

Assessment of two different diagnostic guidelines criteria (National Cholesterol Education Adult Treatment Panel III [ATP III] and International Diabetes Federation [IDF]) for the evaluation of metabolic syndrome remission in a longitudinal cohort of patients undergoing Roux-en-Y gastric bypass

Donají Rodríguez-Ortiz, MD,^a Azucena Reyes-Pérez, MD,^a Pablo León, MD,^a Hugo Sánchez, MD,^a Maureen Mosti, RN, CBN,^a Carlos A. Aguilar-Salinas, MD, PhD,^b David Velázquez-Fernández, MD, MSc, PhD,^a and Miguel F. Herrera, MD, PhD,^a México D.F., México

Background. Bariatric surgery has proven to provide durable weight loss and control of comorbid conditions, including the metabolic syndrome (MS). Existing definitions of MS have caused substantial confusion regarding their concordance for identifying the same individuals. The aim of this study was to assess the value of 2 different diagnostic guidelines criteria (National Cholesterol Education Adult Treatment Panel III [ATP III] and International Diabetes Federation [IDF]) for the evaluation of remission of MS after Roux-en-Y gastric bypass (RYGB).

Patients and methods. A cohort of 381 patients who underwent a primary RYGB, satisfied the criteria for MS, and had at least one postoperative visit were selected. Weight loss and MS remission were analyzed 6 and 12 months after surgery by ATP III and IDF criteria.

Results. Before surgery, 381 (48.9%) and 354 (45.4%) patients fulfilled the criteria for MS according to the ATP III and IDF, respectively. According to the ATP III definition, remission of MS after bariatric surgery occurred in 209 of 239 (87.4%) and 98/102 (96.1%) patients at 6 and 12 months, respectively. According to the IDF definition, this occurred in 180 of 232 (77.6%) and 54 of 64 (84.4%) at the same time periods. On the basis of different percentage of excess body weight loss cut-off values, the area under the curve in receiver operating characteristic analysis at 12 months was slightly better for ATP III (0.77) than IDF criteria (0.68) for remission of MS.

Conclusions. With the use of the IDF definition, the remission rate of MS was 10% more rigorous than with use of the ATP-III criteria. This feature is attributable to a greater discrimination of patients with high blood pressure, glycemia, and dyslipidemia. The IDF criteria seem more accurate to evaluate MS remission. (Surgery 2015;■:■-■.)

From the Center for Nutrition, Obesity and Metabolic Disorders,^a The American British Cowdray Medical Center; and Department of Endocrinology and Metabolism,^b Instituto Nacional de la Nutrición, Salvador Zubirán, México D.F., México

Accepted for publication November 21, 2015.

Reprint requests: Miguel F. Herrera, MD, PhD, Center for Nutrition, Obesity and Metabolic Disorders, The American British Cowdray Medical Center, México D.F., México. E-mail: miguelfherrera@gmail.com.

0039-6060/\$ - see front matter

© 2015 Elsevier Inc. All rights reserved.

<http://dx.doi.org/10.1016/j.surg.2015.11.015>

OBESITY IS A SYSTEMIC, CHRONIC, AND MULTIFACTORIAL DISEASE.¹ According to the World Health Organization, the frequency of obesity has almost doubled since 1980.² In Mexico, its prevalence has increased dramatically in the past decades. Among the members of the Organization for Economic Cooperation and Development, Mexico is the

Table I. MS criteria based on ATP III and IDF criteria

	<i>Diagnosis of MS by ATP III criteria (≥3 of the following criteria)</i>	<i>Diagnosis of MS by IDF criteria (Abnormal waist plus any of the remaining factors)</i>
Waist circumference	>102 cm for males >88 cm for females	≥90 cm in males ≥80 cm in females
Triglycerides	>150 mg/dL	≥150 mg/dL or with specific treatment
HDL cholesterol	<40 mg/dL for males <50 mg/dL for females	<40 mg/dL in males <50 mg/dL in females or with specific treatment
Blood pressure	≥130/85 mm Hg	≥130/85 mm Hg or specific treatment for previously diagnosed arterial hypertension
Fasting plasma glucose	≥100 mg/dL	≥100 mg/dL or previously diagnosed T2D

ATP III, National Cholesterol Education Adult Treatment Panel; HDL, high-density lipoprotein; IDF, International Diabetes Federation; MS, metabolic syndrome; T2D, type 2 diabetes.

second country, after the United States, with a greater prevalence of obesity.³

The intra-abdominal and visceral adipose tissues are metabolically hyperactive and linked with the pathogenesis of insulin resistance, hypertriglyceridemia, and low levels of high-density lipoprotein (HDL) cholesterol.⁴ There is a well-established relationship between the deposition of abdominal fat and the development of metabolic syndrome (MS).^{5,6} This term is a group of interconnected components that increase the risk for having cardiovascular events and type 2 diabetes (T2D), which are currently the main causes of mortality worldwide.⁷

