IFSO

ORIGINAL CONTRIBUTIONS

Improvement in Muscle Strength and Metabolic Parameters Despite Muscle Mass Loss in the Initial Six Months After Bariatric Surgery

Roberto Viña Coral[1] · André Vicente Bigolin[1] · Mayara Christ Machry[1] · Rodrigo Koprovski Menguer[1] · Júlio Carlos Pereira-Lima[2] · Isabela Contin[2] · Paula Veigas Stock[2]

Abstract

Background An aggravation in pre-existing sarcopenia or the onset of sarcopenia may occur in the scenario of extensive and fast weight loss in the initial months following bariatric surgery. The accurate identification of sarcopenia criteria and its metabolic repercussions is vital for its correct management. The aim of this study is to evaluate the correlation between the diagnosis criteria for sarcopenia and metabolic repercussions during the first 6 months following bariatric surgery.

Methods A prospective single-center cohort study was conducted. Convenience sampling was performed among patients with severe obesity undergoing preoperative evaluation for bariatric surgery. Metabolic parameters, nutritional evaluation, and skeletal muscle evaluation were assessed before surgery and 6 months later.

Results A total of 129 patients were selected, 62 participants were included in the final analysis. Mean age was 37.7 years and 88.4% of participants were women. Mean body mass index was 41.8 kg/m2 and 47.8% of patients were sedentary. Sleeve gastrectomy was performed in 41 patients and Roux-en-Y gastric bypass in 21 patients. Significant improvement regarding muscle strength and function after surgery was observed. Sarcopenia criteria were not met by any participant before and after surgery. Blood glucose and ferritin levels remained independently associated with change in muscle strength.

Conclusions Functional evaluation methods did not reflect the reduction in skeletal muscle mass demonstrated in bioelectrical impedance analysis 6 months after bariatric surgery in comparison to the preoperative baseline. Improvement in muscle strength was followed by improvement in metabolic parameters.

Keywords Bariatric surgery · Sarcopenia · Muscle strength and function

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Key points
- Reduction in skeletal muscle mass was detected after surgery.
- Function evaluation methods did not reflect the reduction in skeletal muscle mass.
- Improvement in muscle strength was followed by improvement in metabolic parameters.

✉ Roberto Viña Coral
roberto_coral@hotmail.com

1 Department of Digestive System Surgery, Santa Casa de Misericórdia Hospital, Universidade Federal de Ciências da Saúde de Porto Alegre (UFCSPA), Porto Alegre, RS, Brazil

2 Department of Gastroenterology and Endoscopy, Santa Casa Hospital, Universidade Federal de Ciências da Saúde de Porto Alegre (UFCSPA), Porto Alegre, RS, Brazil

Introduction

Sarcopenia is a condition defined by progressive and generalized impairment of skeletal muscle quantity and quality — strength and performance [1]. It involves muscle mass/fat ratio imbalance characteristic of aging, but also obesity. Obesity exacerbates sarcopenia as it increases the infiltration of fat into muscle and lowers physical function [1–4]. Sarcopenia is associated with unfavorable health outcomes, such as metabolic syndrome, cardiovascular disease, liver impairment, and osteoporosis [3–11]. Adverse outcomes also include functional and physical disability, decreased quality of life, and mortality [1, 2].

Bariatric surgery remains the most effective treatment for severe obesity and related comorbidities [12–17]. According to the International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO), at least 830,000 patients underwent weight

loss surgery throughout 61 countries in 2019 [18]. The increasing number of post-bariatric patients brings challenges in the evaluation of weight loss quality and its effects.

An aggravation in pre-existing sarcopenia or the onset of sarcopenia may occur in the scenario of extensive and fast weight loss in the initial months following bariatric surgery and its identification and metabolic effects are not well documented [19–22]. Although the impact of sarcopenia in patients after weight loss operations is still uncertain, an early and accurate identification of this outcome and its repercussions is vital for its correct management. The objective of this study is to evaluate the correlation between sarcopenia diagnosis criteria and metabolic repercussions during the first 6 months following bariatric surgery.

