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ORIGINAL ARTICLE

Long-term cardiometabolic results after bariatric surgery: Control of comorbidities, weight loss and regain at 5 years of follow-up

Resultados cardiometabólicos de largo plazo tras cirugía bariátrica: control de comorbilidades, pérdida y reganancia de peso a los 5 años de seguimiento

Fredy Orlando Mendivelso-Duarte, MD, MSc, FETP[1],
Ricardo Alberto Borda-Hernández, Lic, MStat[2]

1 Department of Surgery, Clínica Reina Sofía, Colsanitas, Bogotá, D.C., Colombia.
2 Department of Mathematics and Statistics, School of Sciences, Universidad El Bosque, Bogotá, D.C., Colombia.

Abstract

Introduction. Bariatric and metabolic surgery (BMS) has shown its efficacy in achieving short-term weight loss. However, there is limited evidence regarding long-term clinical and metabolic outcomes.

Methods. Retrospective longitudinal study with patients who underwent laparoscopic Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG) interventions at CBM in Bogotá, Colombia, between 2013 and 2021. Weight change, comorbidity control, and metabolic outcomes were collected at the onset, 3-, 6-, and 12-months post-surgery, and annually up to the fifth year. Comorbidity control rates were assessed using Kaplan-Meier test. A Cox proportional hazards model was used to evaluate the effect of covariates on weight regain.

Results. Of 1092 patients with BMS (71.4% SG and 28.6% RYGB), 67% were women, with a median age of 48 years, BMI 35.5 kg/m^2. After five years of follow-up, the control rate in diabetes mellitus was 65.5%, in hypertension 56.6%, and dyslipidemia 43.6%. The weight regain rate was 28% with no differences between SG vs RYGB (p=0.482). The mean time to nadir weight was 14 months. Age at the time of CBM was the best independent predictor of weight regain (HR=1.02, 95%CI: 1.01-1.04), but with a modest clinical effect.

Conclusion. BMS is safe and shows long-term benefits in weight loss and control of comorbidities in the Colombian population.

Keywords: morbid obesity; bariatric surgery; gastric bypass; vertical banded gastroplasty; weight loss; comorbidity.

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Corresponding author: Fredy Orlando Mendivelso-Duarte, Calle 127 # 20-78, Bogotá, D.C., Colombia. Tel.: 3043844102.
E-mail: fmendivelso@colsanitas.com
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Resumen

Introducción. La cirugía bariátrica y metabólica (CBM) es efectiva en lograr pérdida de peso a corto plazo. Sin embargo, existe evidencia limitada en desenlaces clínicos y metabólicos a largo plazo.

Métodos. Estudio longitudinal retrospectivo con pacientes llevados a baipás gástrico en Y de Roux (RYGB) o gastrectomía en manga (MG) por laparoscopia en Bogotá, D.C., Colombia, entre 2013 y 2021. El cambio de peso, control de comorbilidades y resultados metabólicos se recopilaron al inicio del estudio, 3, 6 y 12 meses después de cirugía, y anualmente hasta el quinto año. Las tasas de control de comorbilidades se evaluaron mediante la prueba Kaplan-Meier. Se utilizó un modelo de riesgos proporcionales de Cox para evaluar el efecto de covariables en la reganancia de peso.

Resultados. De 1092 pacientes con CBM (71,4 % MG y 28,6 % RYGB), 67 % eran mujeres, con mediana de edad 48 años e índice de masa corporal de 35,5 Kg/m^2. Después de cinco años de seguimiento, la tasa de control en diabetes mellitus fue 65,5 %, en hipertensión 56,6 % y en dislipidemia 43,6 %. La tasa de reganancia de peso fue 28 %, sin diferencias entre MG vs RYGB (p=0,482). El tiempo promedio hasta peso nadir fue 14 meses. La edad al momento de CBM fue el mejor predictor independiente de reganancia (HR=1,02, $IC_{95\%}$ 1,01-1,04), pero con efecto clínico modesto.

Conclusión. La CBM es segura y muestra beneficios a largo plazo en la pérdida de peso y control de comorbilidades en población colombiana.

Palabras clave: obesidad mórbida; cirugía bariátrica; derivación gástrica; gastroplastia vertical; pérdida de peso; comorbilidad.

