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What is the impact of Roux-en-Y gastric bypass on metabolic syndrome?

Qual é o impacto do bypass gástrico em Y-de-Roux na síndrome metabólica?

Andressa Bressan Malafaia[1], Fernando Issamu Tabushi[1], Ronaldo Mafia Cuenca[2], Timoteo Abrantes de Lacerda Almeida[3], Jorge Alberto Langbeck Ohana[4], Paulo Afonso Nunes Nassif[1]

ABSTRACT

Introduction: Excess overall body fat, often defined by body mass index, has long been recognized as a risk factor for metabolic and cardiovascular diseases, type 2 diabetes mellitus, and osteoporosis. It also affects nonmetabolic disorders such as nonalcoholic fatty liver disease, among others. However, several observations highlight that fat distribution plays a more important role in these associations than excess fat itself. Conversely, peripheral adiposity, characterized by large hip and thigh circumferences, has also been associated with the metabolic profile.

Objective: To review the literature impact of Roux-en-Y gastric bypass on metabolic syndrome in a medium period of time.

Method: This is a narrative review of the literature using review articles, original articles, and case reports published between 2009 and 2024, in Portuguese and English. The search queried the Scielo, PubMed, Google Scholar, and Capes Periódicos databases using the following descriptors: obesity, metabolic syndrome, type 2 diabetes mellitus, and Roux-en-Y anastomosis in Portuguese and English. The inclusion criteria were articles related to metabolic syndrome, focusing on the preoperative, 1- to 6-month postoperative, and 1- to 2-year postoperative periods.

Results: 31 articles were included.

Conclusion: Roux-en-Y gastric bypass improves metabolic syndrome, waist-to-height ratio, and indicators of the patient's cardiometabolic risk profile.

KEYWORDS: Obesity. Roux-en-Y gastric bypass. Metabolic syndrome. Type 2 diabetes mellitus. Surgery.

RESUMO

Introdução: O excesso geral de gordura frequentemente definido pelo índice de massa corporal há muito é reconhecido como fator de risco para doenças relacionadas ao metabolismo, cardiovasculares, diabete melito tipo 2 e à osteoporose. Também afeta distúrbios não metabólicos, como doença hepática gordurosa não alcoólica, dentre outros. No entanto, várias observações ressaltam que, mais do que o próprio excesso de gordura, a distribuição da gordura desempenha papel importante nessas associações. Por outro lado, a adiposidade periférica, caracterizada por grandes circunferências de quadril e coxas, também tem sido associada ao perfil metabólico.

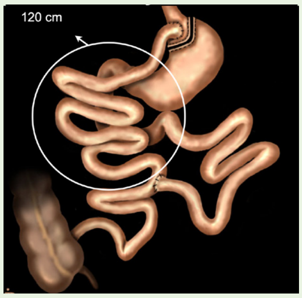
Objetivo: Revisar a literatura quanto ao impacto que o bypass gástrico em Y-de-Roux tem na síndrome metabólica em médio prazo.

Método: Trata-se de revisão narrativa da literatura que utilizou artigos de revisão, originais e relatos de casos no período de 2009 a 2024, nos idiomas português e inglês. Na busca foram consultadas as bases de dados Scielo, PubMed, Google Acadêmico e Capes Periódicos por meio da aplicação dos seguintes descritores: obesidade, síndrome metabólica, diabete melito tipo 2, anastomose em-Y de Roux em português e inglês. Os critérios de inclusão foram artigos relacionados à síndrome metabólica, com foco no pré-operatório, pós-operatório de 1 a 6 meses, e pós-operatório de 1 a 2 anos.

Resultado: Foram incluídos 31 artigos.

Conclusão: Houve melhora com a aplicação do bypass gástrico em Y-de-Roux na síndrome metabólica, na relação cintura/estatura, e nos indicadores do perfil de risco cardiometabólico do paciente.

PALAVRAS-CHAVE: Obesidade. bypass gástrico em Y-de-Roux. Síndrome metabólica. Diabete melito tipo 2. Cirurgia.