Methods

Subjects

A prospective single-center cohort study was conducted. Convenience sampling was performed among patients with severe obesity undergoing preoperative evaluation for bariatric surgery at the same obesity treatment referral center between September of 2017 and December of 2018. Criteria included: (1) Age between 18 and 65 years old; (2) Obesity with BMI ≥ 40 or BMI ≥ 35 associated with comorbid conditions and not responding to medical treatment for 2 years; (3) No psychological contraindication for surgery; (4) No previous bariatric surgery.

Sample size calculation was performed using WinPEPI (Programs for Epidemiologists for Windows) Version 11.43. Level of significance of 5%, power of 80% and minimal effect size of 0.37 standard deviations between pre- and postoperative assessments were considered to obtain a minimum of 60 patients. This sample size also sustains correlations of at least 0.4 between variables.

Time frame of 6 months was selected as it is the period of most accelerated and extensive weight loss, consequently the most vulnerable interval for occurrence of skeletal muscle mass variations. Early identification of sarcopenia parameters would also favor an early intervention for a better management in the long term.

Pre- and postoperative evaluation

Overall evaluation was performed before surgery and 6 months later.

Sarcopenia parameters were defined and measured according to European consensus recommendations [1]. Skeletal muscle mass was evaluated through bioelectrical impedance analysis (BIA) [1]. Skeletal muscle strength was evaluated through hand grip test (HG) Handgrip Strength (HGS) test [23]. Skeletal muscle performance was evaluated through Timed get-up and go test (TGUG) [24] and Gate Speed test (GS) [25, 26]. Metabolic and nutritional evaluations were determined by laboratory blood testing. Physical Activity Questionnaire (IPAQ) [27] was applied for sample characterization. Sarcopenia was determined according to the European consensus cutoff points: grip strength of < 27 kg for men and < 16 kg for women; GS test ≤ 0.8 m/s; and TUG test ≥ 20 s.

Bodyweight and height were measured using standard equipment. Body mass index (BMI) was calculated as weight/height^2. Volume of lean body mass and fat and was estimated through BIA (InBody 720, Biospace, Seoul, Korea). HG test was evaluated with a Jamar dynamometer and the median of three measurements was considered. TGUG test is a measure of the time needed for the subject to stand up from a chair, walk for 3-m distance, turn around, return and sit down again. GS test is a measure of gait speed throughout a 4-min walk. IPAQ validated questionnaire evaluates the time each subject spends being physically active in the last 7 days — including work, house and yard routine, commute, and spare time for recreation, exercise or sport. Patients are classified in levels of activity that include irregularly active B (no activity), irregularly active a (physical activities for 150 min a week or 5 times a week), and active (physical activities for more than 150 min a week or more than 5 times a week). Laboratory testing parameters included the following biological markers: hemogram, fasting blood glucose, glycosylated hemoglobin (HbA1c), total cholesterol, triglyceride, LDL-cholesterol, HDL-cholesterol, total cholesterol, triglycerides, high density lipoprotein cholesterol, alanine aminotransferase (ALT), aspartate aminotransferase (AST), vitamin B12, folic acid, vitamin D, zinc, uric acid, ferritin and iron.

Surgical Procedures

All patients went laparoscopic sleeve gastrectomy (SG) or Roux-en-Y gastric bypass (RYGB) at the same obesity treatment center and according to patient and multidisciplinary team judgement. RYGB was preferably performed in patients who presented with metabolic syndrome or gastroesophageal reflux disease.

Roux-en-Y gastric bypass included a 4.5-cm width gastric pouch with a 100-cm biliopancreatic limb and a 100-cm roux limb; gastrojejunostomy was 4.5-cm width and not calibrated. Sleeve Gastrectomy was performed at 3 cm from the pylorus using a 32F Fouchet calibration tube.