Introduction

Obesity is a chronic and multi-causal metabolic disease that has currently reached epidemic proportions. It is characterized by an abnormal or excessive accumulation of fat, which is harmful to health [1-3]. Obesity is the main risk factor for generating disability and death from non-communicable diseases (NCD), such as ischemic heart disease, stroke, high blood pressure (HTN), cancer, chronic respiratory diseases, diabetes mellitus (DM) and chronic kidney disease. Recently, its direct effect on mortality from COVID-19 in all age groups was evident [4].

According to figures from the World Health Organization (WHO), since 1975 obesity has almost tripled worldwide. In 2016, 39% of adults ages 18 and older were overweight and 13% were obese. The WHO has projected by 2030 that 60% of the world's population, or 3.3 billion people, could be overweight (2.2 billion) or obese (1.1 billion) if trends continue [1]. The most recent National Survey of Nutritional Situation in Colombia reported that 37.8% of the country's adults were overweight, while 18.7% were obese. The high prevalence of overweight and obesity (56.5%) constitutes a public health problem [5].

Obesity management requires a multidisciplinary approach and has broader goals than just weight reduction. It includes the reduction of cardiovascular risk, a better state of health and quality of life with the prevention and control of comorbidities, pain management and psychosocial alterations, including affective and eating disorders, low self-esteem and alteration of body image [6].

Bariatric and metabolic surgery (BMS) is recommended for people with a body mass index (BMI) greater than 35 kg/m^2, regardless of the presence, absence or severity of comorbidities. BMS should be considered in people with metabolic disease and BMI of 30-34.9 kg/m^2. Short-term results of BMS consistently show safety and efficacy [7,8]. In recent publications, sleeve gastrectomy (SG) is the most common bariatric procedure worldwide (50.2%), followed by Roux-en-Y gastric bypass (RYGB) (36.9%) [9,10].

This study aimed to analyze the experience of a center of excellence (CE) in bariatric surgery in the city of Bogotá, Colombia, and determine its effectiveness up to 5 years after the procedure in the control of weight and comorbidities (HTN, DM, and dyslipidemia).

Methods

Design and participants

A retrospective longitudinal panel data study was carried out in an adult population with a clinical diagnosis of morbid obesity. The surgical interventions (SG and RYGB) were performed at the Center of Excellence Clínica Reina Sofía of Colsanitas, in the city of Bogotá, Colombia, between 2013 and 2021.

We worked with the entire population and included patients of both sexes with their first BMS intervention. Cases of revisional surgery, planned multivisceral resection, and disassociation from the insurance plan were excluded. Failure to attend post-surgical control and specialized medical follow-up to manage their comorbidities, as well as those who did not perform specific follow-up labs, were excluded from the analysis (Figure 1).

Variables and monitoring

Information on medical and surgical history, demographic data, anthropometric measurements, physiological variables, clinical laboratory results, and baseline physical examination were collected. The variables of weight change, comorbidity control (DM, HTN, and dyslipidemia) and metabolic outcomes (HbA1c, glucose and lipid profile) were collected at baseline, 3, 6, and 12 months after surgery and annually until the fifth year. No information on pharmacological treatments for comorbidities was recorded.

Outcomes in weight and control of comorbidities at the fifth year

Weight regain was defined as an increase in BMI > 5 from nadir weight (lowest weight in kilograms measured after surgery) [11-13]. DM control was established with HbA1c values = 6-6.4% [14,15]. Standardized control of blood pressure levels in obese patients was defined as systolic blood pressure (SBP) levels of 120-140 mmHg and diastolic blood pressure (DBP) of 80-89 mmHg [11]. Finally, dyslipidemia control was established with low-density cholesterol (LDL) values less