Roux-en-Y gastric bypass and, in the circle, measure of the food loop (120 cm)

Central Message

Obesity, particularly abdominal obesity, is associated with resistance to the effects of insulin on the peripheral use of glucose and fatty acids, components of the pathophysiology of type 2 diabetes mellitus, and obese people present these alterations even before developing this disease, such as hyperinsulinemia and increased adipocyte cytokines. All these factors significantly increase cardiovascular risk, either alone or in combination. In addition, total adiposity and subcutaneous fat accumulation during adolescence are positively and independently associated with the development of cardiovascular disease in adulthood.

Perspective

This review aimed to evaluate the impact of Roux-en-Y gastric bypass on metabolic syndrome, comparing preoperative, postoperative 1 to 6 months, and postoperative 1 to 2 years to measure the results of the procedure as a form of treatment. There was an improvement in metabolic syndrome and waist-to-height ratio in the evaluation of the cardiometabolic risk profile and, therefore, it may be an appropriate indication for this circumstance.

[1]Mackenzie Presbyterian Institute, São Paulo, SP, Brazil;
[2]University of Brasília, DF, Brazil;
[3]University of Miami, Florida, United States;
[4]Unimed Prime Hospital, Belém, Pará, Brazil.

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INTRODUCTION

The growth in the prevalence of obesity has become a major health problem worldwide, both in adults and in children and adolescents. In addition, total adiposity and subcutaneous fat accumulation during adolescence are positively and independently associated with the development of cardiovascular disease in adulthood.[1]

Overall excess fat, often defined by body mass index (BMI), has long been recognized as a risk factor for metabolism-related diseases, cardiovascular disease, type 2 diabetes mellitus (T2DM), and osteoporosis. It also affects non-metabolic disorders, such as non-alcoholic fatty liver disease, neoplasms, polycystic ovary syndrome, glomerulopathy, among others.[1] However, several observations emphasize that, more than the excess fat itself, the distribution of fat, especially in the central regions of the body (also called visceral, omental or intra-abdominal fat) plays an important role in these associations. On the other hand, peripheral adiposity, characterized by large hip and thigh circumferences, has been associated with metabolic profile.[2]

Adipose tissue is a key-actor in the pathogenesis of insulin resistance associated with obesity. Dysfunctional hypertrophic adipocytes are highly lipolytic, which results in increased release of free fatty acids into the circulation, as well as impairing normal adipokine secretion. In addition, hypertrophic adipocytes can cause local hypoxia leading to cell death, attracting macrophages and inflammatory cytokines, causing constant and low-grade local inflammation, which, consequently, compromises insulin signaling and causes or potentiates several other problems.[2]

Overexpression of inflammatory cytokines has been associated with increased accumulation of LDL-cholesterol in the coronary endothelial walls, causing propagation of atherosclerotic plaques and thus increasing the incidence of acute myocardial infarction. In addition, this increase in the mobilization of free fatty acids causes a greater entry of triglycerides into the skeletal muscle, causing increased glucose production in the liver and insulin production, low HDL-cholesterol values, excess androgens, among others.[2] Thus, although not all overweight or obese patients are metaphorically dysfunctional, most have insulin resistance, which increases the risk of developing some diseases in which endothelial dysfunction is present.[2]

The objective of this study was to review the literature regarding the impact that Roux-en-Y gastric bypass (Figure) has on metabolic syndrome in the medium term.

METHOD

This is a narrative review of the literature in which review articles, originals and case reports from 2009 to 2024 were used, in Portuguese and English. In the search, the Scielo, PubMed, Google Scholar and Capes Periódicos databases were consulted through the application of the following descriptors: obesity, metabolic syndrome, type 2 diabetes mellitus, Roux's Y-anastomosis and their English counterparts. The inclusion criteria were articles related to metabolic syndrome, focusing on the preoperative, postoperative period of 1 to 6 months, and postoperative period of 1 to 2 years, resulting in the inclusion of 31 articles.

