

Factors associated with weight loss trajectory in adults after sleeve gastrectomy

Factores asociados a la trayectoria de pérdida de peso en adultos post gastrectomía vertical en manga

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ABSTRACT

Introduction: sleeve gastrectomy (SG) showed an increasing trend, as a primary bariatric procedure, within the last few years, based on outcomes in terms of weight loss and improvement or remission of the comorbidities. Multiple factors have been reported to influence weight loss trajectories after bariatric surgery (BS), therefore the aim of the study was to determine, if there are differences between weight loss trajectories based on time according to demographic and clinical factors at 3, 6 and 12-months post SG.

Method: retrospective review of 267 patients who underwent laparoscopic SG, between 2010 and 2019, assisted in a public hospital in the city of Buenos Aires, Argentina, were included. A two-factor repeated-measures analysis of variance (ANOVA) and a multiple linear regression analyses were performed.

Results: the global percent of weight loss (%EWL) at 3, 6, and 12 months postoperative (post-op) averaged 39,1 %, 60,3 %, and 73,4 % respectively and differences were significant according to time. Regarding differences between intergroup factors, at 12 months post-op, patients younger than 50 years, with an initial BMI lower than 50 kg/m², childhood-adolescence obesity onset, and not having T2DM, lost 15,2 %, 14,8 %, 13,9 %, and 9,5 %, more EWL, compared to the group with aged 50 and over initial BMI greater than or equal to 50 kg/m², having T2DM and adulthood obesity onset, respectively. All differences were significant.

Conclusion: detection of factors that act as barriers or facilitators to weight loss post-op may allow establishing more realistic objectives according to each patient's characteristics, and may optimize the post-op follow-ups.

KEYWORDS

Bariatric Surgery, Sleeve Gastrectomy, Percentage of Excess Weight Loss, Factors Associated, Postoperative.

RESUMEN

Introducción: la Gastrectomía Vertical en Manga (GVM), ha presentado una tendencia creciente en los últimos años como cirugía primaria, con base en la evidencia sobre los resultados en la pérdida de peso y en la mejoría o resolución de comorbilidades. Se han reportado múltiples factores influyentes en la trayectoria postoperatoria de la pérdida de peso, por lo tanto, el objetivo del estudio fue determinar si existen diferencias entre las trayectorias de pérdida de peso en el tiempo según factores demográficos y clínicos a los 3, 6 y 12 meses post GVM.

Método: se incluyeron retrospectivamente 267 pacientes sometidos a una GVM laparoscópica, entre 2010 y 2019, asistidos en un hospital público de la Ciudad de Buenos Aires, Argentina. Se realizó un análisis de la varianza (ANOVA) de 2 factores para medidas repetidas y un análisis de regresión lineal múltiple.

Resultados: el porcentaje de exceso de peso perdido (EPP) del total de la muestra, a los 3, 6, and 12 meses postoperatorio (POP) fue en promedio 39,1 %, 60,3 %, and 73,4 %, respectivamente, siendo significativas las diferencias. Con respecto a las diferencias según factores inter-grupo, a los 12 meses POP, los pacientes menores

de 50 años, con un índice de masa corporal menor a 50 kg/m², inicio de la obesidad en la niñez o adolescencia y sin diabetes tipo 2 (DM2), perdieron 15,2 %, 14,8 %, 13,9 %, y 9,5 % más de EPP, comparados con el grupo con 50 años o más, índice de masa corporal (IMC) inicial mayor o igual a 50 kg/m², con DM2 e inicio de obesidad en la adultez respectivamente. Todas las diferencias resultaron significativas.

Conclusión: la detección de factores que actúan como barreras o facilitadores de la pérdida de peso POP, permiten establecer objetivos más realistas y adaptados a las características de cada paciente, como así también optimizar el abordaje en el seguimiento POP.

PALABRAS CLAVE

Cirugía Bariátrica, Gastrectomía Vertical, Porcentaje de Exceso de Peso Perdido, Factores Asociados, Postoperatorio.