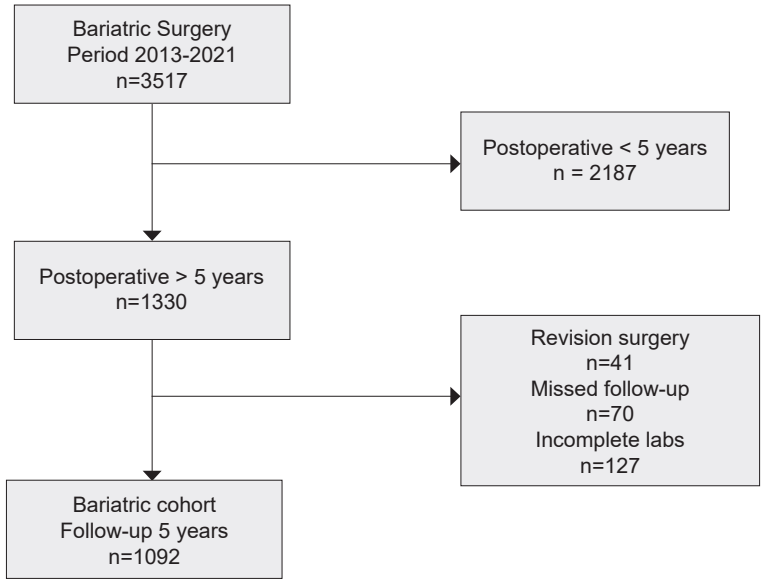

Figure 1. Patient selection flowchart.
Source: Authors' own elaboration.

than 100 mg/dl, and high-density cholesterol (HDL) greater than 60 mg/dl [7].

Statistical analysis

The quantitative variables were analyzed by calculating measures of frequency, central tendency and dispersion; categorical data, with absolute and relative frequencies. The assumptions of normal distribution in continuous variables were analyzed graphically and with the Shapiro-Wilk test. In the bivariate analysis, the Chi square statistics, Fisher's exact test and the Wilcoxon signed rank test were used. Analysis of variance (ANOVA) for panel data was implemented to identify differences in metabolic markers across follow-up. In the hypothesis contrast, a p-value less than 0.05 was considered as a criterion for rejecting the null hypothesis of the test statistic.

The time-to-event analysis (DM, HTN, and dyslipidemia control) was performed with the non-parametric Kaplan-Meier estimator. Time curves to comorbidity control were compared according to procedure type (SG and RYGB) using the log-rank test. The cumulative risk function in the control of comorbidities (cumulative incidence rate) was calculated by the maximum likelihood method and the Nelson-Aalen estimator. Finally, to identify the effect of covariates of clinical and surgical importance on weight regain evaluated in the fifth year, semiparametric Cox proportional hazards models (univariate and multivariate) were implemented. The risk estimator was reported as Hazard Ratio (HR) for each covariate in the model with its respective 95% confidence interval (95%CI) and p-value. In the fit of the best Cox model, the assumptions of proportionality of risks for continuous covariates (Schoenfeld residuals) and linearity in logarithms (Martingale and Dfbeta residuals) were evaluated. The data set was analyzed with the R programming language version 4.2.

Results

Of 1092 participants, 780 underwent SG (71.4%) and 312 RYGB (28.6%) as their first bariatric procedure. The highest frequency of BMS was performed in women (67%) and in young adults aged 18 to 64 years (92.0%). Among the most relevant presurgical conditions, the median age of the patients included in the study was 48 years (range: 40 - 57). Similarly, the BMI was 35.6 Kg/m^2 (range: 34.1 - 40.6), SBP 124 mmHg (range: 113 - 133), LDL 91.98 mg/dl (range: 66. 7 - 119.4), HDL 45.24 mg/dl (range: 38.3 - 54.5), blood glucose of 98.4 mg/dl (range: 89.6 - 120.9) and glycosylated hemoglobin (HbA1c) in the subset of patients with DM (n=316) was 8.7% (range 7.9 - 9.4%).

History of active tobacco and alcohol consumption was less than 4% and 1%, respectively; 92.8% of the patients had a diagnosis and received specialized treatment for at least one chronic condition, among which dyslipidemia (52.1%), sleep apnea-hypopnea syndrome (OSAS, 52.2%), HTN (42.2%), DM (28.9%) and gastroesophageal reflux disease (GERD, 25.4%) were prominent. There were no deaths during the BMS procedures or in the 5 years of follow-up (Table 1).

The change in weight and BMI indicators during the postsurgical period at months 12, 36 and 60 showed a significant decrease for each time point compared to the baseline measurement. Likewise, the physiological and laboratory variables presented values with a tendency towards normal clinical reference figures (Table 2). The median weight before BMS was 96 kg (range: 88.8 - 102.3) and in the fifth year it decreased to 81 kg (range: 77 - 90). The BMI registered the same behavior, with a change from a median of 35.5 Kg/m^2 (range: 34.1 - 40.6) to 30.9 Kg/m^2 (28.7 - 35.2) (Figure 2). The median nadir weight was 72.2 kg (range: 63.7 - 73.7) and the average time to reach the nadir was 14 months. The percentage of patients with weight gain evaluated in the fifth year of follow-up was 28.1%.

