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ORIGINAL CONTRIBUTIONS

Endothelial Function of Patients with Morbid Obesity Submitted to Roux-en-Y Gastric Bypass With and Without Obstructive Sleep Apnea-Hypopnea Syndrome

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Abstract

Background Obesity is associated with obstructive sleep apnea-hypopnea syndrome (OSA) and both induce endothelial dysfunction. However, the effect of OSA on endothelial function after bariatric surgery has not been investigated yet.

Objectives This study aims to evaluate the impact of weight loss on endothelial function in patients with and without obstructive sleep apnea (OSA) in the first 6 months after bariatric surgery.

Setting This study was conducted at a university hospital, in Brazil.

Methods The sample consisted of 56 patients homogeneously divided into groups with and without OSA. All patients underwent Roux-en-Y gastric bypass (RYGB), and the diagnosis of OSA was performed by polysomnography. The patients were evaluated preoperatively and 6 months after surgery. The evaluations included anthropometric measures, electrical bioimpedance, clinical symptoms of OSA, and endothelial function (flow-mediated dilation). RYGB improved the anthropometric, bioimpedance, and endothelial function results in both groups.

Results Patients presented a significant clinical improvement in OSA symptoms throughout the study. However, patients with OSA had an improvement in the endothelial function 2.5% lower ($p < 0.001$) than patients without APNEA syndrome.

Conclusion This study demonstrates that the existence of OSA prior to bariatric surgery interferes in the improvement of endothelial function.

Keywords Obstructive sleep apnea-hypopnea syndrome · Gastric bypass · Vascular endothelium · Morbid obesity · Flow-mediated dilation

Introduction

The global obesity epidemic and the worldwide prevalence of obstructive sleep apnea-hypopnea syndrome (OSA) are increasing [1]. This syndrome is probably the most common respiratory disorder in the USA and Europe, suggesting that between 14 and 49% of middle-aged men have clinical symptoms [2] and morbid obesity is the main risk factor [3]. OSA leads to decreased quality of life (QOL) and functional capacity, together with an increased risk of cardiovascular disease, predisposing to higher rates of morbidity and mortality [2, 4].

Surgical treatment for obesity can be considered when nutritional, pharmacological, and physical activities are not efficient [5]. For morbidly obese patients, this treatment is considered the most effective method in the long term, since it promotes control of weight and comorbidities [5, 6] when compared to the conservative method [7–10]. Currently,

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Roux-en-Y gastric bypass (RYGB) is one of the most performed methods in the world due to its lower morbidity and mortality, better control of comorbidities, and good efficacy, as it leads to a 70% reduction in excess weight [5].

The vascular endothelium is strategically located between blood and smooth muscle and covers the entire cardiovascular system [11]. Its normal function inhibits platelet aggregation, suppresses the proliferation of smooth muscle cells, and stimulates angiogenesis [11, 12]. This is due to the humoral regulation of vascular tone, which is mainly due to the production of nitric oxide (NO), but also prostacyclin (PGI_2) and hyperpolarizing endothelium-derived factor (EDHF), which together promote vascular vasodilation [11, 12]. Clinically, studies have demonstrated that endothelial function assessed by the flow-mediated dilation (FMD) technique is a predictor of cardiovascular events [12–14] and all-cause mortality [14]. Weight reduction improves endothelial function, and in morbidly obese patients, this improvement was more evident in patients submitted to bariatric surgery [15].

OSA is related to several pathophysiological mechanisms triggered by hypoxia [2, 16] and sleep fragmentation [17] that induce sympathetic activation, inflammation, altered blood coagulation, and endothelial dysfunction [18–20]. RYGB improves comorbidities [5], including OSA [10, 21, 22] and endothelial function [15, 23]. However, the effects of bariatric surgery on endothelial function in patients with OSA are still not well understood. The objective of this study is to evaluate the impact of weight loss in the first 6 months of RYGB-reduced gastroplasty on endothelial function in patients with and without OSA.

