## CLINICAL RESEARCH

# Nutritional Profile of Patients Before and After Roux-en-Y Gastric Bypass: 3-Year Follow-up

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#### Abstract

*Background* Bariatric surgery is considered the most effective treatment for obesity class II and III. However, postoperative side effects may occur, such as nutritional deficiencies resulting from reduced gastric capacity and alterations in nutrient absorption along the gastrointestinal tract.

*Methods* A total of 170 patients (136 women and 34 men) submitted to Roux-en-Y gastric bypass (RYGB) between 2000 and 2005 were retrospectively assessed. Anthropometric and laboratory data were evaluated and the use of vitamin and mineral supplements, before and 1, 6, 12, 24, and 36 months following surgery, was assessed, as well.

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D. S. Casagrande Research on Research Group, Department of Surgery, Duke University Medical Center, 834 Marilee Glen Ct, Durham, NC, USA *Results* Mean excess weight loss at 24 and 36 months was  $81.5\pm19.2$  and  $78.5\pm20.8$  %, respectively. Anemia was present in 6.5 % of subjects prior to the surgery and increased to 33.5 % at 36 months. The levels of total cholesterol, low-density lipoprotein cholesterol, triglycerides, and glycemia were reduced, while high-density lipoprotein cholesterol was increased. Albumin and vitamin B12 levels showed no significant differences at the end of the study compared to the preoperative evaluation. Folic acid levels increased significantly during the follow-up. Almost 6 % of the patients had used standard vitamin and mineral supplements in the preoperative period and 72.4, 85.3, 74.7, 77.1,

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and 72.4 % at 1, 6, 12, 24, and 36 months following RYGB, respectively.

*Conclusions* Bariatric surgery is an effective treatment for long-term weight loss. However, nutritional deficiency is one of its side effects and should be properly diagnosed and handled, aimed at improving the patient's quality of life and preventing severe complications.

**Keywords** Morbid obesity · Bariatric surgery · Roux-en-Y gastric bypass · Nutritional deficiencies

## Introduction

Although bariatric surgery is considered the most effective treatment for patients with obesity class II and III and is associated with improved quality of life, side effects may occur in the postoperative period, such as nutritional deficiencies resulting from reduced gastric capacity and alterations in nutrient absorption across the gastrointestinal tract. The main nutritional complications in the period after Roux-en-Y gastric bypass (RYGB) surgery are deficiencies in protein, iron, vitamin B complex, liposoluble vitamins (A, D, E and K), calcium, and zinc. Although less frequent, copper, magnesium, and selenium deficiencies may also occur [1–5].

The routine use of multivitamins is a common practice after RYGB due to malabsorption. However, multivitamin supplementation alone may not be enough to prevent postoperative nutritional deficiencies [6]. The American Society for Metabolic and Bariatric Surgery (ASMBS) suggests that patients start using vitamin and mineral supplements as soon as they are discharged from the hospital, at doses twice the conventional amount, as well as a complementary supplementation for specific nutrients [7].

Considering the nutritional aspects after bariatric surgery, the nutritional assessment of patients submitted to this type of procedure is essential to ensure satisfactory results, prevent possible complications, and improve quality of life. The purpose of this study was to describe the nutritional and cardiometabolic profile of patients submitted to Rouxen-Y gastric bypass at an obesity surgery treatment center using anthropometric and biochemical parameters to assess the effect of vitamin and mineral supplements and to determine postoperative nutritional deficiencies.

#### Subjects and Methods

A descriptive and exploratory retrospective cohort study was conducted, with data collected from clinical records of patients submitted to RYGB, between 2000 and 2005, by a multidisciplinary care team. The patients' data representing before and 1, 6, 12, 24, and 36 months following surgery were analyzed.

Patients who did not have data from all assessments in their clinical records, women who got pregnant following surgery, and patients who were submitted to any additional surgical procedure within the analyzed period were excluded from the study. Out of a total of 480 patients, 170 were eligible to participate in the study.

The following variables were assessed: patient age (years); gender; follow-up time (months); body mass index (BMI, in kilograms per square meter); waist circumference (centimeters); initial excess weight; percentage of excess weight loss (%EWL); and biochemical tests (hematocrit, hemoglobin, iron, ferritin, folic acid, vitamin B12, albumin, fasting glucose, total cholesterol, triglycerides, low-density (LDL-c) and high-density lipoprotein cholesterol (HDL-c)). Regarding the use of vitamin and mineral supplements, the following were considered: multivitamin, iron, folic acid, and vitamin B12. Supplement dosage and composition were not analyzed.