Control of all three comorbid conditions assessed in the study was significantly greater five years after BMS versus baseline ($p<0.001$) (Table 2). Before surgery, 14.8% of obese patients with HTN had blood pressure levels under control; after BMS and in the fifth year of follow-up, this percentage increased to 56.6%. In obese patients with DM, none met therapeutic control goals at the time of surgery; however, at the fifth year of

Table 1. Demographic characteristics and preoperative comorbidities of patients according to type of surgical procedure.

Characteristics	Sleeve gastrectomy		Roux-en-Y		Total	
	n=780 (%)		n=312 (%)		n=1092	
Gender	n	%	n	%	n	%
Female	511	46.8	221	20.2	732	67.0
Male	269	24.6	91	8.3	360	33.0
Age, years						
18 - 64	712	65.2	298	27.3	1010	92.5
65 or older	68	6.2	14	1.3	82	7.5
BMI, Kg/m^2						
30 - 34	184	16.4	166	15.2	350	32.0
35 - 39	322	29.5	129	11.8	451	41.3
40 - 44	241	22.1	14	1.3	255	23.3
45 or greater	33	3.0	3	0.3	35	3.2
Civil status						
Married	371	34.0	68	6.2	439	40.2
Single	228	20.9	63	5.8	291	26.6
No reported	134	12.3	121	11.1	255	23.3
Free union	11	1.0	46	4.2	57	5.2
Separated/Divorced	31	2.8	8	0.7	39	3.6
Widow/er	5	4.6	6	0.5	11	1.0
History						
Smoking	33	3,0 %	9	0,8 %	42	3,8 %
Alcohol	11	1,0 %	1	0,1 %	12	1,1 %
Comorbidities before surgery						
Dyslipidemia	402	36,8 %	167	15,3 %	569	52,1 %
OSAS	389	35,6 %	181	16,6 %	570	52,2 %
HTN	349	32,0 %	112	10,2 %	461	42,2 %
Diabetes	236	21,6 %	80	7,3 %	316	28,9 %
GERD	210	19,2 %	67	6,1 %	277	25,4 %
NAFL	147	13,5 %	56	5,1 %	203	18,6 %
COPD	150	13,7 %	35	3,2 %	185	16,9 %
Pre-Diabetes	132	12,1 %	43	3,9 %	175	16,0 %
Depression	37	3,4 %	14	1,3 %	51	4,7 %
DVT	12	1,1 %	3	0,3 %	15	1,4 %

BMI: body mass index; HTN: hipertension; OSAS: obstructive sleep apnea-hipopnea syndrome; GERD: gastroesophageal reflux disease; NAFL: non-alcoholic fatty liver; COPD: chronic obstructive pulmonary disease; DVT: deep venous thrombosis.
Source: Authors' own elaboration.

follow-up, 65.5% had control figures with HbA1c. Finally, 20.4% of obese patients with dyslipidemia had control figures at the time of surgery, and after the fifth year, the percentage of control in lipid profile increased to 43.6% (Figure 3). The median time until HTN control was 43 months (95% CI 42 - 45), in dyslipidemia 25 months (95% CI 15 - 27) and in DM 15 months (95% CI 9 - 42). When comparing the cumulative incidence rate curves in the control of comorbidities according to the type of BMS, significant differences were observed in the control of dyslipidemia in favor of patients operated on with SG (p=0.008). There was no difference by type of surgery in HTN and DM.

Table 2. Anthropometric changes and metabolic markers after 1, 3 and 5 years of follow-up.