INTRODUCTION

Bariatric surgery (BS) has globally expanded due to the failure of nonsurgical treatments for morbid obesity (MO) or class III obesity. Treatment is also prescribed for patients undergoing class II obesity with comorbidities.^(1,2,3,4) In that sense, an increase in the BS effectiveness could be observed within sustained weight loss in the short term. Regarding the different surgical procedures, and despite Roux-en-Y Gastric Bypass (RYGB) was implemented as one of the main techniques, sleeve gastrectomy (SG), an entirely restrictive technique, subsequently showed an increasing trend within the last few years, currently outweighing the ratio procedure with regard to RYGB.^(4,5,6,7)

In 2012, in a position statement updated in 2017, the American Society for Metabolic, and Bariatric Surgery (ASMBS) agreed to acknowledge SG as the primary bariatric surgery, needless of a second procedure as it had been considered at baseline and is based on evidence which showed similarities as for weight loss, and the improvement or remission of the comorbidities between RYGB and SG.^(8,9,10,11) According to the 6th statement from the International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO), between 2016 and 2020, SG was implemented as primary surgery in 50,2 % of the reported subjects worldwide, followed by BGYR, implemented in 36,9 % of cases, from a total amount of 255,620 procedures.^(4,12)

In relation to the results on weight loss and in addition to the surgical technique, multiple factors have been reported to be influential in weight-loss trajectories after BS, both modifiable and non-modifiable. Age and preoperative body mass index (BMI), were shown as the factors with greater influence. Younger patients with lower preoperative BMI have shown greater weight loss.^(13,14,15,16,17,18,19) Results in relation to biological sex are controversial, although differences among men and women are not often found.^(13,14,15,16)

To report weight loss after bariatric surgery, the percentage of excess weight loss (%EWL) is a common metric, considering “a treatment success” in terms of weight loss, and aiming to obtain a greater or equal 50 % EWL between 12 – 18 months postoperative (post-op).^(1,2,3) That cut-off has shown an adequate specificity and sensibility. (20) An %EWL lower than 50 %, considered a “treatment failure”, is one of the main criteria to assess the conducting of a revision surgery.^(4,15,21)

Among the predictors of insufficient weight loss, comorbidities such as arterial hypertension (AHT) and type 2 diabetes mellitus (T2DM) have been reported, even though in some cases the effect disappears adjusting by age.^(14,15,17,18)

There is scarce research related to the topic performed in public hospitals in Latin America with the SG technique. In this sense, the objective of this study was to determine, in a group of patients with morbid obesity that undergo SG, if there are differences between weight loss trajectories based on time according to biological sex, obesity onset, age at surgery, baseline BMI, and the presence of T2DM, at 3, 6 and 12-months post-op.

METHOD

An observational, longitudinal, analytical, and retrospective study was conducted. Through an intentional non-probabilistic sampling, patients with severe obesity, between 21 and 70 years old, both sexes, with a follow-up for at least 12 months post-op, assisted in a public hospital in the city of Buenos Aires, Argentina, who underwent laparoscopic sleeve gastrectomy (LSG), between 2010 and 2019, were included. Patients with a severe psychiatric disorder, pregnancy or breastfeeding, diagnosis of binge eating disorder prior to surgery, oncological disease, Type 1 diabetes, and severe gastrointestinal issues, were excluded. Demographic, anthropometric, and clinical data pre and post-op were obtained from standardized medical and nutritional files. The files with incomplete information were also excluded.