Table 1 Sample characteristics

Variable	Overall sample (n=62)	SG (n=41)	RYGB (n=21)
Age (years), mean ± SD	38.4 ± 10.8	38.1 ± 11.1	39.0 ± 10.4
Sex, n (%)			
Female	52 (83.9)	33 (80.5)	19 (90.5)
BMI (kg/m^2), mean ± SD	42.2 ± 5.4	42.2 ± 5.7	42.1 ± 4.9
Level of physical activity, n (%)			
Inactive	23 (37.1)	17 (41.5)	6 (28.6)
Irregularly active B	15 (24.2)	9 (22.0)	6 (28.6)
Irregularly active A	16 (25.8)	11 (26.8)	5 (23.8)
Active	7 (11.3)	3 (7.3)	4 (19.0)
Very active	1 (1.6)	1 (2.4)	0 (0.0)

Statistical Analysis

Quantitative variables were expressed as mean and standard deviation and categorical variables as absolute and relative frequencies. Comparison of means was performed through Student's t-test. Association between numerical variables was calculated through Pearson correlation coefficients. Generalized estimating equations (GEE) model with Bonferroni adjustment was used to compare variables between the two time points of assessment (before and after surgery), as the numbers in comparison were small. To control for confounding factors, linear regression model with backward extraction was run to identify factors independently associated with variation in muscle strength. Variables with $p < 0.20$ on bivariate analysis in association with change in handgrip strength were included in a multivariate linear regression model with backward extraction to identify factors independently associated with this outcome. Level of

significance was set at 5% ($p < 0.05$). All analyses were performed using SPSS Version 21.0.

Ethical Considerations

Written informed consent was obtained from all individual participants included in the study.

The study protocol and the informed consent procedure were approved by the institutional ethics committee under the registration number 73910017.0.0000.5335.

Results

A total of 129 patients were selected. Fifty-seven patients were excluded — 21 patients refused to participate, 3 patients accidentally became pregnant, and 33 patients were lost to follow-up. A total of 62 participants were included in the final analysis and their characteristics are presented in Table 1. Mean age was 37.7 years and 88.4% of participants were female. Mean BMI was 41.8 kg/m^2. SG was performed in 41 patients and RYGB was performed in 21 patients. According to IPAQ questionnaire, 47.8% of patients were sedentary.

Body composition assessment through BIA demonstrated an average weight loss of 31% — a mean 11.5 kg/m^2 reduction in BMI (from 68.8 to 22.8% excess BMI). The average lean body mass and fat mass lost was 4 kg and 25 kg, respectively. The mean ratio of appendicular lean mass to height (kg/m^2) was significantly reduced from 9 to 7.7. The mean body fat percentage was significantly reduced from 49.1 to 36.9% (Table 2).

Significant improvement was observed regarding muscle function evaluated by the TGUG test and gait speed test postoperatively. HG test results remained stable (Table 3).

Table 2 Comparison of BIA results before surgery and 6 months after surgery

Variable	Before surgery Mean ± SE	6 months Mean ± SE	Difference (95%CI)	P
Total body weight (kg)	113.5 ± 2.2	82.5 ± 1.6	− 31.0 (− 33.2 to − 28.9)	< 0.001
BMI (kg/m^2)	42.2 ± 0.7	30.7 ± 0.5	− 11.5 (− 12.2 to − 10.8)	< 0.001
Lean body mass (kg)	32.5 ± 0.8	28.5 ± 0.6	− 4.1 (− 4.6 to − 3.5)	< 0.001
Fat mass (kg)	55.8 ± 1.3	30.8 ± 1.2	− 25.0 (− 26.8 to − 23.2)	< 0.001
Appendicular lean mass (kg)	24.4 ± 0.6	20.9 ± 0.5	− 3.4 (− 3.8 to − 3.1)	< 0.001
Appendicular lean mass/height^2 (kg/m^2)	9.0 ± 0.1	7.7 ± 0.1	− 1.3 (− 1.4 to − 1.2)	< 0.001
Appendicular lean mass/BMI (m^2)	0.58 ± 0.01	0.69 ± 0.02	0.11 (0.56 to 0.12)	< 0.001
Fat mass/Lean mass ratio	1.74 ± 0.03	1.11 ± 0.05	− 0.63 (− 0.69 to − 0.57)	< 0.001
Body fat percentage, %	49.1 ± 0.5	36.9 ± 1.0	− 12.2 (− 13.5 to − 10.9)	< 0.001
Basal metabolic rate	1617 ± 27.0	1486 ± 22.0	− 131 (− 150.6 to − 111.5)	< 0.001
Waist-to-hip ratio	1.02 ± 0.0	0.95 ± 0.01	− 0.07 (− 0.08 to − 0.06)	< 0.001
Obesity grade (%)	195.8 ± 3.2	142.4 ± 2.5	− 53.4 (− 56.5 to − 50.2)	< 0.001
Visceral fat (m^2)	19.9 ± 0.1	14.0 ± 0.5	− 5.9 (− 6.9 to − 4.9)	< 0.001