Characteristics	Pre-surgical	Post-surgical					
		1 Year n=1092	p-value [a]	3 Years n=1092	p-value [b]	5 Years n=1092	p-value [c]
BMI (Kg/m^2)	35.5 [34.1-40.6]	27.4 [25.6-28.3]	< 0.001	30.2 [28.3-31.5]	< 0.001	30.9 [28.7-35.2]	< 0.001
Weight (Kg)	96 [88.8-102.3]	75.2 [66.4-76.8]	< 0.001	78 [74-88]	< 0.001	81 [77-90]	< 0.001
Systolic blood pressure (mmHg)	124 [113-123]	128 [124-133]	< 0.001	129 [124-134]	< 0.001	122 [116-129]	0.115
Diastolic blood pressure (mmHg)	89.4 [86.7-89.4]	80 [69-91]	< 0.001	65 [57-72.2]	< 0.001	75 [67-83]	< 0.001
Creatinine (mg/dl)	0.93 [0.81-1.1]	0.71 [0.63-0.82]	< 0.001	0.76 [0.66-0.9]	< 0.001	0.75 [0.66-0.86]	< 0.001
Fasting blood glucose (mg/dl)	98.4 [89.6-120.9]	88.6 [82.9-97.6]	< 0.001	91.3 [84.2-101.0]	< 0.001	85.9 [81.2-91.9]	< 0.001
HbA1c (%) *	8.7 [7.9-9.4]	6.4 [6.2-6.6]	< 0.001	6.5 [6.2-6.7]	< 0.001	6.5 [6.3-6.8]	< 0.001
Total cholesterol (mg/dl)	165.3 [138.9-195.2]	192.8 [165.5-220.6]	< 0.001	180.2 [158.7-203.7]	< 0.001	174.5 [150.5-201]	< 0.001
HDL cholesterol (mg/dl)	45.2 [38.3-54.5]	55.1 [45.8-64.9]	< 0.001	49.9 [41.5-59.8]	< 0.001	44.8 [37.4-53.6]	0.245
LDL cholesterol (mg/dl)	91.9 [66.7-119.4]	112.1 [99.9-137.6]	< 0.001	103.5 [84.1-124.7]	< 0.001	104 [86.1-127.3]	< 0.001
Triglycerides (mg/dl)	120.6 [90.9-165.7]	115.4 [87.9-157.1]	0.002	106 [79-151.7]	< 0.001	127.5 [94.6-188.8]	< 0.001
B12 vitamin (pg/ml)	534.8 [390-812.2]	497 [366-714.1]	< 0.001	563 [390-823.5]	0.266	487 [360-686.5]	< 0.001
25-Hydroxy-Vitamin D (ng/ml)	29 [23.4-35.8]	27.2 [21.8-33.9]	< 0.001	29 [23.4-35.8]	0.874	27.2 [21.8-33.9]	< 0.001

BMI: body mass index; HbA1c: glycosylated hemoglobin; HDL: high density colesterol; LDL: low density colesterol.
Data are shown as Median and Interquartile Range [IQR].
The p-value was calculated with the Wilcoxon signed rank test and the ANOVA test for repeated measures.
[a] Pre-surgical versus 1 year. [b] Pre-surgical versus 3 years. [c] Pre-surgical versus 5 years
* Only the test is included for the 316 diabetic patients
Source: Authors' own elaboration.