The study variables included sex (female/male); age at the time of surgery (<50 years/≥50 years); Initial BMI (<50

kg/m²/ ≥50 kg/m²); obesity onset (childhood or adolescence/adulthood); T2DM (yes/no). The primary outcome was the percentage of excess weight loss (%EWL) at 3, 6, and 12 months post-op surgery, calculated as follows:

$$EWL\% = [(Initial\ weight) - (Postop\ weight)] / [(Initial\ weight) - (Ideal\ weight)] \times 100$$

Where the ideal weight is defined by the weight corresponding to a BMI of 25 kg/m² and initial BMI corresponds to preoperative BMI at the time of admission to the bariatric surgery program, that is, during the first evaluation. A multidisciplinary team (bariatric surgeons, registered dietitians, internists, and psychologists) evaluated all patients preoperatively and after the surgery at 3, 6, and 12 months. All patients underwent standard pre and post-op bariatric evaluation and received verbal and written dietary, exercise, and behavioral recommendations. Postoperatively, patients were advised to follow the same structured dietary intervention, follow-up schedule, and supplementation protocol; thereafter, were individualized according to specific needs. The surgeries were performed by the same team of trained surgeons.

Ethics

The study protocol was reviewed and approved by the institutional review board and was in accordance with the Declaration of Helsinki declaration.

Statistical Analyses and Sample Size Estimation

Categorical variables were expressed as absolute and relative frequencies and quantitative data were presented as mean and standard deviation (SD) since they met the assumption of normality. The assumption of normality was evaluated through statistical (Kolmogorov Smirnov test) and graphical (histogram, box-plot, Q-Q plot) methods. A two-factor repeated-measures analysis of variance (ANOVA) was used as a statistical method to detect any significant differences in the %EWL and sex, age categories, preoperative BMI, the onset of obesity, and T2DM, among the 3-time points of assessment (3,6 and 12 months post-op). Post hoc Bonferroni tests were performed for comparison of differences between and within these time points. Sphericity was assessed using Mauchly's test with a Greenhouse-Geisser correction being applied if sphericity was violated.

Further, multiple linear regression analyses was performed to determine if sex, age categories, initial BMI categories, T2DM, and obesity onset groups were significantly different concerning %EWL at 12 months after surgery. The single coefficients (β) in the linear regression model were used to describe the effects of the respective independent variables on the dependent variable, adjusted for all other variables in the model, the higher the single coefficient, the higher the association. A negative β implied that the corresponding independent variable was negatively. All analyses were performed in R Studio Version 4.0.5 (2021) and ANOVA profile graphs were made with SPSS version 24 software. Two-tailed P-values of 0,05 or less was considered statistically significant.

Regarding sample size, for the F statistic for repeated measures of 2 factors, with a maximum of 4 measurements in each subject, a power of 95 %, assuming the requirement of correction for lack of sphericity and an expected correlation between groups of at least 0,5, a minimum 235 participants were required.

RESULTS

A total of 267 patients (74 %; N=197 female) were included. Overall, the mean (SD) age was 43 (10,8) years at the time of surgery (range 20- 68 years). The mean preoperative BMI was 46,5 (SD 6,1) kg/m² (range 35,5- 65 kg/m²). The baseline characteristics of the patients are shown in Table 1. Overall, %EWL and the percentage of patients with EWL 50 % (considered "successful treatment"), progressively increased from 3 to 12 months. The greatest increase was observed between 3 and 6 months postop.

Trajectory of excess weight loss according to between-subjects factors (longitudinal analysis)

The post-op %EWL increased significantly over time, in all the comparisons between groups ($p < 0,001$). Regarding the effect of the interaction of time with age, biological sex, initial BMI, obesity onset, and T2DM, in all cases, was significant. In addition, the following factors were associated with more favorable weight trajectory groups: < 50 years ($F = 11,951$; $p < 0,001$); initial BMI < 50 kg/m², ($F = 3,491$; $p = 0,031$); childhood or adolescence obesity onset ($F = 7,093$; $p = 0,004$); and not having diabetes ($F = 18,9$; $p < 0,001$).

In the case of biological sex, %EWL, also increased significantly over time after surgery in both, males and females, but with similar magnitude, and no significant differences were observed ($F = 0,138$; $p = 0,787$).

Regarding %EWL values at different post-surgical times points, at 3 months, minimum and maximum were found between 32 and 42 % on average, at 6 months between 50,4 a 64,5 %, and at 12 months, between 62,3 a 77,8 %, according to the between-subject factors comparisons.