Methods

Study Outline

This case-control study was approved by the Research Ethics Committees of the the Pontifical Catholic University of Rio Grande do Sul (PUCRS) and the Federal University of Santa Maria (UFSM) (assessment no. 157368). The preoperative evaluations and the postoperative follow-up of the patients were performed at a medical clinic in the city of xxxxxxxxxxxxxxxxxx. Endothelial function was performed at the Diagnostic Service by Graphic Methods of the xxxxxxxxxxxxxxxxxxxxxxxxxxxx (xxxx). All patients enrolled in the study signed the informed consent term. Data were collected during the period from July 2016 to May 2017. The population comprised morbidly obese patients who underwent preoperative evaluation of bariatric surgery. The sample was divided into two groups, without OSA (control group) and group with OSA (OSA group), verified through polysomnography. After surgery, the patients were followed for 6 months and were reevaluated. Patients were not using continuous positive airway pressure (CPAP) during the study.

Sample Calculation

The sample calculation was based on a previous study [24]. We estimated that 28 patients would be required in each study group (without or with OSA). The FMD for the group with OSA is approximately 4.2% for a standard deviation of 2%. After the RYGB intervention (with or without OSA), we estimated a difference of 1.4% between means. These values were maintained for a power of 80% and for a $\alpha = 0.05$. The sample was composed of 56 obese patients divided into two groups (without OSA or control group and with OSA or OSA group) undergoing RYGB.

Eligibility Criteria

The patients included in the study were as follows: volunteers of both sexes, aged ≥ 16 years, BMI ≥ 35 kg/m^2, with comorbidities or with BMI ≥ 40 kg/m^2, and who were undergoing preoperative evaluation for bariatric surgery through the RYGB technique, with and without diagnosis of OSA through polysomnography. In the present study were excluded patients with diseases such as the following: decompensated hyperthyroidism (TSH < 0.01); neoplasms or immunosuppressive diseases; Cushing's syndrome or chronic use of corticosteroids; patients with chronic obstructive pulmonary disease (COPD); patients with diabetic nephropathy, rheumatoid arthritis, diabetics, smokers, patients who did not present alterations in endothelial function at the initial evaluation, and who would undergo other types of bariatric surgery, other than RYGB.

Procedures for Data Collection

The candidates for bariatric surgery who were in their first consultation for surgical evaluation were screened through the Berlin Questionnaire (BQ) [24, 25] and the Epworth Sleepiness Scale (ESS) [25, 26] and Quality Index of Pittsburgh Sleep [27] for the screening of patients at risk of OSA. After identification of the patients suspected of having OSA, they were referred by the attending physician for the polysomnography examination, to confirm or not the diagnosis.

The laparoscopic Roux-en-Y gastric bypass technique involves the creation of a 15-mL stapled gastric pouch, a one-layer, side-to-side gastrojejunostomy (inside staples and outside sutures), a 75- to 150-cm antecolic, antegastric Roux-limb, and a stapled side-to-side jejunojejunostomy.

Polysomnography

Polysomnography examinations followed the international guidelines [28, 29], and OSA diagnoses were made according to the international standards established by the American Academy of Sleep Medicine (AASM) [30]. The evaluation was overseen by a trained specialist using a digital polygraph (Homed brand Icelera™ Fast-poly model, São Paulo) with six channels for electroencephalography (EEG); two channels for electrooculography; two channels for electrocardiogram; two channels for chin electromyogram; two channels for leg electromyogram; two extra channels for legs, bruxism, or EEG; one channel for SpO_2; and one channel for heart rate. Additionally, air flow sensors, thoracic and abdominal straps, a microphone for snoring, position sensor, pressure transducer with flow cannula, and pressure transducer with cannula for snoring were used. The PSG evaluated sleep stages 1, 2, and 3 (N1, N2, and N3), rapid eye movement (REM) sleep, apnea-hypopnea index (AHI), AHI in REM sleep (AHIREM), average peripheral oxygen saturation during sleep (SpO_2med), average heart rate during sleep (HRmed), micro-arousal index (MAI), and total sleep time (TST). These were associated with pulse oximetry and a video system integrated with infrared to monitor the polysomnographic variables and vital signs. OSA severity is defined as mild for AHI ≥ 5 and < 15, moderate for AHI ≥ 15 and ≤ 30, and severe for AHI > 30/h (consensus) [29].