Table 3 Comparison of muscle parameters before surgery and 6 months after surgery

Variable	Before surgery Mean ± SE	6 months Mean ± SE	Difference (95%CI)	P
Handgrip strength (kg)	25.7 ± 1.2	25.4 ± 1.0	− 0.3 (− 0.7 to 0.9)	0.647
Timed Up and Go (s)	9.9 ± 0.2	8.9 ± 0.2	− 1.0 (− 1.4 to − 0.6)	< 0.001
Gait speed (m/s)	0.62 ± 0.01	0.69 ± 0.01	0.07 (0.04 to 0.09)	< 0.001

Sarcopenia criteria were not met by any participant during the 6-month follow-up period.

Significant decrease in fasting blood glucose was detected (mean — 13.3 mg/dL). Parameters such as total cholesterol and triglycerides were also significantly improved. Vitamin B12 and D levels increased significantly after surgery (Table 3).

Comparison of muscle strength and function scores, metabolic variables, and anthropometric parameters between surgical techniques revealed no significant difference (Table 4).

After adjustment by the multivariate model, change in blood glucose and ferritin levels remained independently associated with change in muscle strength, as shown in Tables 5 and 6. Percent weight loss was borderline significant after adjustment. For every 1 mg/dL reduction in blood glucose levels after surgery, there was an average increase of 0.08 units in handgrip strength after multivariate adjustment (Fig. 1). For every 1-unit reduction in ferritin levels after surgery, there was an average increase of 0.02 units in handgrip strength.

Discussion

Reduced skeletal muscle mass may be associated with the development of metabolic disease, such as type 2 diabetes. Likewise, skeletal muscle mass gain and strength is related with a lower risk of type 2 diabetes [28]. Although a reduction in skeletal muscle mass after surgery was detected in some studies [29, 30], as well as, in our sample, this muscle mass decrease did not affect muscle function and was not enough to independently affect blood glucose levels. In our study, loss of skeletal muscle mass did not present any correlation with metabolic factors worsening. Moreover, patients in this sample presented an increase in muscle strength after surgery, although their significantly lean body mass loss, an outcome that has been correlated with improvement in glucose metabolism disorders [31]. The inverse relation between muscle strength and type 2 diabetes presented a linear positive correlation that may be due to a greater peripheral insulin action.

Serum ferritin levels are an important marker of systemic inflammation and their values are directly correlated with other inflammatory markers levels, like HbA1c [32]. Serum ferritin also reflects body iron stores. It is suggested that increased serum ferritin levels in patients with obesity may be associated to a raise in fatty acids values and consequently, to an aggravation of insulin resistance due to iron metabolism imbalance [33]. A linear correlation between reduction in serum ferritin levels and increase in muscle strength was found in our analysis.

Table 4 Comparison of laboratory parameters before surgery and 6 months after surgery