The highest %EWL at 12 months post-op was observed in the group of patients with initial BMI less than 50 kg/

m2 and the lowest, in those 50 years or older at the time of surgery.

The greatest magnitude of the difference in %EWL at 3 and 6 months post-op, was observed according to initial BMI, where participants with BMI less than 50 kg/m² lost 10,4 and 14,1 % more EWL respectively, compared to the group with a BMI greater than or equal to 50 kg/m². On the other hand, at 12 months post-op, the greatest magnitude of the difference in %EWL was observed according to age at the time of surgery. Participants under the age of 50 lost 15,2 % more EWL, compared to the group aged 50 and over.

In the same way, all independent variables were associated with the %EWL at the end of follow-up (12 months post-op), except biological sex, in the multiple regression analysis (Previous bivariate analysis showed the same results). The variables with the greatest magnitude of the effect, according to the value of the adjusted β coefficient, were the initial BMI, followed by T2DM. Those with BMI < 50 kg/m² prior to surgery were more likely to have 13,8 % more EWL on average and the group without T2DM, a 10,9 % more EWL, compared to those patients with an initial BMI of 50 kg/m² or more and those with DM2, respectively. These five parameters together explained 25 % of the variance of %EWL.

DISCUSSION

In this study, the global %EWL at 3, 6, and 12 months post-op averaged 39,1 %, 60,3 %, and 73,4 %, respectively. Such values can be found among the ranges reported by Oslan et al.⁽¹¹⁾, in a systematic review in which %EWL post-LSG was 31,51 % 3 months post-op (5 studies); between 49,4-67,3 % 6 months post-op (4 studies), and between 69,7-83 % 12 months post-op (5 studies), from a total amount of 254 participants.

Wozniowska 2020⁽²²⁾, reported a similar value in 555 participants 3 months post-op (36,2 %; 95 %CI 28-44); 6 months post-op resulted lower (51,4 %; 95 %CI 40,6 – 60,8), and 12 months post-op resulted higher (76,92; 95 %CI 62,2 – 90,9). Finally, Sanchez Santos et al.⁽²³⁾, reported a slightly lower value 12 months post LSG (70,6 %; SD 24,8).

On another note, the ratio of patients in this study who achieved the objective of 50 %EWL or higher has increased over time, achieving 17,2 % (n=46) 3 months post-op; 73 % (n=195) 6 months post-op, and 86,9 % (n=232) 12 months post-op. In the research conducted by Déusebio et al.⁽¹⁶⁾, the value 12 months post-op was a little lower (79,8 %) and included patients with LSG and RYGB independently of the surgical method.

Regarding the comparisons between groups, in our research %EWL greater average value 12 months post-op was found in the group of patients under 50 kg/m² (77,88 %EWL) initial BMI, and the lower value in subjects aged 50 or over at the moment of surgery (62,4 %EWL), from which similarities could be observed with published evidence, in which factors with greater influence in weight loss were age and preoperative BMI.^(13,17,19,24)

In our study, %EWL was also substantially higher within people under 50, compared to those patients aged 50 or more than 50, based on time (p<0,001). This may occur due to common physiological factors in elderly people, such as a decreased metabolic rate, and/or fat oxidation capacity, or a decreased lipolytic activity, in addition to greater limitations for dietary and physical activity adherence. Additionally, in animals conducting research, the absence or cutback of estrogen has been described to increase ghrelin levels, stimulating appetite to a larger extent.^(18,25,26,27,28) In relation to this, almost 30 % of the participants in this study aged 50 or over were postmenopausal women.

Conversely, Manning et al.⁽²⁴⁾, found an important interaction between time, age, and sex, observing a decrease in weight loss after 6 months (p= 0,012) and 12 months post-op (p=0,018), in the LSG group (n=432), in women aged over 50. Regarding Chang et al.⁽¹⁷⁾, age was one of the main predictors, and the chance of an EWL over 50 % 12 months post-op increased almost twice every additional 10 years of age, adjusted by other variables (OR = 1,82; 95 % CI 1, 27–2, 59, p < 0,001.)