Evaluation of Endothelial Function

Endothelial function is in accordance with the American Heart Association Guidelines [31], with adjustments [13, 32]. Evaluation of endothelial function of the brachial artery was done by high-resolution vascular ultrasound (Esaote MyLabe Gold, vascular transducer LA332 3.5–10 MHz, Esaote Healthcare do Brazil, de São Paulo) in the region above the cubital fossa of the left arm. The cuff positioned around the arm was insufflated with 50 mmHg above systolic blood pressure, and arterial changes in the first 60 s of reactive hyperemia after disinflation accounted for endothelium-dependent vasodilation. In order to assess baseline blood flow and blood flow in the first 15 s after disinflation, a pulsed-wave Doppler velocity signal was used. The sonographer was encouraged to use a Doppler beam-vessel angle at 60°. Endothelium-independent vasodilation was considered after the interventions, which is regarded as an increase of arterial diameter after sublingual nitroglycerin (0.4 mg). Settings of depth and gain imaging were kept constant throughout the study. Vascular responses to reactive hyperemia and nitroglycerin are expressed as percentage changes in relation to the diameter immediately before cuff inflation and nitroglycerin administration [31]. All arterial diameter measurements were done off-line by two evaluators using a semiautomatic quantitative analysis system, and the second evaluator was blind to the measurements done by the first evaluator. All measurements were done twice, and if any difference above 0.01 mm between evaluations was observed, the measurements were repeated.

Physical and Biochemical Assessments

Anthropometric variables and body composition measurements were collected in the fasted state of 2 h. For the accomplishment (of the corporal composition evaluation) of these measurements, an electrical bioimpedance exam was done, with the equipment InBody 370 (InBody Co LTD, South Korea), which is a tetra-polar bioimpedance apparatus, a stadiometer, and a tape measure for the measurements of the cervical and abdominal circumference, which were performed with the subject standing and wearing underwear under an apron. Measurements were performed twice (interval of 5 min), and the percentages of fat mass, trunk fat, and total body water quantity were expressed by the mean of the measurements. The systemic arterial pressure was evaluated by the auscultatory method. The heart rate was measured through a Nonin GO2 (Nonin Medical USA) pulse oximeter.

In order to perform the biochemical tests, the patients had 8 h of fasting, and the glucose levels were measured by Trinder assay (calorimetry) in the equipment *LAB MAX 240*® (Tokyo, Japan). Cholesterol, triglycerides, high-density lipoproteins (HDLc), glucose, and urea were measured using *LAB TEST* commercial kits (Lagoa Santa, MG, Brazil) and analyzed in the equipment *LAB MAX 240*® (Tokyo, Japan). Low-density lipoproteins (LDLc) were calculated by Friedewald's formula.

Statistical Analysis

To analyze the data, we used frequency tables and descriptive measures, such as the following: mean, standard deviation, quartiles (q1, md, q2). The Shapiro-Wilk normality test ($n < 2000$) was applied. Fisher's exact test was applied to the qualitative variables. Two-way ANOVA with repeated measures (time, group, and interaction) was used to compare the two groups at the moments (pre- and postoperative) and the differences between the groups (control vs. OSA) followed by Tukey post hoc. The variables with two measures were analyzed by the Student *t* test. Pearson correlation coefficient was applied in the deltas of variation (Δ = postoperative − preoperative) of the variables. The level of significance used in all tests was 0.05. Statistical analysis of the data was performed using the Statistical Analysis System (SAS), version 9.0.

Results

The flowchart shown in Fig. 1 shows the follow-up of patients throughout the study period. After allocation of 31 control group patients, three patients did not continue the study leaving a total of 28 patients in the group. Thirty-five patients were initially allocated to OSA group, but three patients did not undergo surgery, two patients did not continue the study, and two patients did not perform endothelial function assessment, with a total of 28 patients in the study. The preoperative polysomnography showed an AHI of 47.43 (± 24.82) episodes per hour, with 10 patients classified as OSA moderate and 18 severe. In the OSA group, the percentages of oxygen saturation (SaO_2) were as follows: minimum 74.8% (± 10.7), medium 93.2% (± 2.3), and maximum 97.4% (± 2.1).