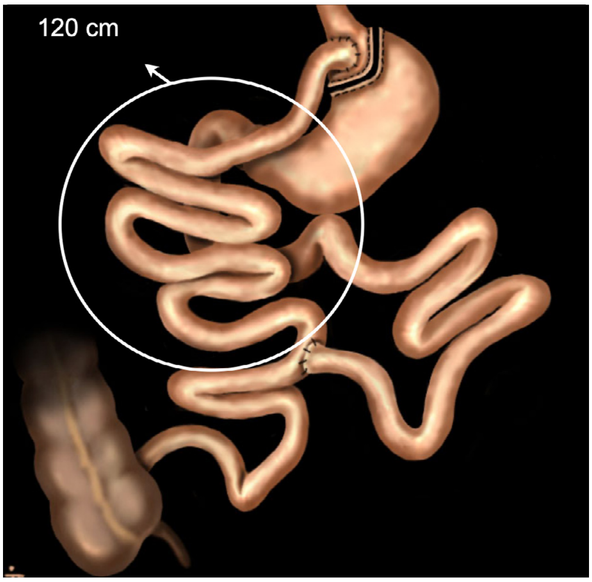

FIGURE — Roux-en-Y gastric bypass 120 cm

DISCUSSION

Metabolic syndrome

In 1988, Reaven[3] paid attention to the simultaneous occurrence of cardiovascular risk factors (dyslipidemia, hypertension and hyperglycemia) that occurred simultaneously in some patients, calling this association syndrome X, which is currently called metabolic syndrome (MS). The first concept that integrated this clinical condition was described by Jean Vague in 19564, who recognized the association between android obesity, diabetes, hyperlipidemia, and atherosclerosis as an entity. In current terms, MS is composed of some objectively measurable elements, such as hypertension, DM2, dyslipidemia, and obesity. In addition to these, there are non-cardiac factors, such as liver disease (including steatosis, alcoholic and non-alcoholic hepatitis), kidney disease, severe obesity, polycystic ovary syndrome, and obstructive sleep apnea.[2]

The diagnostic criteria for MS have changed in recent decades, but the most widely used definition comes from the latest International Diabetes Federation consensus: centripetal obesity; elevated triglycerides (TG) ≥150mg/dl; reduced HDL-cholesterol <40 mg/dl in men and <50 mg/dl in women or specific treatment for this dyslipidemia; high blood pressure ≥130/85 mmHg; Elevated fasting blood glucose ≥100 mg/dl or T2DM previously diagnosed. SM is defined when at least 3 of these components are present.[5]

The average prevalence of MS is 31%, and it has increased alarmingly due to the increase in the prevalence of obesity. MS is associated with a 2-fold increase in the risk of coronary heart disease and cerebrovascular disease and a 1.5-fold increase in the risk of all-cause mortality.[1]

Clinical interventions

To modify the course of MS and obesity, it is believed that lifestyle modifications play an important role in primary prevention. However, several studies have shown little relevance in reducing cardiovascular disease morbidity based solely on lifestyle changes, due to the questionable durability of patient adherence to such interventions, especially over time. Even though current anti-obesity strategies may not be feasible in the long term, weight reduction significantly decreases associated cardiovascular complications.[6]

Jensen et al.[7] have shown that reducing body weight by 3-5% can result in significant declines in cardiovascular events, while greater losses of 5-10% certainly lead to more benefits.[7] Recent advances have reported that not only is strict management of obesity beneficial, but also early detection and targeted improvement of other conditions, such as hypertension, dyslipidemia, and obstructive sleep apnea, are of equal importance in reducing obesity in decreasing cardiovascular events.[2]

Obesity seems to be multifactorial, so combinations of strategies and interventions are indicated for success in controlling the disease. There are currently 3 treatment modalities for obesity: lifestyle management (which individually has not shown good results in preventing cardiovascular disease), pharmacological options when interventions in lifestyle habits fail and, in more extreme cases, bariatric surgery.[2]