Several organizations have proposed different diagnostic criteria, causing substantial confusion regarding their concordance for identifying the same individuals.⁸ Visceral adiposity, hypertriglyceridemia, arterial hypertension, hyperglycemia, and low HDL cholesterol levels are the traits considered in the most-used MS diagnostic criteria. Although all definitions are based on similar principles, cutoff values and some diagnostic criteria differ between them. Two of the definitions most commonly used are the ones proposed by the National Cholesterol Education Adult Treatment Panel III (ATP III)⁹ and by the International Diabetes Federation (IDF).¹⁰ In contrast with the ATP III-based MS definition, the IDF criteria require an abnormal waist circumference to make the diagnosis, include the application of different cut-off values for waist circumference according to the ancestral origin of the population, and take into consideration the specific treatment for each MS component.¹¹

Bariatric surgery has proven to induce long-lasting weight loss and control of comorbid conditions, including the traits of MS.¹² The aim of this study was to assess the value of 2 different diagnostic guidelines criteria (ATP III and IDF) for the evaluation of MS remission in a longitudinal cohort of obese patients undergoing a Roux-en-Y gastric bypass (RYGB).

PATIENTS AND METHODS

A review of our prospectively constructed database was performed. A total of 779 patients who underwent RYGB between 2004 and 2013 were scrutinized. All patients who fulfilled the following 3 criteria were included in this study: (1) A primary RYGB, (2) MS criteria according to ATP III or IDF criteria, and (3) a minimum of 1 follow-up visit within the first year after RYGB. Data for the analysis were obtained immediately before surgery and at 6 and 12 months of follow-up. A range plus/minus 3 months was allowed in all time periods. The protocol was executed in accordance with the Helsinki Declaration and was approved by the Ethics Committee of the American British Cowdray Medical Center.

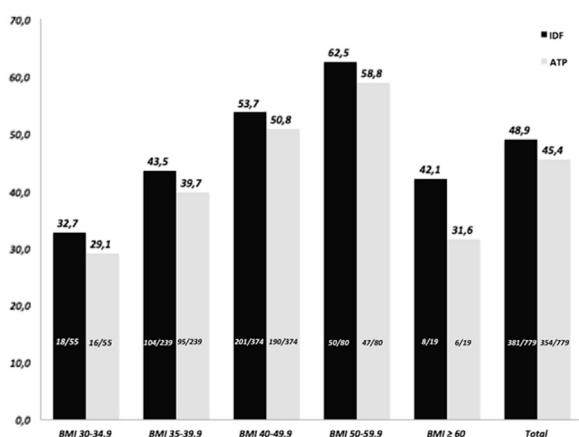
According to the ATP II definition, MS was determined with the presence of 3 or more diagnostic criteria, whereas for the IDF criteria, MS was diagnosed when patients displayed 2 or more factors in addition to central obesity (defined as an abnormal waist circumference). Diagnostic criteria for MS according to both definitions are shown in [Table I](#).

Remission of MS was considered as follows: fewer than 3 criteria for the ATP III definition;

Table II. Demographic information of the included patients based on MS criteria groups

	Diagnosis of MS by ATP III (n = 354)	Diagnosis of MS by IDF (n = 381)
Sex, male/female	181/173	190/191
Age, mean ± SD	40.9 ± 11.3	40.9 ± 11.3
BMI, mean ± SD	43.2 ± 6.3	43.2 ± 6.4
Abnormal waist circumference, n	355	374

ATP III, National Cholesterol Education Adult Treatment Panel; BMI, body mass index; IDF, International Diabetes Federation; MS, metabolic syndrome; SD, standard deviation; T2D, type 2 diabetes.

**Fig 1.** Prevalence of MS based on the BMI before bariatric surgery.

and the normalization of waist circumference or abnormal waist circumference plus one additional criterion for the IDF criteria. Weight loss and remission of MS were evaluated at 6 and 12 months after RYGB. Excess body weight loss (EBWL) was calculated as follows:

$$EBWL = \frac{(\text{Weight at Surgery} - \text{Weight at 6 or 12 months})}{(\text{Weight at Surgery} - \text{Ideal Body Weight})}$$

All biochemical and laboratory variables were measured at the central laboratory of the American British Cowdray Medical Center with commercially available reagents. The laboratory is certified by the American College of Pathologists and the ISO 9001–2000.