Table 1 shows the clinical characteristics of patients throughout the study. The groups were homogeneous according to sex (control group 9 men, OSA group 14 men, $p = 0.277$) and age (control group 34.7 ± 10.4, OSA group 39.6 ± 9.2 years, $p = 0.072$). All patients were white in both groups. None of the women were in menopause. Control and OSA groups were similar in all variables analyzed at the preoperative time. In both groups, reductions in BMI, cervical circumference, waist circumference, percentage of fat mass, waist/hip ratio, heart rate, diastolic blood pressure, glucose, total cholesterol, triglycerides, uric acid, urea, and creatinine were observed throughout the study. The heart rate showed a reduction in both groups ($p < 0.001$), but there were no differences between the groups ($p = 0.568$), but this decrease was more significant in the OSA group (control group = 3.8 ± 7.2 vs. OSA group 8.9 ± 4.4; interaction $p = 0.049$). However, systolic blood pressure reduced only in the OSA group. The other variables were similar between the groups. Drug use was similar in both groups at all times evaluated (Table 2).

Table 3 shows the endothelial function data of the patients throughout the study. All variables analyzed were similar between groups at preoperative time. The comparison between the pre- and postoperative moments shows that %FMD increased in both groups (control group = 11.4, OSA group = 7.9), with control group facing an increase 2.5% higher than OSA group ($p = < 0.001$) (data represented in Fig. 2a). The basal flow increased only in the control group. HR flow increased in both groups. Basal flow and HR flow did not differ between groups. The increase in the PostNtg% was higher in the control group than in the OSA group (2.4 vs. 0.6), but there was no intragroup difference (pre vs. post). The other variables did not show differences intra (pre vs. post) and between groups (control group vs. OSA group).