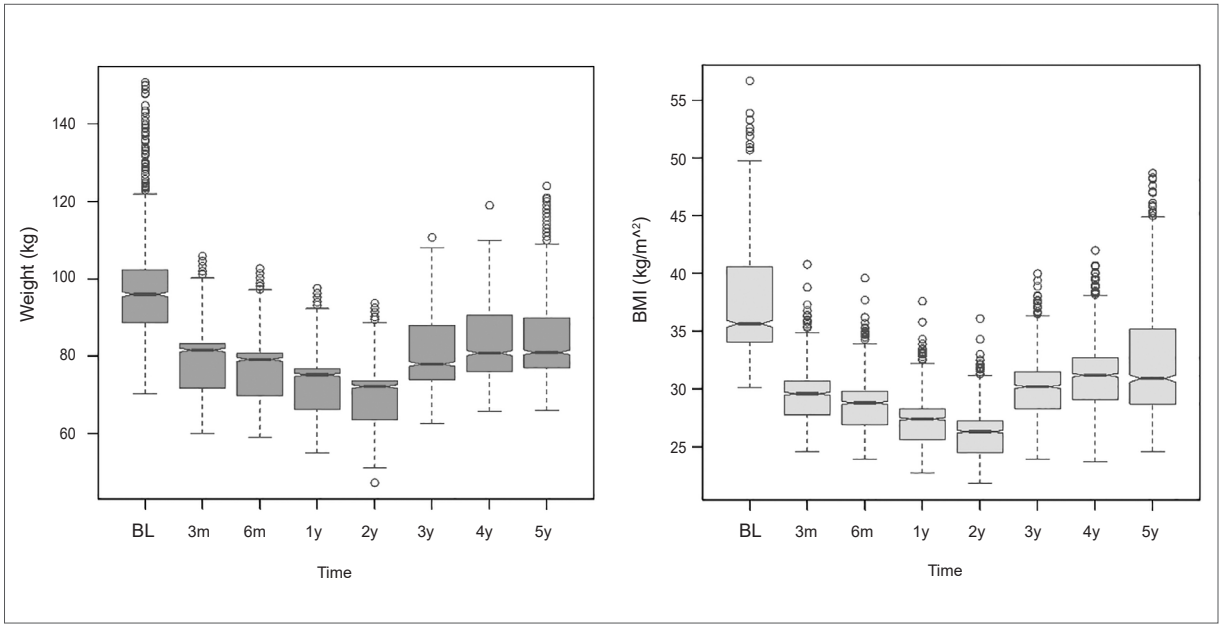

Figure 2. Changes in weight and BMI after BMS.
BL: Base Line. Months (m), Years (y).
Source: Authors' own elaboration.

The multivariate Cox regression model identified a set of covariates that increased the risk of weight gain in BMS patients. Age (HR= 1.02; 95% CI 1.01 - 1.04), alcohol consumption (HR= 2.81; 95% CI 0.77 - 10.21), depression (HR= 1.33; 95% CI 0.80 - 2.21), and dyslipidemia (HR= 1.20; 95% CI 0.93 - 1.55); however, only age was clinically and statistically significant (Figure 4).

Discussion

In this research we address several knowledge gaps on long-term weight change and gain and health outcomes after BMS in a Colombian Center of Excellence, highlighting standardized assessment and complete clinical follow-up. Long-term weight loss after BMS was similar to the results of several studies with five or more years of follow-up, which reported that this loss was maintained in more than 70% of patients [16].

High rates of control or compliance with the therapeutic goal were identified in the comorbidities with the highest cardiometabolic risk (HTN, DM, and dyslipidemia), most of which are evident from the first year of surgery. In the particular case of DM, a modifying effect on the course of the disease was observed objectively evaluated with HbA1c levels [12,17].

Although this study did not evaluate the influence of different pharmacological therapy regimens during the postoperative period, several authors report that among patients with DM and a BMI greater than 30 kg/m^2, for five-year results, BMS plus intensive medical therapy was more effective in reducing or, in some cases, resolving hyperglycemic states, compared to patients who only received conservative medical measures [15,17,18]. Schiavon and collaborators designed a randomized clinical trial (RCT) in