Statistical analysis. Microsoft Excel (Redmond, WA) and IBM SPSS Statistics version 21.0 (IBM, Armonk, NY) were used for statistical analysis. Data were expressed as mean ± standard deviation whenever a normal distribution was determined. Univariate analysis was used for individual variables

Table III. Preoperative distribution of the number of MS criteria according to ATP III and IDF

	ATP III		IDF*	
	n	%	n	%
3 criteria for MS	201	56.8	172	45.1
4 criteria for MS	112	31.6	147	38.6
5 criteria for MS	41	11.6	62	16.3
Total patients	354	100	381	100

*All patients had an abnormal abdominal circumference plus 2, 3, or 4 additional criteria Kappa = 0.58, $P < .0001$.

ATP III, National Cholesterol Education Adult Treatment Panel; IDF, International Diabetes Federation; MS, metabolic syndrome.

depending on the intrinsic variable scaling, whereas bivariate analysis was performed to assess potential statistical associations or correlations. The t test and analysis of variance were used to analyze continuous variables. For categorical variables, $R \times C$ tables were used with the chi-square and Fisher exact test, whereas Kendall's tau was used for ordinal variables in all statistical contrasts. Parametric and nonparametric correlations were performed through the use of Pearson's, Kendall's tau-b for concordance paired values and Spearman's tests.

RESULTS

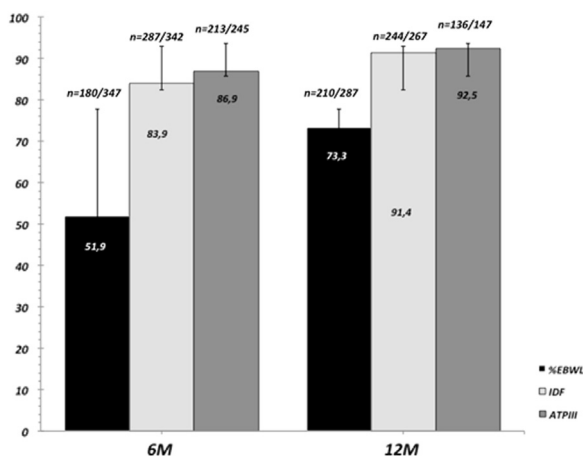
From the 779 scrutinized patients, 381 fulfilled the inclusion conditions. All patients met the diagnostic criteria for MS according to ATP III and 354 according to the IDF. Clinical follow-up was 72.9% (278/381) at 6 months and 53.8% (205/381) at 12 months. Demographic information of each group is shown in Table II.

Before surgery, an abnormal waist circumference was found in 355 (94.9%) patients according to ATP III criterion, whereas it was abnormal in 374 (100%) according to the IDF and in 355 according to both. A total of 205 patients (53.8%) fulfilled diagnostic criteria for T2D, and 129 were on oral medication. Arterial hypertension had been documented in 222 patients (58.3%) and 158 were on treatment (62.9%). Hypertriglyceridemia was present in 238 (63.6%), but only 27 patients (11.3%) were treated with drug therapy and 260 (69.5%) patients had low levels of HDL cholesterol. Preoperative prevalence of MS according to the degree of obesity is shown in Fig 1. More than half of our cohort of patients had a body mass index (BMI) between 40 and 49.9 kg/m². The preoperative distribution of criteria according to each definition of MS is shown in Table III. Before surgery, the diagnosis of MS was established in 354 patients with the use of ATP III and in 381 with the

Table IV. Discordant cases with diagnosis of MS based on ATP III and IDF criteria before and 6 and 12 months after surgery

	Before surgery		6 mo		12 mo	
	ATP III n (%)	IDF n (%)	ATP III n (%)	IDF n (%)	ATP III n (%)	IDF n (%)
Hypertension	7 (25.9)	21 (77.8)	2 (9.5)	15 (71.4)	0	1 (20)
Hyperglycemia	3 (11.1)	19 (70.4)	3 (14.3)	9 (42.9)	1 (20)	2 (40)
Abnormal waist	27 (100)	27 (100)	7 (33.3)	21 (100)	0	2 (40)
Decreased HDL	10 (37)	10 (37)	16 (76.2)	16 (76.2)	1 (20)	1 (20)
Hypertriglyceridemia	4 (14.8)	6 (22.2)	8 (38.1)	8 (38.1)	1 (20)	1 (20)
Total of discordant cases	27		21		5	

ATP III, National Cholesterol Education Adult Treatment Panel; HDL, high-density lipoprotein; IDF, International Diabetes Federation.

**Fig 2.** Percentage of EBWL and MS remission frequency according to the ATP III and IDF criteria at 6 months and 1 year postoperatively.

use of IDF (discordant diagnosis was observed in 27 patients; 3.7%). Concordance for MS criteria between ATP III and IDF at basal time, 6 and 12 months postoperatively, is displayed in Table IV. As it can be observed, discordance is explained by the fact that IDF criteria were superior for categorizing patients with arterial hypertension, hyperglycemia, and dyslipidemia.