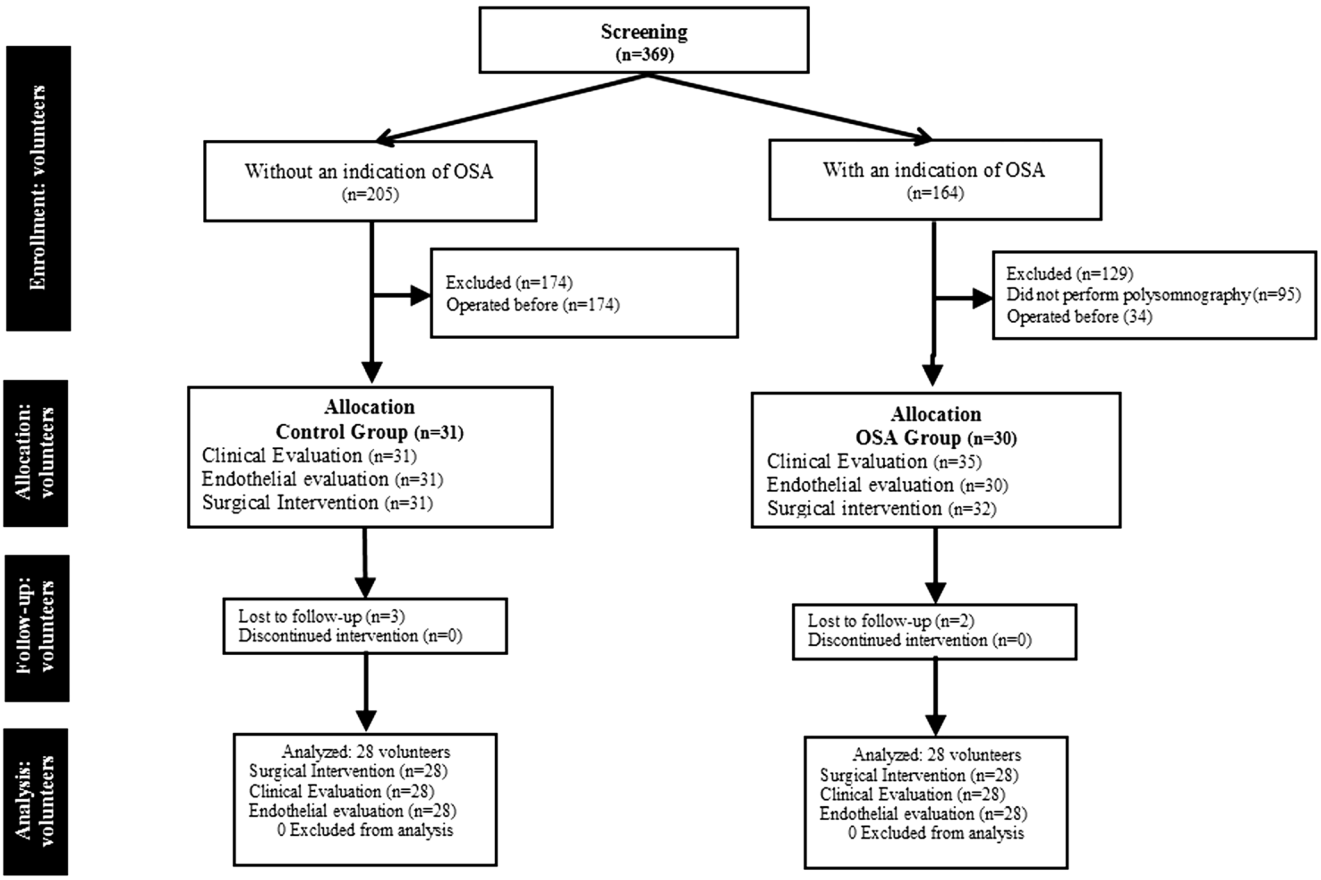

Fig. 1 Flowchart. OSA obstructive sleep apnea-hypopnea syndrome

Table 1 Clinical characteristics of the patients in the preoperative and 6 months postoperative moments

Variables	Control group ($n = 28$)		OSA group ($n = 28$)		ANOVA 2 vias		
	Pre	Post	Pre	Post	Time	Group	Interaction
Body mass index (kg/m^2)	41.6 ± 3	28.9 ± 2.4*	43.2 ± 5.5	30.3 ± 3.4*	*< 0.001*	0.117	0.844
Cervical circumference (cm)	42.7 ± 3.9	37.2 ± 3.1*	43.5 ± 5.1	38.4 ± 3.6*	*< 0.001*	0.584	0.598
Abdominal circumference (cm)	122.3 ± 11.5	90.6 ± 8.5*	124.8 ± 14.1	93.8 ± 10*	*< 0.001*	0.186	0.883
Fat mass (%)	49 ± 5.4	34.1 ± 8*	49 ± 6.5	33.9 ± 8.7*	*< 0.001*	0.947	0.925
Total body water (kg)	42.8 ± 8	38 ± 6.4*	45.9 ± 1.2	41.1 ± 9.5*	*0.005*	0.066	0.953
Hip/waist ratio	1.05 ± 0.1	0.9 ± 0.1*	1 ± 0.1	0.9 ± 0.1*	*< 0.001*	0.281	0.150
Snoring fat (kg)	22.8 ± 3.6	22.8 ± 3.6	26.5 ± 2.9	25 ± 4.8	0.507	0.080	0.136
Heart rate (bpm)	69.8 ± 9.1	66 ± 4.3*	71.9 ± 6.8	62.3 ± 4.8*	*< 0.001*	0.568	*0.049*
Systolic blood pressure (mmHg)	129.6 ± 10.1	124.6 ± 15.7	133.6 ± 11.4	124.5 ± 14*	*0.003*	0.446	0.369
Diastolic blood pressure (mmHg)	90.2 ± 9.7	80.4 ± 9*	94.7 ± 12	82.5 ± 11.5*	*< 0.001*	0.103	0.564
Glucose (mg/dL)	100 ± 23.4	81.4 ± 7.2*	102.3 ± 38.3	83.3 ± 11.2*	*< 0.001*	0.626	0.958
Total cholesterol (mg/dL)	193.3 ± 44.3	160.9 ± 39*	192.3 ± 38.3	162.5 ± 31.7*	*< 0.001*	0.937	0.886
HDLc (mg/dL)	48.1 ± 13.4	44.7 ± 8.6	46.4 ± 1.4	48.4 ± 2	0.724	0.632	0.194
LDLc (mg/dL)	112.7 ± 4.8	97.6 ± 34.9*	114.1 ± 35.6	95.8 ± 25.6*	*0.012*	0.982	0.811
Triglycerides (mg/dL)	161.6 ± 92.4	93.7 ± 43.3*	165.6 ± 10.2	90.8 ± 27.5*	*< 0.001*	0.978	0.812
Uric acid (mg/dL)	5.6 ± 1.5	4.6 ± 1.4*	6 ± 1.8	5 ± 1.4*	*< 0.001*	0.393	0.974
Urea (mg/dL)	29.3 ± 6.7	25.5 ± 7.6*	30.5 ± 7.2	27.1 ± 6.4*	*< 0.001*	0.436	0.765
Creatinine (mg/dL)	0.82 ± 0.2	0.73 ± 0.2*	0.83 ± 0.2	0.74 ± 0.2*	*< 0.001*	0.768	0.902