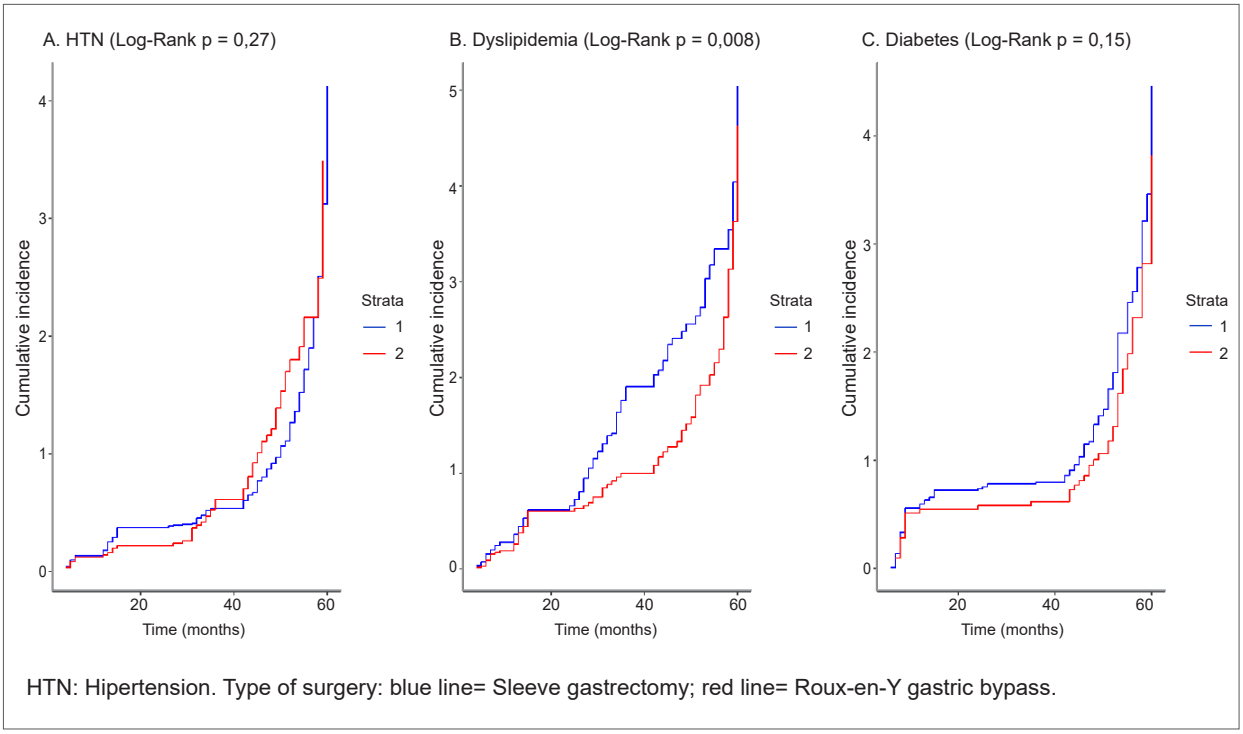

Figure 3. Five-year cumulative incidence rates in the control of comorbidities in patients with extreme obesity brought to BMS
HTN: Hipertension. Type of surgery: Blue= Sleeve gastrectomy; Red= Roux-en-Y gastric bypass.
Source: Authors' own elaboration.

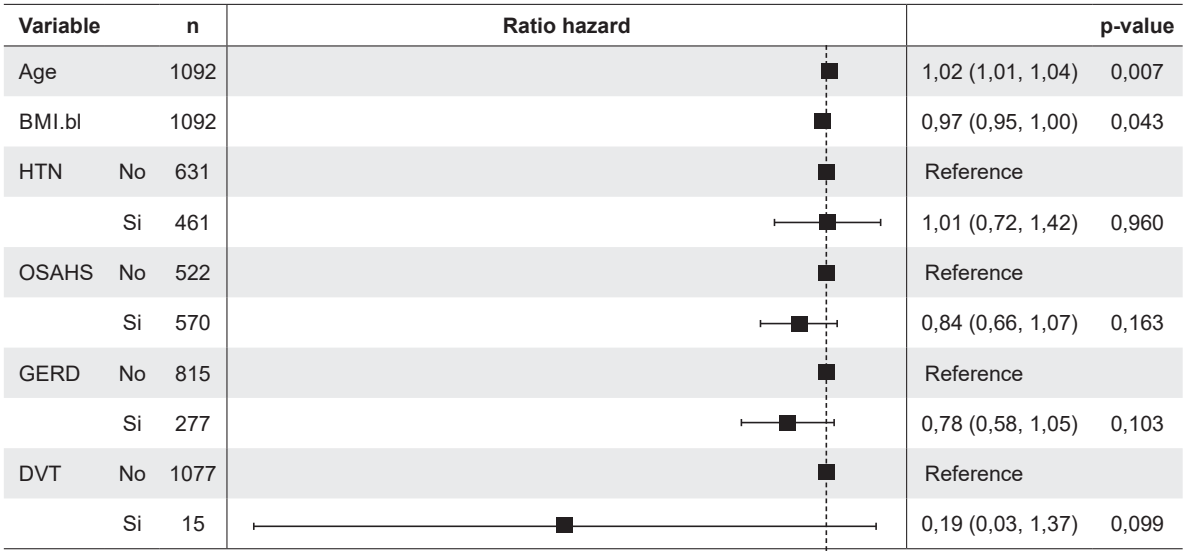

Figure 4. Covariates related to weight gain at the fifth year (Multivariate Cox Model).
BMI.bl: baseline body mass index (Kg/m2); HTN: Hipertension; OSAHS: Obstructive sleep apnea-hipopnea síndrome; GERD: gastroesophageal reflux síndrome; DVT: Deep venous thrombosis. Source: Authors' own elaboration.

patients with morbid obesity with the objective of evaluating the three-year effects of BMS on blood pressure (BP) compared to pharmacological treatment alone, and their conclusions indicate that BMS is an effective strategy for medium-term BP control and HTN remission, with less need for medications [11,19]. The results of the Colombian group, despite not being an RCT, confirm these findings, both in the medium and long-term [8,20,21].