All patients included in our analysis underwent a primary RYGB. Major postoperative complications occurred in 9 patients (gastrointestinal bleeding requiring transfusion in 4, intra-abdominal bleeding requiring reoperation in 2, gastric leaks in 2, and acute renal insufficiency in 1). All complications resolved soon after surgery, and there were no subsequent complications or clinical conditions that may have affected the 6-month and 12-month analysis. Fig 2 shows the %EBWL mean \pm standard deviation and the percentage of remission of the MS at 6 and 12 months after RYGB. Observed trends for the %EBWL and

remission of MS persisted 6 and 12 months after surgery. The magnitude of %EBWL was associated with the percentage of remission of MS at 6 and 12 months regardless of the applied diagnostic criteria. On the basis of different %EBWL cut-off values, the area under the curve in the receiver operating characteristic analysis for MS remission at 6 and 12 months was slightly better for ATP III (0.77) than IDF criteria (0.69) (Fig 3). The best cut-off values of %EBWL for predicting MS remission at 6 months using ATP III criteria was a 48.3% (sensitivity = 70.3% and specificity = 47%) and 48.7% using IDF criteria (sensitivity = 58.2% and specificity = 54.5).

The relationship between the number of MS criteria and the %EBWL was specifically scrutinized by stratified analysis. Nevertheless, there was no association between the number of MS traits present before surgery and the amount of weight loss at 6 months and 1 year. In contrast, patients with less weight loss remained with a significantly greater number of MS traits at 6 and 12 months when both criteria were used (Fig 4). A more detailed assessment of the MS components and other metabolic traits throughout the investigated time periods (preoperatively and at 3, 6, 9, and 12 months postoperatively) is shown in Fig 5. RYGB exhibited a superior effect on the frequency of T2D remission and cholesterol levels but with a lesser impact on the waist circumference.

DISCUSSION

Obesity is associated with an increased risk for hypertension, hyperglycemia, respiratory problems, and cardiovascular disease.¹³ Central obesity is particularly associated with MS, with a resulting increase in the mortality rate caused by cardiovascular disease.¹⁴ Several definitions of MS have been suggested; the most frequently used are the definitions established by the ATP III and the IDF.^{8,11,15}