Italic data highlights the significant data in the two-way ANOVA

Values expressed as mean ± DP. *OSA group*, obstructive sleep apnea-hypopnea syndrome group; *HDLc*, high-density lipoprotein cholesterol; *LDLc*, low-density lipoprotein cholesterol; *Pre*, preoperative; *Post*, postoperative

*Difference versus preoperative

Table 4 shows the results of OSA. The clinical evaluation instruments, used in the preoperative period and follow-up of 6 months of OSA evolution after the RYGB, showed clinical remission of the symptoms in the postoperative period. The Berlin Questionnaire was negative in 100% of the subjects ($p < 0.001$), the Epworth Scale reduced by approximately 15-fold ($p < 0.001$), and the Pittsburgh Sleep Quality Index (PSQI-BR) was good for all patients ($p < 0.001$). In the OSA

Table 2 Medications used by patients throughout the study

Drugs	Control group ($n = 28$)		OSA group ($n = 28$)	
	Pre	Post	Pre	Post
Antidepressants	9 (32%)	6 (21%)	12 (43%)	8 (29%)
Benzodiazepines	5 (18%)	2 (7%)	4 (14%)	2 (7%)
Angiotensin converting enzyme inhibitors	4 (14%)	0 (0%)	5 (18%)	0 (0%)
Diuretics	4 (14%)	0 (0%)	5 (18%)	0 (0%)
Angiotensin receptor II antagonists	11 (39%)	0 (0%)	7 (25%)	0 (0%)
Calcium channel antagonists	2 (7%)	0 (0%)	2 (7%)	0 (0%)
B-Blockers	11 (39%)	2 (7%)	14 (50%)	1 (4%)
Hypothyroidism	5 (18%)	5 (18%)	4 (14%)	4 (14%)
Bronchodilator	5 (18%)	1 (4%)	5 (18%)	0 (0%)
Hypolipid (statins)	4 (14%)	0 (0%)	4 (14%)	0 (0%)
Glycemic control	7 (25%)	1 (4%)	5 (18%)	1 (4%)
Proton-pump inhibitors	9 (32%)	0 (0%)	5 (18%)	1 (4%)

Data presented in absolute values (n) and percentage (%). *OSA group*, obstructive sleep apnea-hypopnea syndrome group

Table 3 Endothelial function of the patients at the moments before and 6 months postoperatively

Variables	Control group ($n = 28$)		OSA group ($n = 28$)		ANOVA 2 vias		
	Pre	Post	Pre	Post	Time	Group	Interaction
Basal flow (cm/s)	36.5 ± 7.4	43.3 ± 9*	36.2 ± 9.7	41.3 ± 9.4*	*0.006*	0.476	0.621
Basal diameter (mm)	3.2 ± 0.6	3 ± 0.5	3.5 ± 0.6	3.4 ± 0.7	0.150	*< 0.001*	0.545
HR flow (cm/s)	84.8 ± 31.7	128.3 ± 18.4*	83.9 ± 30.8	122.3 ± 16.1*	*0.001*	0.470	0.594
%FMD	3.4 ± 2.9	14.8 ± 4.6*	3.2 ± 2.2	11.1 ± 3.6*#	*< 0.001*	*0.003*	*0.010*
Pre Ntg (mm)	3.2 ± 0.6	3 ± 0.5	3 ± 2.2	3.4 ± 0.7	0.572	0.536	0.140
%Post Ntg	22 ± 8.4	24.4 ± 6.2	18.8 ± 6.2	19.4 ± 5.5#	0.074	*0.006*	0.387

Italic data highlights the significant data in the two-way ANOVA

Values expressed as mean ± SD. *OSA group*, obstructive sleep apnea-hypopnea syndrome group; *HR*, reactive hyperemia; *%FMD*, percentage flow-mediated dilation; *Ntg*, nitroglycerin; *%Post Ntg*, percentage dilatation after Ntg; * difference versus pre; # difference versus CG