Weight gain after BMS is becoming a common clinical problem due to the increase in the number of procedures performed. Consequently, its early identification and intervention are necessary to reduce the potential recurrence of comorbid conditions [22]. Although this study identified several baseline characteristics (e.g., age, BMI, depression, and alcohol consumption) associated with risk of weight gain, its contribution was not significant in the multivariate analysis and only the age variable can be considered as an independent predictor of recurrence within the Cox model, but with modest or almost no clinical significance. Despite this, our findings can be used to counsel patients regarding expected weight loss after BMS. The above may be a consequence of a certain degree of homogeneity between predictors and recruited patients; however, future efforts should consider combinations of clinically relevant variables identified here, pharmacological therapy, quality of life indicators, and functional status accompanied by metabolomic/genomic data [23].

Changes in the gut microbiome and systemic levels of amino acids and sugars are directly affected by anatomical changes in the gastrointestinal tract after BMS. Considering alterations in metabolomics and genomics may lead to better characterization and prediction of bariatric surgery outcomes and optimize more personalized treatment strategies [24]. Although BMS can be performed safely in all age groups with satisfactory postoperative weight loss, most authors recommend that BMS in obese patients with comorbidities should be offered earlier in life to allow patients to gain greater benefits.

Although the SG and RYGB procedures showed similar patterns of weight loss and remission of obesity-related disease at medium and long-term follow-up, the highly prevalent rates of GERD at baseline may limit the long-term success of this procedure. Patients who for this reason needed revision surgery were not included in the study; however, several authors recommend routine endoscopy during follow-up, given the high rates of esophagitis and Barrett's esophagus that can appear in these patients after BMS [25].

Among the limitations of this study, we highlight that it was not randomized, so direct comparisons cannot be made between the surgical procedures (SG-RYGB), since there may be inherent differences between these treatment groups. There was also no non-surgical control group, so the observed changes may not necessarily be entirely attributable to BMS. Measurements on quality of life were not included in the pre-surgery and during patient follow-up.

This study has many strengths, including the fact that it is a study with a large number of BMS cases, standardized and comprehensive data collection. There is excellent completeness of follow-up (especially for weight, blood pressure, HbA1c, and lipid profile over 5 years).

Conclusions

We found that among Colombian patients with morbid obesity and indication for BMS, the majority maintained a large part of their weight loss in the long term and achieved the therapeutic goal in the control of cardiometabolic risk comorbidities, especially in diabetes mellitus. Post-surgical follow-up should be carried out by interdisciplinary groups, in an exhaustive and long-term manner. The importance of optimizing patient follow-up is highlighted, particularly around 14 months when they reach nadir weight; This is a "critical" period or inflection point during which weight regain begins and can influence a decrease in quality of life and adherence to treatment recommendations.

Compliance with ethical standards

Informed consent: The research protocol was evaluated and approved by the institution's research and ethics committee (Resolution CEIFUS-08821). According to Resolution 008430 of 1993 of the Ministry of Health, this is a risk-free investigation. Taking into account that this is a retrospective investigation with analysis of administrative data from medical records, it was not necessary to complete informed consent.

Conflict of interest: The authors declare no conflicts of interest.

Use of artificial intelligence: No technologies assisted by Artificial Intelligence (AI) were used in the development of this research.

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Author's contributions

- Conception and design of the study: Fredy Orlando Mendivelso-Duarte, Ricardo Alberto Borda-Hernández.
- Acquisition of data: Fredy Orlando Mendivelso-Duarte, Ricardo Alberto Borda-Hernández.
- Literature review: Fredy Orlando Mendivelso-Duarte, Ricardo Alberto Borda-Hernández.
- Drafting the manuscript: Fredy Orlando Mendivelso-Duarte, Ricardo Alberto Borda-Hernández.
- Critical review and final approval: Fredy Orlando Mendivelso-Duarte, Ricardo Alberto Borda-Hernández.

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