The role of bariatric surgery

Over the past decade, a number of clinical trials have shown that significant reduction in short- and long-term cardiovascular disease events can be achieved with bariatric surgery in up to 15% of obese patients.[8] However, because it is an invasive approach, it involves risks and costs, and is currently recommended for patients with severe obesity in whom conventional weight reduction strategies have failed.[2]

For 2 decades, bariatric surgery was performed only for indications specified by the 1991 National Health Institute consensus conference. The goal of the operation was weight loss, and patients had to have a BMI greater than 40 or greater than 35 and significant comorbidities to qualify. In 2015, the second consensus conference of the Diabetes Surgery Summit published guidelines that support the use of metabolic surgery and further expanded its indications for the treatment of type 2 diabetes mellitus in patients with a BMI between 30 and 34.9 if hyperglycemia is inadequately controlled by oral or injectable medications. The American Diabetes Association's 2018 diabetes treatment standards included this in the recommendations. Bariatric surgery used for the primary purpose of treating diabetes or metabolic syndrome is known as "metabolic surgery".[7]

Bariatric surgery has been shown to be a very effective and long-lasting method to induce weight loss in morbidly obese patients, and consequently improving comorbidities associated with obesity and reducing mortality from cardiovascular causes.[6] The most commonly performed bariatric procedures are laparoscopic Roux-en-Y gastric bypass (RYGB) - considered the gold standard procedure by many surgeons - and sleeve gastrectomy. Together, the 2 procedures constitute nearly 80% of all bariatric operations worldwide.[9,10]

RYGB is considered a mixed technique: the smaller stomach is connected directly to the jejunum, and the duodenum is diverted, significantly reducing the surface area for absorption by reducing the gastric volume itself, and excluding the duodenum and proximal jejunum from gastrointestinal transit. In contrast, GV involves an easier surgical technique that does not involve any digestive anastomosis, and is achieved by reducing the size of the stomach by removing 70-80% of its volume in the portion of great curvature, transforming it into a tube.[10,11]

The results presented by the Metabolic Syndrome are satisfactory. Bariatric surgery induces significant and long-lasting weight loss and improves MS in all its 3 components: hyperglycemia/T2DM, hypertension and dyslipidemia – all risk factors for cardiovascular diseases. Consequently, this risk is reduced after bariatric surgery.[12] There are 3 main reasons why RYGB induces weight loss, namely: the restrictive effect due to the small size of the gastric pouch, generating a feeling of early satiety; the incomplete absorption of calories and nutrients secondary to the exclusion of part of the digestive tract; and the accelerated transit to the final portions of the small intestine.[13]

T2DM and obesity often coexist – it is estimated that 85% of patients with T2DM are overweight or obese. For obese diabetic patients who fail in lifestyle management and medical therapy, bariatric surgery is the most effective treatment and can achieve long-term remission of 23% to 60% of patients, depending on the baseline severity and duration of their diabetes. Bariatric surgery demonstrated glucoregulatory effects, probably by neuroendocrine mechanisms, i.e., independent of weight loss. This mechanism is primarily mediated by 2 enteric hormones: glucagon-like peptide-1 and gastric inhibitor polypeptide. In addition, RYGB is considered a satiogenic-incretinic operation, as it stimulates hormones involved in weight loss and improvement of comorbidities, especially DM2.[14,15]

In recent years, the efficacy of bariatric surgery in the treatment of T2DM has been evaluated and compared to drug therapy (lifestyle change, weight management counseling, home blood glucose monitoring, and blood glucose control medications). All clinical trials (with 1 exception) demonstrated that the use of bariatric surgery was superior to drug therapy in achieving the pre-designated glycemic goal.[16]