A Filizola® digital scale with a capacity of 300 kg was used for weight measurement, with the patient wearing light clothes and no shoes; height was measured with a vertical Tonelli & Gomes® stadiometer with a capacity of 2.20 m. Waist circumference (WC) was measured using a non-elastic tape, defined as the largest waist diameter [8]. Patients with WC≥102 cm (men) and >88 cm (women) were considered at risk of increased metabolic complications, in accordance with the National Cholesterol Education Program (NCEP-ATPIII) [9]. BMI was calculated using weight (in kilograms) divided by the height squared (in square meter) and classified according to FAO/ WHO 1995 for adults [10]. Initial excess weight is the difference between the preoperative weight and the ideal weight, calculated using a BMI of 25 kg/m<sup>2</sup>. The %EWL in the postoperative period was calculated according to Deitel et al. [11] using the following formula: [(initial weight-current weight)  $\times$  100]/initial excess weight.

The biochemical tests were classified according to reference values from the Laboratory of Hospital São Lucas da PUCRS. The blood samples were drawn after a 12-h fast at the Clinical Pathology Laboratory of Hospital São Lucas da PUCRS. Ferritin, folic acid, and vitamin B12 were measured by chemiluminescence (Centaur, Siemens Medical Solutions Diagnostics, Tarrytown, NY). Fasting glucose, albumin, total cholesterol, HDL-c, triglycerides, and iron measurements were made using the Dry Chemistry method (Fusion 5.1, Johnson & Johnson Company, Rochester, NY). LDL-c was calculated using Friedewald's formula: [(total cholesterol-HDL-c)-(triglycerides/5)]. Hemoglobin was measured using the sodium lauryl sulfate method (Sysmex XT-2000, Sysmex Corporation, Kobe, Japan). Hematocrit was measured using the cumulative pulse height method (Sysmex XT-2000, Sysmex Corporation).

The project was submitted and approved by the Scientific and Research Ethics Committee of Hospital São Lucas da PUCRS (protocol 10/05146) and by the Research Ethics Committee of Instituto de Cardiologia do Rio Grande do Sul– Fundação Universitária de Cardiologia (protocol 4404/10).

#### **Statistical Analysis**

Statistical analysis was performed using SPSS (Statistical Package for the Social Sciences) software, version 17.0. Qualitative variables were described through absolute and relative frequencies, while quantitative variables were described using mean and standard deviation values or median and interquartile range values. The comparison of anthropometric and biochemical parameters in relation to assessment times was performed using analysis of variance (ANOVA), with the outline of repeated measurements, complemented by the Bonferroni multiple comparisons test, Tukey multiple comparisons test, *t* test, or Friedman's nonparametric test, when the variation coefficient was above 50 %.

The comparison of excess weight loss in relation to different body mass index categories and age ranges was performed using ANOVA, complemented by Tukey's multiple comparisons test. The comparison of excess weight loss in relation to diabetes status was performed using the *t* test. The significance level established for this study was 5 %.

#### Results

This study analyzed 170 patients before and 1, 6, 12, 24, and 36 months after RYGB. Prior to surgery, the sample was characterized by a mean age of  $39.5\pm10.8$  years, 80 % women, and a mean weight of  $130.7\pm27.9$  kg, BMI of  $48.8\pm9.0$  kg/m<sup>2</sup>, and an initial excess weight of  $63.8\pm25.5$  kg. %EWL at 1, 6, 12, 24, and 36 months following surgery were  $21.5\pm7.8$  % ( $13.0\pm6.1$  kg),  $58.3\pm13.6$  % ( $35.4\pm10.8$  kg),  $77.2\pm18.2$  % ( $46.1\pm13.3$  kg),  $81.5\pm19.2$  % ( $49.7\pm16.6$  kg), and  $78.5\pm20.8$  % ( $47.7\pm17.4$  kg), respectively. A progressive reduction in excess weight was observed until 24 months, with significant weight regain after this period. At the end of the follow-up, mean BMI reduction was 17.8 kg/m<sup>2</sup>. Figure 1 shows %EWL over the follow-up.

As shown in Fig. 2, at 36 months following RYGB, % EWL was significantly higher among subjects younger than 30 years (p < 0.05) compared to those older than 40 years ( $86.8 \pm 3.7$  versus 75.5 $\pm 3.6$  %). However, the only age range that did not show weight regain at the end of the follow-up is represented by patients older than 50 years.