| Variable	Before surgery Mean ± SE	6 months Mean ± SE	Difference (95%CI)	P
Hemoglobin (g/dL)	12.8 ± 0.2	12.5 − 0.2	− 0.3 (− 0.7 to 0.1)	0.164
Fasting glucose (mg/dL)	96.3 ± 2.6	83.0 ± 1.3	− 13.3 (− 18.1 to − 8.5)	< 0.001
Glycated hemoglobin (A1C) (%)	5.6 ± 0.2	5.4 ± 0.2	− 0.2 (− 0.8 to 0.4)	0.518
Total cholesterol (mg/dL)	185.6 ± 4.0	163.7 ± 4.2	− 21.9 (− 30.3 to − 13.5)	< 0.001
Triglycerides (mg/dL)	128.0 ± 7.5	88.7 ± 6.0	− 39.3 (− 53.7 to − 24.9)	< 0.001
High-density lipoprotein (HDL) cholesterol (mg/dL)	50.0 ± 1.9	50.0 ± 2.5	0.0 (− 5.8 to 5.7)	0.994
Gamma-glutamyltransferase(U/L)	34.0 ± 2.1	24.3 ± 3.6	− 9.7 (− 16.7 to − 2.7)	0.007
Aspartate aminotransferase(U/L)	21.2 ± 1.1	27.5 ± 2.7	6.3 (0.4 to 12.1)	0.034
Alanine aminotransferase(U/L)	26.1 ± 2.0	31.7 ± 5.9	5.6 (− 6.8 to 18.0)	0.379
Vitamin B12 (pg/mL)	419.5 ± 22.2	630.6 ± 54.6	211.2 (103.0 to 319.3)	< 0.001
Folic acid (ng/mL)	8.5 ± 0.6	9.5 ± 0.8	1.0 (− 0.8 to 2.8)	0.284
Vitamin D (ng/mL)	22.7 ± 1.0	27.9 ± 1.4	5.2 (2.4 to 7.9)	< 0.001
Zinc (µg/dL)	42.8 ± 9.7	47.8 ± 11.6	5.0 (− 20.6 to 30.6)	0.702
Uric acid (mg/dL)	5.1 ± 0.2	4.4 ± 0.2	− 0.7 (− 1.2 to − 0.2)	0.006
Ferritin (ng/mL)	146.0 ± 22.2	217.7 ± 33.0	71.8 (11.0 to 132.5)	0.021
Iron (µg/dL)	77.7 ± 4.2	96.2 ± 16.1	18.4 (− 13.6 to 50.5)	0.259

Table 5 Comparison of change in muscle strength and function scores, metabolic variables, and anthropometric parameters between surgical techniques

Variable	SG (n=41) Mean ± SE	RYGB (n=21) Mean ± SE	P
Handgrip strength (kg)	− 0.69 ± 4.99	0.50 ± 5.11	0.380
Timed Up and Go (s)	− 1.19 ± 1.57	− 0.73 ± 1.56	0.271
Gait speed (m/s)	0.08 ± 0.09	0.05 ± 0.12	0.423
Blood glucose (mg/dL)	− 15.6 ± 20.4	− 18.1 ± 21.6	0.691
Glycated hemoglobin (%)	0.25 ± 2.22	− 1.12 ± 2.23	0.101
Appendicular lean mass (kg)	− 3.37 ± 1.34	− 3.55 ± 1.52	0.641
Appendicular lean mass/height^2 (kg/m^2)	− 1.23 ± 0.43	− 1.34 ± 0.58	0.397
Lean body mass (kg)	− 4.18 ± 2.07	− 3.80 ± 2.50	0.526
Appendicular lean mass/BMI (m^2)	0.11 ± 0.05	0.11 ± 0.06	0.933
Fat mass/Lean mass ratio	− 0.60 ± 0.22	− 0.69 ± 0.28	0.185
Percent weight loss (%)	− 26.8 ± 5.8	− 27.8 ± 4.5	0.471
BMI (kg/m^2)	− 11.3 ± 2.9	− 11.8 ± 2.5	0.594
Body fat percentage (%)	− 11.5 ± 5.0	− 13.5 ± 5.8	0.157
Fat mass (kg)	− 24.6 ± 7.8	− 25.7 ± 6.5	0.574
Visceral fat	− 5.41 ± 3.95	− 6.95 ± 4.09	0.157
Obesity grade (%)	− 52.7 ± 13.6	− 54.7 ± 11.6	0.558
Waist-to-hip ratio	− 0.07 ± 0.03	− 0.08 ± 0.05	0.321

The contradictory association between loss of skeletal muscle mass, increase in muscle strength and improvement in metabolic parameters may strengthen the hypothesis that skeletal muscle tissue in the patient with severe obesity is of lower functional and metabolic quality. Young patients with severe obesity have a greater quantity of skeletal muscle mass than the one expected for their weight, yet evidence suggests it is of lower quality. Due to fat infiltration into muscle tissue, its function may be impaired. A prior study evidenced a negative correlation between muscle strength and the degree of fat infiltration in the muscle tissue [34]. These findings reinforce the importance of adequate interpretation of skeletal muscle mass