The 2 most popular hypotheses on how RYGB improves T2DM are the anterior and posterior gut hypothesis. The anterior intestine study proposes that the exclusion of the intestine (duodenum and upper part of the jejunum) results in the inhibition of signals that induce DM2, responsible for insulin resistance. After it, the foregut is no longer stimulated by nutrients, leading to better glycemic control. The hindgut hypothesis proposes that the rapid release of partially digested nutrients into the distal gut leads to early secretion of glucagon-like peptide by the hindgut (lower part of the ileum), resulting in improved diabetic status.[17]

Another component of MS is arterial hypertension. It is known that there is a strong relationship between obesity and the development of chronic arterial hypertension. Weight loss, either by intensive medical lifestyle modification program or by bariatric surgery, improves obesity-related hypertension or contributes to its remission. A clinical trial conducted with 100 hypertensive patients (using 2 or more antihypertensive drugs) and obese patients (with BMI between 30 and 39.[9]) demonstrated that in 1 year bariatric surgery associated with medical therapy reduced the use of antihypertensive drugs by more than 30% and 46% of the patients had remission of the disease.[6]

Finally, the most common dyslipidemias found in obese people are hypertriglyceridemia, high LDL-cholesterol and decreased HDL-cholesterol values. Dyslipidemia associated with obesity is a well-established risk factor for cardiovascular disease. Clinical studies have shown improved lipid profiles after bariatric procedures, with RYGB being the most studied procedure.[18]

Hypovitaminosis after RYGB

Morbidly obese patients undergoing bariatric surgery are at high risk of developing micronutrient deficiencies due to extensive changes in the anatomy and physiology of the gastrointestinal tract.[19] In 2016, the American Society of Bariatric and Metabolic Surgery updated its nutritional guidelines for operated patients, where great variability in vitamin deficiencies was described, both pre- and postoperatively. The prevalence of preoperative vitamin deficiencies was then identified as 30% for vitamin B12 and 90% for vitamin D. Postoperative deficiencies had a prevalence of up to 20% for vitamin B12 and 100% for vitamin D.[20]

Notably, RYGB compromises the absorption of vitamin B12 because almost no gastric acid remains in the gastric pouch, and consequently the release of food-bound B12 is substantially decreased. In addition, the production of intrinsic factor - a parietal cell-derived protein necessary for intestinal absorption of B12 - is decreased or absent in the diverted stomach. In addition, B12 malabsorption is potentiated by the late introduction of pancreatic enzymes into the distal jejunum.[19]

As already described, vitamin D deficiency is the most common preoperative deficiency, and is related to insufficient sun exposure and reduced hepatic hydroxylation.[21] To prevent this post-surgical deficiency, oral vitamin D supplementation of 800 IU daily is generally recommended by the American Association of Clinical Endocrinologists and The Obesity Society.[22]

BMI

The accumulation of adipose tissue in the abdominal region is considered a risk factor for several morbidities and, in view of the relevance of visceral fat in the study of MS, several methods have been proposed to evaluate the distribution of body fat and quantification of intra-abdominal adiposity.

Among the least invasive, BMI stands out, which is a widely used international measure, developed in the nineteenth century, which, because it uses only weight and height, is easy, fast and reproducible. The calculation consists of dividing the mass in kilograms by the height squared in meters.[23]

However, there are several limitations of BMI, which include: non-differentiation of lean mass and fat mass, making it difficult to evaluate muscular patients; non-differentiation of visceral and subcutaneous fat; and having special tables for children and the elderly.[23]

The tool routinely used for its measurement is by calculating BMI, obtained by the formula where the individual's weight is divided by their height squared. This number can be classified into levels according to the World Health Organization classification shown in Table 1, presenting itself as a good measure widely used in epidemiological and clinical studies. Because it is easy to reproduce, it has significant prognostic and diagnostic value.

TABLE 1 — BMI classification in adults

BMI (Kg/m2)	Classification
18.5 - 24.9	Eutrophy (adequate)
25.0 - 29.9	Overweight
30.0 - 34.9	Obesity grade I
35.0 - 39.9	Obesity grade II
> 40.0	Obesity grade III

Adapted from the World Health Organization (WHO), 1995 and 1997

The American Society of Bariatric Surgery and the International Federation of Obesity Surgery sought to improve the classification of the obese population for adequate evaluation among them. Thus, they created a new one that has levels on which we based ourselves to classify the patients included in this study (Table 2).