There was a significant correlation between %EWL and the different BMI cutoff points along the postoperative periods. Patients with preoperative BMI under 40 kg/m<sup>2</sup> showed a significantly higher %EWL (p<0.001) compared

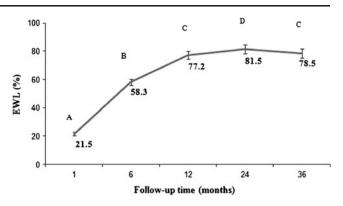


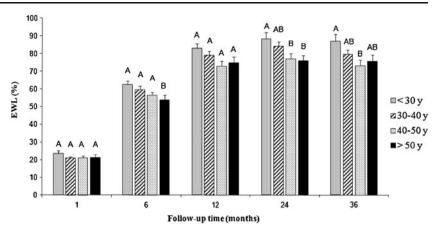
Fig. 1 Percentage distribution of excess weight loss (*EWL*) following RYGB. Percentages followed by *different letters* significantly differ by ANOVA using the outline of repeated measurements, complemented by the Bonferroni multiple comparisons test, at a significance level of 5 %

to those classified as superobese (>50 kg/m<sup>2</sup>) 36 months following surgery (93.9±4.4 versus 66.3±2.4 %). Figure 3 shows %EWL over the follow-up according to the different BMI ranges. Excess weight loss was significantly higher in non-diabetic subjects (p<0.05) starting in the sixth month (60.2±1.2 versus 52.9±2.5 %) until the end of the study (81.2±1.9 versus 70.0±3.1). Figure 4 shows %EWL in diabetic versus non-diabetic subjects along the follow-up.

The study showed waist circumference reduction until 12 months after RYGB, with no significant alteration after this period. The smallest mean value was obtained at 24 months following surgery, with 39.7 % (54) of women and 44.1 % (15) of men showing desirable values. At the end of the study, 38.2 % (13) of men had a waist circumference under 102 cm and 35.3 % (48) of women had a waist circumference under 88 cm.

In the biochemical analysis, hematocrit levels displayed a significant reduction 1 year following surgery, while hemoglobin and iron were reduced at 1 month postoperatively. However, ferritin concentration increased significantly 1 month following surgery when compared to other postoperative evaluations and decreased at 24 months following surgery when compared to the preoperative period.

Women with regular menstruation represented 66.2 % of the sample, and their hematocrit, hemoglobin, and ferritin levels were significantly lower (p<0.05) than the postmenopausal women in the sample in a majority of the assessment periods. In addition, women in the study had lower levels (p<0.05) in all hematologic parameters mentioned above, including iron, compared to men in the study. Vitamin B12 and folic acid showed the lowest mean values before RYGB, with significant increases at 1 and 12 months, respectively. Albumin levels did not show a statistically different change at any assessment time after surgery. A significant reduction was observed in fasting glucose and total cholesterol starting in the first month, and in triglycerides Fig. 2 Percentage distribution of excess weight loss (*EWL*) following RYGB according to age ranges. Percentages followed by *different letters* significantly differ, for each assessment period, by ANOVA, complemented by Tukey's multiple comparisons test, at a significance level of 5 %



and LDL-c levels starting in the sixth month. Meanwhile, HDL-c showed a reduction 1 month following surgery, with a significant increase in subsequent periods. This continued until the end of the follow-up. Table 1 shows the anthropometric and biochemical characteristics of the sample.

Regarding the classification of obesity, in the preoperative period and 1 month following surgery, 100 % of the patients had a level of obesity ( $\geq$ 30 kg/m<sup>2</sup>) that was reduced to 46.5 % by the 36th month. At 24 months, 60 % of the patients were no longer classified as obese, and at the end of the study, 16.5 % of the patients showed a BMI within the normal range (18.5–24.9 kg/m<sup>2</sup>). Table 2 shows the BMI classification according to the evaluation time.

Prior to surgery, 14.7 % of subjects presented with diabetes mellitus (DM), with disease remission at the end of the follow-up and a significant improvement of the lipid profile: recommended lipids levels were in 80.6 % of the patients for total cholesterol, 93.5 % for triglycerides, 58.8 % for LDL-c, and 91.7 % for HDL-c. Assessment at 24 months post-operative showed the highest prevalence of patients with values below the normal range for hematocrit (44.7 %) and hemoglobin (34.1 %), and the highest number of iron deficiency cases (17.1 %) was seen in the first month. Ferritin values below the normal range were seen in 5.3 % of subjects at the beginning of the study versus 23.5 % at the

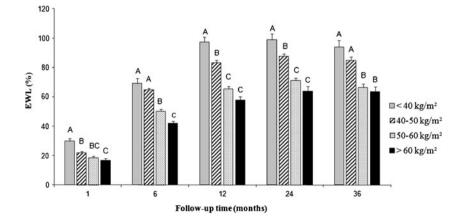
Fig. 3 Percentage distribution of excess weight loss (*EWL*) following RYGB according to BMI categories. Percentages followed by *different letters* significantly differ, for each assessment period, by ANOVA, complemented by Tukey's multiple comparisons test, at a significance level of 5 %

end, and low levels of folic acid were observed in 6.5 versus 0.6 %. The highest deficiencies of vitamin B12 (7.1 %) and albumin (5.9 %) were observed at the end of the study. Table 3 shows the alterations observed in biochemical tests.