Fig. 1 Association between blood glucose variations and hand grip variations through Pearson correlation coefficients (r=0.378; p=0.011)
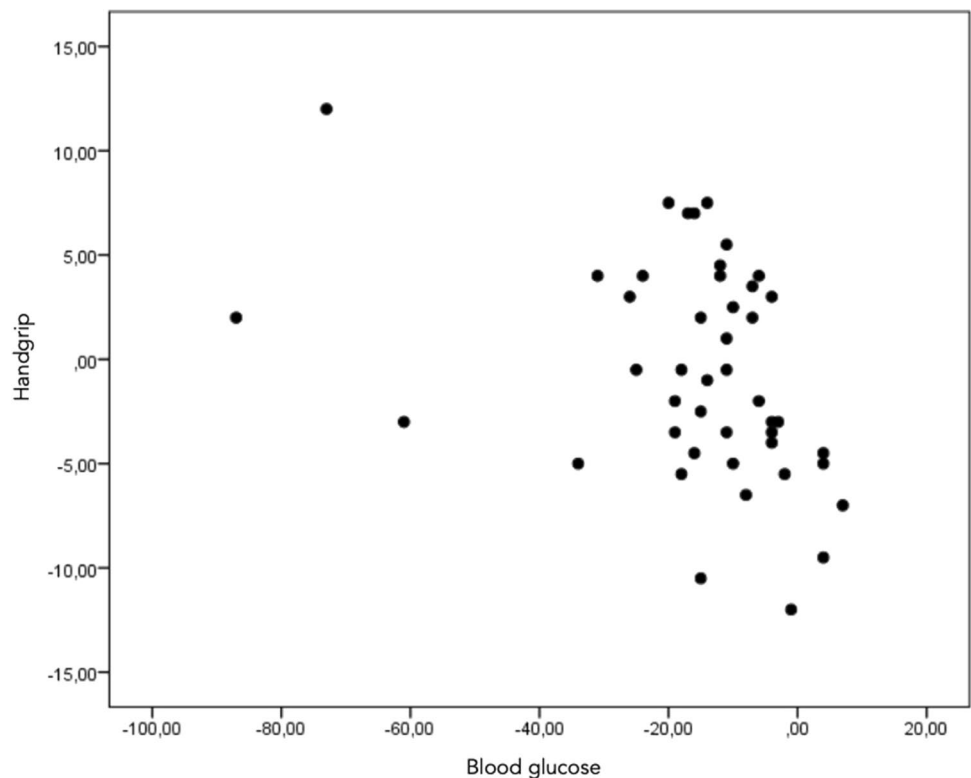
evaluation parameters and diagnosis criteria for sarcopenia. An isolated measurement of skeletal muscle mass may induce a false diagnosis. Loss of muscle mass after bariatric surgery may be considered a metabolic adaptive process, since factors related to muscle quality (like strength) and metabolic syndrome markers show significant improvement after surgery.

The high rate of weight loss in the early postoperative period of our patients did not induce the development of sarcopenia that reinforces the safety of bariatric surgery as a weight loss strategy. Nevertheless, further studies on continuous loss of skeletal muscle mass must be conducted to evaluate the occurrence and long-term outcomes of this initial loss of lean body mass.

Limitations of this study included the inclusion of two different metabolic procedures; high dropout rate and loss of follow up; non-individual analysis of the group of patients with diabetes; the lack of direct markers of glucose intolerance; and general aspects of non-intervention studies, such as the lack of control over physical training and postoperative nutritional supplementation.

Conclusion

Functional evaluation methods (TGUG test, GS test and HG test) did not reflect the reduction in skeletal muscle mass demonstrated in BIA 6 months after bariatric surgery in comparison to the preoperative baseline. Improvement in muscle strength was followed by improvement in metabolic parameters.

Declarations

Ethics Approval and Consent to Participate The study protocol and the informed consent procedure were approved by the institutional ethics committee under the registration number 73910017.0.0000.5335.

All procedures performed in studies involving human participants were in accordance with the ethical standards of institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Written informed consent was obtained from all individual participants included in the study.

Conflict of Interest The authors declare no competing of interests.

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