In a sample with 252 subjects post SG, Fernandez Ananin et al.⁽²⁹⁾, reported a higher %EWL in subjects aged under 60 in comparison to subjects aged 60 or over 60 (63 vs 54 %, respectively; p<0,05) 12 months post-op, also reflecting age influence.

Concerning preoperative BMI, patients with BMI lower than 50 kg/m² showed in this study an increase in %EWL in comparison to the group with higher or equal 50 kg/m² BMI post-op, based on time. As regards the mean differences, the group of subjects with BMI > 50 kg/m² presented 14,8 %, lower EWL. In a meta-analysis, Livhits et al.⁽³⁰⁾, informed that 9 out of 11 studies found an inverse association between preoperative BMI and %EWL. Patients with BMI > 50 kg/m² (n= 908) presented an average of 10 % lower EWL (IC 95 % –3,7 %; –16,5 %; p= 0,002), in comparison to those who presented BMI < 50 kg/m² (n=2384) 12 months post-op. However, heterogeneity was significant among studies (I² 98 %; p<0,0001.) In accordance with this, Barzin et al.⁽³¹⁾, observed that a higher amount of patients with preoperative BMI under 50 kg/m² reached a higher or equal %EWL 1 year post-op (p= 0,017), adjusted by age, sex, surgical procedure (LSG vs RYGB), AHT y T2DM, unlike the results obtained from the systematic review of Kourounis et al.⁽³²⁾, in which preoperative BMI was not a predictor of %EWL post-op in 5 of 9 studies, where SG was included as one of the implemented techniques.

There were only 2 studies that presented an inverse correlation.

Regarding biological sex, in this study weight loss significance was not substantially different between men and women at 3, 6, and 12 months post-op ($p=0,787$). Similarly, in Ortega et al.⁽³³⁾, major differences were not found according to sex ($p=0,3$), adjusted by age, sex, surgical technique, and T2DM. Chang et al.⁽¹⁷⁾, did not find differences either, in a sample with 247 patients ($p=0,09$), composed of only 10,6 % men 12 months post-op. Finally, Nickel et al.⁽¹⁹⁾, observed a decreased weight loss in women 6 months post-op, and no differences were found 12 months post-op. The lack of differences may be due to potential bias in the analysis, owing to women being the majority of participants. The same distribution, with prevalence among women (between 70 % to 90 % of the sampling), was reported in most of the published studies.^(13,17,19,33)

Concerning to the presence of T2DM and its relation to weight loss, evidence is controversial. On one side, patients undergoing insulin secretion deficiency and higher glycemia have been reported to present an increased weight loss post BS, due to the anabolic role of insulin. The authors establish that what was previously mentioned is biologically plausible since a decreased insulin production would have a reduced anabolic effect post-op.^(34,35) On another note, in light of elevated circulating insulin levels, consistent with insulin resistance, insulin would perform its anabolic effect, facilitating lipogenesis and resulting in a decreased weight loss post-op. Another related factor may be an increase in calorie intake through “snacking” behavior, as prevention or treatment methods for hypoglycemia episodes, observed in light of the fast weight loss in patients who suffer from diabetes.⁽³⁶⁾ In accordance with the second hypothesis, patients who obtained 50 %EWL in a longer period, and subjects who never reached it, were noticed to present a high prevalence of worst glycemic profile.

In this study, a minor amount of weight loss in patients suffering from T2DM was found, and it was observed an increase in the differences as time progressed. At 12 months post-op, in patients who did not present T2DM, %EWL resulted an average of 76,8 % against 62,9 % in patients suffering from T2DM, with significant differences, similar to the deviation reported by Ortega et al.⁽³³⁾, (77 % vs 67 %; $p < 0,0001$.) The presence of T2DM was associated to %EWL, even adjusted by age, sex, obesity onset, and preoperative BMI. In a multicenter study conducted in 29 hospitals and including 1565 patients, Sanchez Santos et al.⁽²³⁾, obtained as a result of a multiple regression analysis that the chance of “treatment failure” (%EWL lower than 50 %) 12 months post-op increased in patients presenting an initial BMI higher than 50 kg/m², aged over 50, and suffering from T2DM, similarly to our study. Regarding research from Chang et al.⁽¹⁷⁾, T2DM was linked to a lower weight loss post-op, although the differences when adjusting for age were no longer significant.