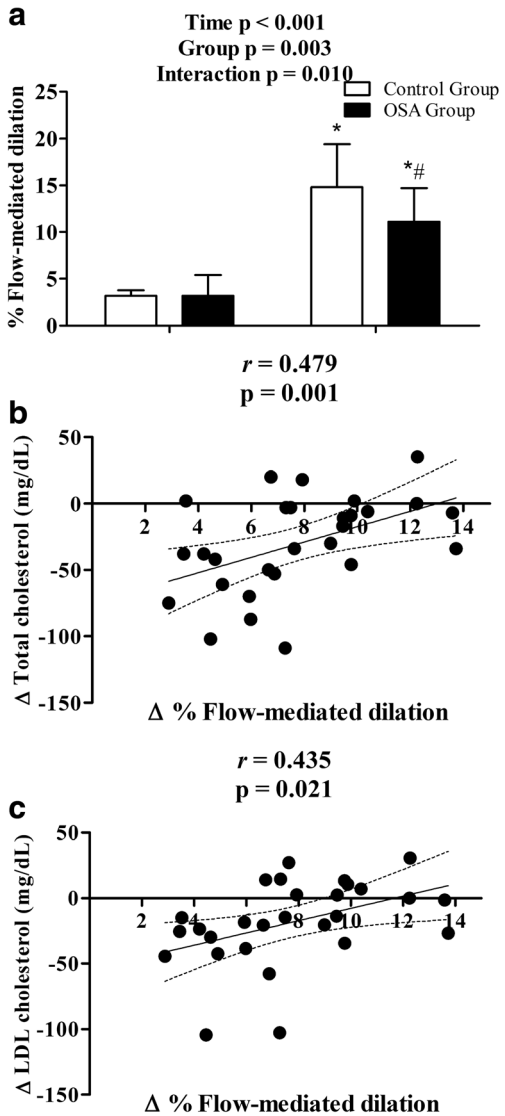

Fig. 2 Endothelial function of both groups (**a**) and correlations of OSA (obstructive sleep apnea-hypopnea syndrome) group Δ% FMD with total cholesterol (**b**) and LDLc (**c**). %FMD percentage flow-mediated dilation, deltas of variation (Δ = postoperative − preoperative), LDLc low density lipoprotein cholesterol

group, the variation deltas (Δ = postoperative − preoperative) of the %FMD correlated with the Δ of the total cholesterol ($r = 0.479$; $p = 0.001$) and with the Δ LDLc ($r = 0.435$; $p = 0.021$), and results are shown respectively in Fig. 2b, c. The control group did not correlate %FMD with anthropometric, physiological, and biochemical variables.

Discussion

The main result of this study shows that patients with OSA present an important improvement of endothelial function 6 months after bariatric surgery. This improvement in endothelial function is related to the improvement of total cholesterol and LDLc.

This study describes that after 6 months, RYGB patients already present an expected weight reduction, improved biochemical variables, endothelial function, and OSA. Sjostrom et al. [10] followed 4047 patients who underwent bariatric surgery ($n = 2010$) and who underwent clinical treatment for weight loss ($n = 2037$) for more than 10 years, where mortality

Table 4 Clinical evaluation for OSA (Berlin Questionnaire), Sleepiness Level (Epworth Excessive Sleepiness Scale), and Pittsburg Sleep Quality Index (PSQI-BR)

Variables	Pre	Post	*p*
Berlin positive	28	0	*< 0.001*
Berlin negative	0	28	
ESE Epworth	14.8	0.85	*< 0.001*
PSQI (good)	4	28	*< 0.001*
PSQI (bad)	3	0	
PSQI (w/sleep disturbance)	11	0	

Italic data highlights the significant data in the two-way ANOVA

The data were presented in absolute numbers and as an average. Berlin positive and Berlin negative (absolute numbers); *ESE Epworth*, Epworth Excessive Sleepiness Scale (scoring); *PSQI*, Pittsburg Sleep Quality Index (classification)

was higher with conservative treatment. In prospective study [9] with a 2-year follow-up of patients undergoing bariatric surgery (423) compared to patients with clinical treatment (733), the operated patients had better results in decreasing body mass index, waist/hip ratio, systolic blood pressure, heart rate, triglycerides, and LDLc, as well as higher increases in HDLc levels. Meta-analysis showed that after bariatric surgery, diabetes was controlled in 76.8% of patients, hyperlipidemia improved in 70%, and hypertension was controlled in 61.7% of the patients [22]. In this study, it was possible to demonstrate that in six postoperative months, besides the biochemical variables, the endothelial function and the OSA also improve.