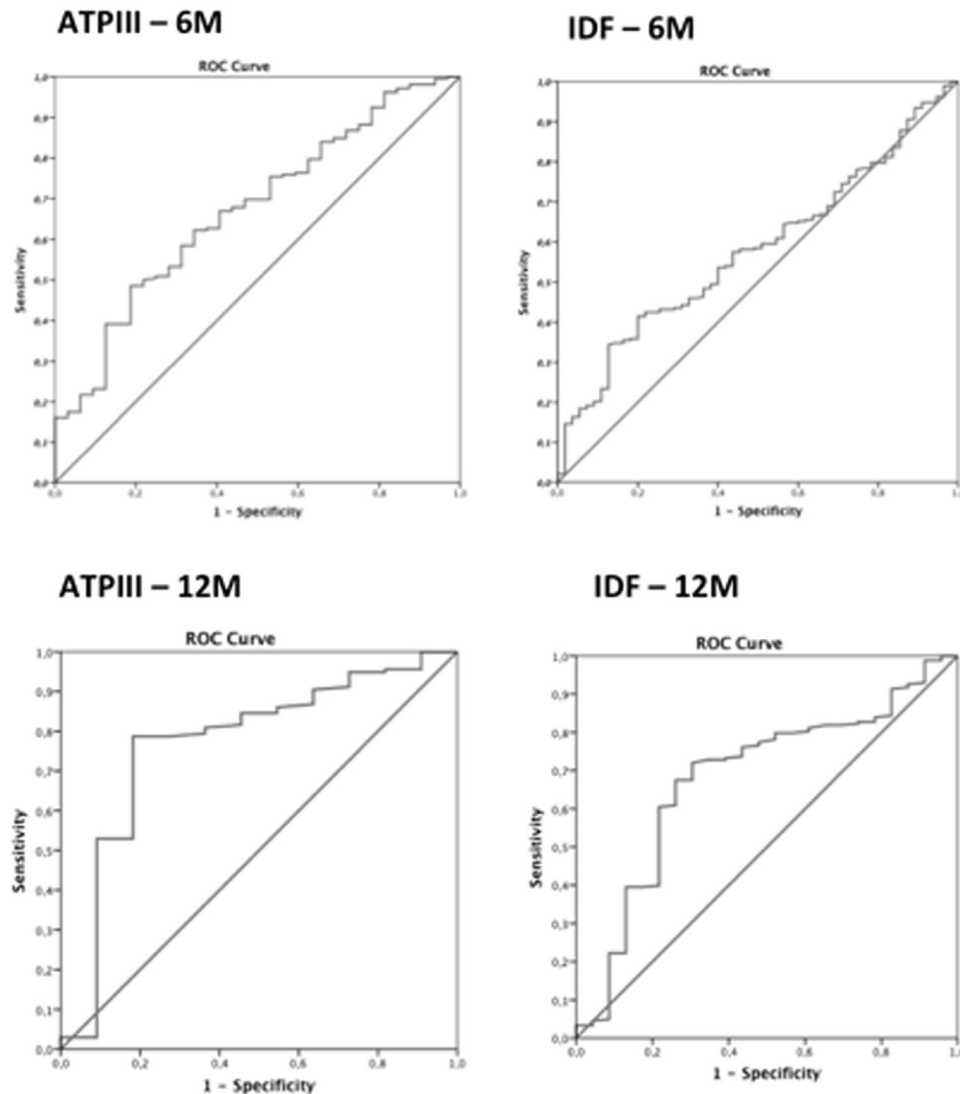


Fig 3. Receiver operating characteristic analysis estimating the %EBWL sensitivity and specificity for remission of MS by the use of ATP III and IDF criteria.

Bariatric surgery has proven to provide durable weight loss and control of comorbid conditions, including the MS. Buchwald et al.¹⁶ demonstrated that with a mean excess weight loss of 61.2%, T2D resolved in 76.8% and improved in 86% of the patients; hyperlipidemia improved in more than 70% of patients, and high blood pressure resolved in 61.7% and improved in 78.5% of patients. Several studies have demonstrated the remission of MS after bariatric surgery in different populations; however, it is difficult to compare the results because the lack of homogeneity in terms of the used criteria, the follow-up periods, and the operative procedures. In a study of 50 patients with MS and a BMI between 30 and 40 kg/m², Heffron et al.¹⁷ found a 65% remission rate 1 year after

laparoscopic adjustable gastric banding. Using the Assessment of Obesity-Related Comorbidities Scale, Inabnet et al.¹⁸ studied remission of MS after RYGB. The remission rate of T2D diabetes at 1 year was 62%. Rossi et al.¹⁹ reported 88.6% of MS remission 6 months after RYGB when the mean excess weight loss was 67.8%. Batsis et al.²⁰ evaluated the resolution of MS 3.4 years after bariatric surgery by using the American Heart Association/National Heart, Lung, and Blood Institute criteria. Remission of the syndrome occurred in 71% of operative patients with a mean excess weight loss of 59% ± 20. Finally, in a study similar to our study, Nora et al.²¹ found 69.7% remission of MS 1 year after surgery. In our patients, maximum weight loss 1 year after surgery was 72.1 ± 26.4%, and

