgery may be useful to predict further MetS reversal or persistence before its ultimate outcome.

**Conflict of Interest** Everton Cazzo, Francisco Callejas-Neto, José Carlos Pareja, and Elinton Adami Chaim declare that they have no conflict of interest.

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