The improvement in OSA symptoms demonstrated in this study is in accordance with previous studies [10, 21, 22, 33]. Buchwald et al. demonstrated in meta-analysis that after bariatric surgery, OSA was resolved in 85.7% of obese patients, which reinforces our results [22], but these favorable results take from 1 to 2 years. RYGB-induced weight loss may reduce the severity of sleep apnea through anatomical changes (increase in airway size, compliance, and changes in lung residual capacity) [1] and by the decrease in adiposity (both visceral and subcutaneous) that relieves physical pressure on the neck, upper airway, and respiratory system [34]. The results of the present study demonstrate the reduction of these physical and anthropometric variables (cervical circumference, abdominal circumference, percentage of fat mass, BMI, WHR). One of these variables is the increased neck diameter, since it is related to the increase in mortality [10] and the reduction of BMI and abdominal circumference, which represents, in part, the decrease of visceral fat, reducing intra-abdominal pressure, thus improving blood oxygenation, also reflecting a favorable effect on the cerebral respiratory center [33].

The results of this study demonstrate that 6 months after RYGB, there is improvement in endothelial function in patients with and without OSA. These results are corroborated by previous studies [15, 23]. Sturm et al. [23] followed patients undergoing bariatric surgery for 18 months and observed a reduction in glycemia, insulin, and HOMA and in the lipid profile and improvement in pressure levels and endothelial function. Gokce et al. [15] compared the effects in obese patients undergoing surgical treatment and clinical treatment and demonstrated that the improvement in endothelial function was more efficient in the surgically treated group. The weight loss obtained after bariatric surgery is associated with a reduction in the thickness of the carotid intima and media layers (an indirect factor of subclinical atherosclerosis) [35], which contributes to an improvement in endothelial function, a decrease in systemic arterial pressure, heart rate, diabetes mellitus, and hypercholesterolemia [36, 37]. Metabolic syndrome increases cardiovascular risk due to the development of atherosclerosis, and molecular mechanisms involve inflammation, oxidative stress, and endothelial dysfunction, which are indirectly reversed by bariatric surgery [21], weight reduction, improvement of lipid profile and glucose, and improvement in pressure levels, which were also demonstrated in this study.

The results of this study show that patients diagnosed with OSA 6 months after RYGB have lower endothelial function than patients without this syndrome. These patients present a greater sympathetic activation [18–20], and RYGB clinically reversed OSA, which possibly decreased sympathetic activity and decreased peripheral resistance, which would explain the reduction of systemic arterial pressure and a more evident heart rate reduction found in this group in the present study. In patients with severe OSA, the thickness of the carotid intima and media layers is larger, as well as plasma levels of inflammatory factors (IL-6 and hs-CRP); on the other hand, the %FMD is lower, suggesting that arterial endothelial damage and inflammation play important roles in the development of atherosclerosis in these patients [38]. Still, severe OSA is associated with endothelial dysfunction independently; visceral fat and adiponectin [16] and OSA severity are related to %FMD and hs-CRP [19], which reinforces that OSA interferes with endothelial dysfunction.

OSA leads to a longer exposure to factors that interfere with endothelial function such as sympathetic activation [18–20], oxidative stress [39], inflammatory markers action [19, 38], and subclinical atherosclerosis [38], which would result in the lower evolution of the endothelial function of these patients 6 months after surgery. It should be noted that in the present study, the endothelial function of these patients is directly related to total cholesterol and LDLc, which suggests that a better preoperative lipid profile favors the recovery of postoperative endothelial function, besides the fact that these patients present a more atherogenic profile than patients without OSA. The absences of measures of carotid artery intima-media thickness, inflammatory markers, oxidative stress, autonomic balance, and non-repetition of polysomnography (6 months after surgery) are limitations of the present study.

Conclusions

The main result of this study shows that weight loss after 6 months of RYGB surgery promotes the improvement of OSA symptoms, but despite this clinical evolution, these patients still present lower endothelial function than patients without apnea. The data show that the OSA compromises the health of the patients, as they may present a greater risk for the formation of atheroma plaques and acute myocardial infarction due to the lower endothelial function. Although the weight loss process is not yet complete 6 months after surgery, current results allow us to verify that bariatric surgery reduces comorbidities, among them OSA, which favors the evolution of clinical improvement and future quality of life of these patients.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Abbreviations OSA, obstructive sleep apnea-hypopnea syndrome; RYGB, Roux-en-Y gastric bypass; FMD, flow-mediated dilation

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