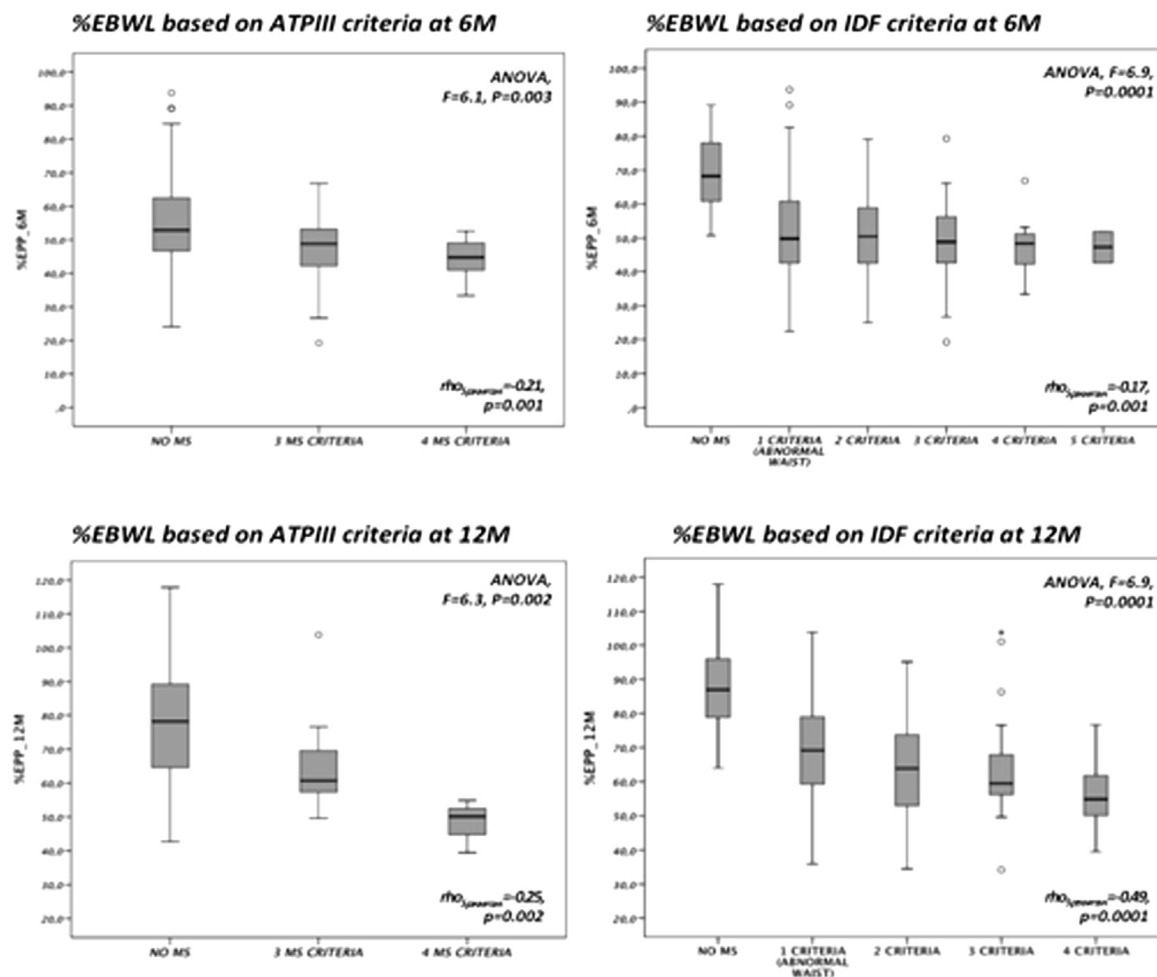


Fig 4. Boxplots showing the magnitude of %EBWL associated with the persistence of abnormal metabolic syndrome traits after 6 and 12 months.

remission of metabolic syndrome was 92.5% and 79.8%, respectively, when the ATP III and the IDF definitions were used.

The ATP III and the IDF definitions for MS have different cutoff diagnostic values. The IDF definition considers central obesity, measured by waist circumference, as the principal element for the diagnosis, whereas the ATP III definition assigns the same value to all components.⁹ Furthermore, the IDF definition establishes a cut-off value for waist circumference according to population ethnicity and also takes into consideration the treatment of each component of the MS.¹⁰ These diagnostic criteria do not identify the same individuals as affected. The use of the IDF definition results in a greater prevalence and the clinical profile of the affected subjects is less severe compared with the results derived from other diagnostic criteria.²² This result is mainly attributable to a lower waist circumference threshold,

especially in overweight individuals. Because our population was entirely composed of obese individuals with a large waist circumference, we explored whether the lack of agreement between diagnostic criteria persisted. As shown in Fig 1, the difference in the prevalence was small. This observation suggests that both criteria have a similar diagnostic performance in obese candidates for bariatric surgery.

The resolution of the MS could be used as an outcome to assess the metabolic effect of bariatric surgery. In our study, MS remission was greater when we used the ATP III compared with the IDF criteria at all time periods. This observation may be attributable to the fact that IDF considers abdominal obesity as a required abnormal trait to be corrected or, if it remains present, only one additional trait may persist. As a result, it will take a greater %EBWL and/or a longer time to achieve the remission with the IDF criteria. Thus,