Concerning obesity onset, we could observe that the group who developed obesity in adulthood showed a 9,5 %EWL decrease 12 months post-op, compared to those who developed obesity in childhood or adolescence, showing significant differences. With regard to the adjustment by age, sex, age, initial BMI, and T2DM, differences stayed significant. Moreover, it was found that 52 % of patients suffering from T2DM were 50 or over 50, and a higher number of subjects presented obesity onset in adulthood, with the possibility of a synergistic effect among the factors.

Other studies analyzed the effect of age at obesity onset and its connection with post BS weight loss and comorbidities development, considering that the greater the years of obesity evolution, baseline presented at childhood or adolescence, the greater comorbidities prevalence like T2DM may be expected.⁽¹⁹⁾ However, according to Wrosek et al.⁽³⁷⁾, the possibility of presenting T2DM was substantially lower in the group that developed obesity at childhood or adolescence (OR = 0,58, IC 95 % 0,38-0,83; $p=0,017$). Similarly, in the study of Nickel et al.⁽¹⁹⁾, age at obesity onset (childhood vs adolescence vs adulthood), adjusted by age, sex, and years of obesity progression were not linked to T2DM and AHT development ($p=0,91$.) Nevertheless, unlike our study, %EWL 12 months post-op was not linked to obesity onset, adjusted by age, sex, preoperative BMI ($p=0,068$), and, as in our sample, authors found a negative association between age and preoperative BMI ($\beta = -0,799$, $p = 0,006$ and $\beta = -1,2$, $p < 0,001$, respectively).

With regard to the limitations found in our study, non-probability sampling, data obtained in only one center, and retrospective design can be mentioned, even though the records used were designed to standardize data collection under a BS team protocol.

In addition, diet, “grazing” or “snacking” behaviors, and physical activity were not included in the analysis. In this sense, methods to estimate adherence rate present multiple biases mainly due to patients suffering from morbid obesity typically reporting fewer amounts of ingestion, which can be at least 40 %. The self-report from patients could not contribute to detecting differences within food intake and physical activity according to the %EWL achieved in other studies.^(18,38,39) It has also been found that many patients increase physical activity; however, most of them remain insufficiently active⁽¹⁵⁾, concurring with what was observed priori in our patients. Due to the difficulties mentioned before, this study was focused on non-modifiable factors that play a role in post BS weight loss. Another limitation found was the relatively short follow-up, mainly due to the lack of follow-ups during longer periods, a constraint reported by multiple BS teams in different countries.

This study was meant to provide information for the early detection of factors that may interfere with or slow

down weight loss; useful factors to establish more realistic and personalized objectives at patient admission to a BS program, optimizing the approach within the postsurgical follow-up in order to prevent weight regain, patient dissatisfaction, and comorbidities relapse

Future studies with more follow-up periods are suggested since complications such as weight regain tend to be detected at 2-3 years post-op,^(6,7,17) and also studies that analyze other key factors of obesity perpetuation and its complications like the environment and the patient's socio-economic vulnerability.^(40,41)

CONCLUSION

Over time, %EWL post-op increased, and it was substantially higher in patients under 50 years old; presenting preoperative BMI lower than 50 kg/m²; also presenting obesity onset in childhood-adolescence, and subjects who did not present T2DM at baseline. Differences according to sex were not observed. Most of the differences in %EWL 12 months post-op were found in comparison to age, followed by preoperative BMI and T2DM. Early detection of factors that act as a barrier or facilitators to weight loss post-op may allow establishing more realistic objectives according to each patient's characteristics, and also may optimize the post-op follow-ups.

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