TABLE 2 — Classification of obesity degree

BMI (Kg/m2)	Classification
27.0 - 29.9	Overweight
30.0 - 34.9	Obesity grade I
35.0 - 39.9	Obesity grade II
40.0 - 49.9	Obesity grade III
50.0 - 59.9	Superobesity
> 60	Super-superobesity

Adapted from the American Society of Bariatric Surgery and International Federation for the Surgery of Obesity

Waist circumference and waist-to-height ratio

Abdominal obesity is composed of subcutaneous and visceral fat, the latter presenting metabolic and functional characteristics that distinguish it from those located in other anatomical regions, representing greater predictive value for cardiovascular disease.

In view of the relevance of visceral fat in the study of metabolic syndrome, several methods have been proposed to evaluate the distribution of body fat and quantification of intra-abdominal adiposity. There are a variety of techniques for assessing body composition, such as anthropometric measurements (waist circumference, waist-to-hip ratio, waist-to-height ratio, taper index, and sagittal diameter) and imaging measurements (computed tomography, magnetic resonance imaging, and ultrasonography).

Hwaung, et al.[24,] Burton[25], and Nevill et al.[26] concluded that waist circumference adjusted for height (known as waist circumference index) is higher than BMI in its association with body fat. This conclusion contrasts with the recent IAC and ICCR (International Atherosclerosis Society and International Chair On Cardiometabolic Risk) consensus report on visceral obesity, which argued that waist circumference thresholds alone are adequate for assessment of abdominal obesity in clinical practice.[27,28]

There is an unmet need to promote a consistent and universal public health message that visceral/central/abdominal obesity is associated with adverse health outcomes.[29] We have advocated the use of the waist-to-height ratio (WHtR) for nearly 25 years as an adjunct to BMI, because it is a better predictor for central obesity as well as a superior predictor for cardiovascular risk factors.[27] But, is the waist circumference index higher than the WHtR in this aspect?

The National Institute for Health and Care Excellence has recognized the value of WHtR as an indicator of early health risk. Recent data from the UK can be used to explore whether the WHtR-based classification identifies more adults at cardiometabolic risk than the BMI and waist circumference-based 'matrix' currently used for screening. Data from the Health Survey for England used 4112 adults aged 18 years and older to identify the cardiometabolic risk indicated by elevated glycated Hb, dyslipidemia, and hypertension. HbA1c, total/HDL cholesterol, and systolic blood pressure were more strongly associated with WHtR than the "matrix". The WHtR $^{0.5}$ cutoff at initial screening translates into a simple message: "your waist should be less than half your height." This allows individuals to be aware of their health risks.[27]

WHtR is a simple anthropometric predictor for central body fat because it is easy to use from the point of view of health education. WHtR value > $^{0.5}$ was proposed as the first-level indicator of health risk. The first objective of this study was to compare WHtR with BMI-based values in its prediction of body fat percentage (BF%).[30] BMI is the most widely used anthropometric index to define the status of weight in relation to height and its units are in kg/m2.[31] Despite the strong correlation between body fat and BMI, BMI cannot distinguish between lean and fat mass.[30,31]

CONCLUSION

The use of Roux-en-Y gastric bypass in the treatment of major obesity improves both the metabolic syndrome, waist-to-height ratio and the indicators of the cardiometabolic risk profile that the patient initially presents, being more significant in the medium term.

Authors' contributions

Andressa Bressan Malafaia - Conceptualization
Fernando Issamu Tabushi - Research
Ronaldo Mafia Cuenca - Methodology
Timoteo Abrantes de Lacerda Almeida - Writing (proofreading and editing)
Jorge Alberto Langbeck Ohana - Writing (original draft)
Paulo Afonso Nunes Nassif - Supervision

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