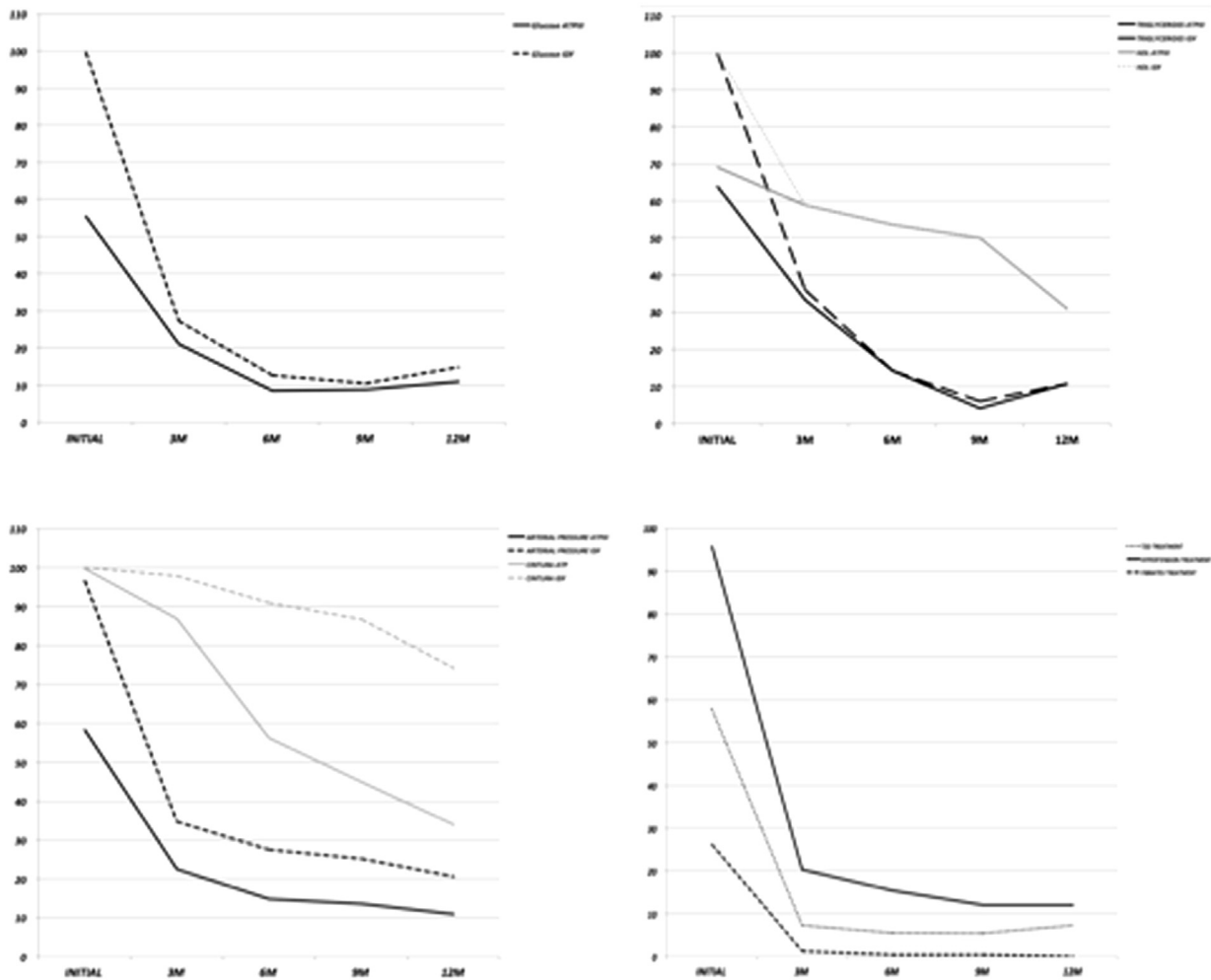


Fig 5. Prevalence of the different MS components before and after bariatric surgery.

the use of the IDF criteria as an outcome of bariatric surgery will have the opposite effect to that described when it is used as a diagnostic tool. When the IDF is used, it is difficult to compare remission of MS with other series, because it has been used very little in patients undergoing bariatric surgery.

Nora et al²¹ previously reported that the percentage of excess body mass index lost represents a good parameter for predicting MS resolution because they found that the area under the curve was between 0.75 and 0.85. In a similar fashion, Rossi et al²³ evaluated the correlation of different anthropometric indexes with MS remission. They found that the percentage of excess body mass index lost was the best indicator of MS remission in morbidly obese patients after RYGB. This fact might point out the relevance of bariatric surgery to provide not only durable weight loss but also

metabolic improvement. It was interesting to see in our results that %EBWL displayed a significant negative correlation with MS remission and the number of MS components ($P \leq .001$). This correlation was demonstrated for the 2 MS criteria used in this work (IDF and ATP III). This association points out the importance of the %EBWL on the number of criteria across all time points. An EBWL of 48% had the greatest sensitivity and specificity to predict MS remission when both criteria were used.

We recognize, among the limitations of our study, the number of patients who were lost to follow-up (27.1% at 6 months and 46.2% at 12 months); however, the relatively large sample size (greater than 205 patients) allowed us to have enough numbers to analyze our primary objective. It is important to mention that the initial profile (sex, age, fat mass, glycemia, blood pressure, HDL,

triglycerides, cholesterol, and low-density lipoprotein) of nonfollowed patients was similar to that of the subjects available for the 1-year analysis (separated Student *t* tests; $P \geq .318$ for all comparisons). Patients lost for follow-up had a BMI 3 kg/m^2 greater than followed patients (Student *t* test; $P = .001$).

In conclusion, our results showed evidence that the use of the IDF and the ATP III criteria in morbidly obese individuals renders contrasting conclusions depending on the purpose of the analysis. When these definitions are used to assess the outcome of bariatric surgery, the remission rate of MS with the IDF definition is roughly 10% more rigorous at 6 and 12 months compared with the ATP-III criteria. This is explained by the fact that IDF criteria were better to discriminate cases with high blood pressure, glycemia, and dyslipidemia. On the basis of these findings, we believe that the use of the IDF diagnostic criteria is more accurate and meticulous to assess MS remission in bariatric patients.

REFERENCES

- Ng M, Fleming T, Robinson M, et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2014;384:746-81.
- World Health Organization. Obesity and overweight; 2014. Available from: <http://www.who.int/mediacentre/factsheets/fs311/en/>. Accessed July 15, 2015.
- OECD. Health at a Glance 2013: OECD Indicators; 2014. Available from: http://dx.doi.org/10.1787/health_glance-2013-en. Accessed July 15, 2015.
- Despres JP, Lemieux I. Abdominal obesity and metabolic syndrome. *Nature* 2006;444:881-7.
- Bergman RN, Kim SP, Hsu IR, et al. Abdominal obesity: role in the pathophysiology of metabolic disease and cardiovascular risk. *Am J Med* 2007;120:S3-8.
- Despres JP, Lemieux I, Bergeron J, et al. Abdominal obesity and the metabolic syndrome: contribution to global cardiometabolic risk. *Arterioscler Thromb Vasc Biol* 2008;28:1039-49.
- World Health Organization. The top ten causes of death. Fact Sheet N°310; 2014. Available from: <http://www.who.int/mediacentre/factsheets/fs310/en/>. Accessed July 15, 2015.
- Kassi E, Pervanidou P, Kaltsas G, Chrousos G. Metabolic syndrome: definitions and controversies. *BMC Med* 2011;9:48.
- Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA* 2001;285:2486-97.
- Alberti KG, Zimmet P, Shaw J. The metabolic syndrome—a new worldwide definition. *Lancet* 2005;366:1059-62.
- Alberti KG, Eckel RH, Grundy SM, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation* 2009;120:1640-5.
- Buchwald H, Estok R, Fährbach K, et al. Weight and type 2 diabetes after bariatric surgery: systematic review and meta-analysis. *Am J Med* 2009;122:248-56.
- Jacobs EJ, Newton CC, Wang Y, et al. Waist Circumference and All-Cause Mortality in a Large US Cohort. *Arch Intern Med* 2010;170:1293-301.
- Schuster J, Vogel P, Eckhardt C, Morelo SD. Applicability of the visceral adiposity index (VAI) in predicting components of metabolic syndrome in young adults. *Nutr Hosp* 2014;30:806-12.
- Pi-Sunyer X. The metabolic syndrome: How to approach differing definitions. *Med Clin North Am* 2007;91:1025-40.
- Buchwald H, Avidor Y, Braunwald E, et al. Bariatric Surgery. A Systematic Review and Meta-analysis. *JAMA* 2004;292:1724-37.
- Heffron SP, Singh A, ZagZag J, et al. Laparoscopic gastric banding resolves the metabolic syndrome and improves lipid profile over five years in obese patients with body mass index 30–40 kg/m^2 . *Atherosclerosis* 2014;237:183-90.
- Inabnet WB III, Winegar DA, Sherif B, Sarr MG. Early outcomes of bariatric surgery in patients with metabolic syndrome: an analysis of the bariatric outcomes longitudinal database. *J Am Coll Surg* 2012;214:550-6.
- Rossi M, Barretto Ferreira da Silva R, Chaves Alcántara G Jr, et al. Remission of metabolic syndrome: a study of 140 patients six months after Roux-en-Y gastric bypass. *Obes Surg* 2008;18:601-6.
- Batsis JA, Romero-Corral A, Collazo-Clavell ML, Sarr MG, Somers VK, Lopez-Jimenez F. The effect of bariatric surgery on the metabolic syndrome: a population-based, long-term controlled study. *Mayo Clin Proc* 2008;83:897-907.
- Nora M, Guimarães M, Almeida R, et al. Excess body mass index loss predicts metabolic syndrome remission after gastric bypass. *Diabetol Metab Syndr* 2014;6:1.
- Rojas R, Aguilar-Salinas CA, Jiménez-Corona A, et al. Metabolic syndrome in Mexican adults. Results from the National Health and Nutrition Survey 2006. *Salud Publica Mex* 2010;52(Suppl 1):S11-8.
- Rossi M, Serpa Neto A, Rossi FM, et al. Percentage of excess BMI lost correlates better with improvement of metabolic syndrome after Roux-en-Y gastric bypass in morbidly obese subjects: anthropometric indexes and gastric bypass. *Surg Obes Relat Dis* 2009;5:11-8.