With regard to vitamin and mineral supplementation, in the preoperative period, 10 (5.9 %) patients were taking a supplement, especially for iron, folic acid, and vitamin B12, compared to 123 (72.4 %) in the 1st month after RYGB, 145 (85.3 %) in the 6th month, 127 (74.7 %) in the 12th month, 131 (77.1 %) in the 24th month, and 123 (72.4 %) in the 36th month. Figure 2 shows the type of supplement taken according to the evaluation time (Fig. 5).

### Discussion

A successful bariatric surgery can be determined by weight loss of over 50 % of excess weight following surgery [12]. The results of excess weight loss were satisfactory and agreed with information provided in the literature, which reports maximum loss at 24 months after surgery [13–16]. In our sample, at 24 months postoperatively, 96.4 % of the patients had lost more than 50 % of their initial excess weight, falling to 92.8 % at the end of the follow-up. By the 36th month, there was a reduction in excess weight loss,



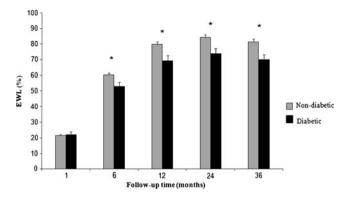


Fig. 4 Percentage distribution of excess weight loss (*EWL*) following RYGB, diabetic versus non-diabetic patients. \*t test: p < 0.05

with significant regain of 3 % of initial weight, when compared to 24 months postoperatively. O'Brien et al. [14], in a systematic review that analyzed medium-term and longterm weight loss after bariatric surgery, also found reduced excess weight loss starting at 36 months postoperatively (mean=62.5 versus 67.5 % at 24 months postoperatively), occurring gradually and progressively for up to 10 years (52.5 %) following surgery. However, Magro et al. [16] reported regain starting in the 48th month postoperatively, with a 4 % increase in initial BMI in this period. In another study, also conducted at our center, Barhouch et al. [15] reported that in the 60th postoperative month, there was an 8.7 % regain of initial weight, demonstrating a greater tendency for weight regain 5 years following surgery. Christou et al. [13] demonstrated that, despite the weight regain following surgery, the long-term mortality rate of 3.1 % remained low. Some factors described in the literature seem to be predictors of weight regain after bariatric surgery, such as dilation of the gastric reservoir and gastrojejunostomy, increased calorie intake of high glycemic index carbohydrates and fats, intolerance to red meat, hormonal alterations resulting from the adaptive process, binge eating, alcohol and drug consumption, and absence of postoperative multidisciplinary follow-up [15-18].

The preoperative biochemical evaluation of patient candidates for bariatric surgery is essential for early detection and correction of nutritional deficiencies to prevent possible side effects [19]. Protein deficiency is uncommon before surgery, ranging from 0 to 1.1 % [4, 20–22]. However, Ernst et al. [19] and Bavaresco et al. [23] found hypoalbuminemia in 12.5 and 15.6 % of obese patients, respectively, before surgery. After RYGB, protein deficiency may occur, with prevalence ranging from 0 to 13 %, especially in the second year following surgery [3], although it is more frequent in primarily malabsorptive procedures [3, 4, 22, 24]. A longterm study [25] that analyzed the nutritional profile of 75 patients 5 years following surgery found hypoalbuminemia in 5.6 % of the sample studied. Among the patients analyzed in our study, there was no significant reduction in albumin levels along the follow-up, and the number of individuals with deficiency increased from 1.2 % in the preoperative period to 5.9 % at 36 months postoperative, in agreement with the results of other studies [4, 20, 22]. The protein deficiency mechanism after RYGB involves multiple factors and is attributed to reduced protein intake, resulting from restricted gastric capacity and insufficient chewing combined with malabsorption and reduced secretion of digestive enzymes. The main consequences are muscle weakness, anemia, alopecia, and edema [3, 26, 27].

The prevalence of anemia, defined by reduced hemoglobin concentrations, ranges from 6.4 to 22 % in the preoperative period [20–22] and reaches 45-52 % two years following surgery [3], with the possibility of reaching 74 % over the long-term (mean of  $46\pm25$  months postoperative), with iron deficiency considered as the most common cause [24, 28]. In our study, 6.5 % of the patients presented with anemia prior to surgery, increasing to 33.5 % three years after RYGB, although all patients received instructions on iron supplementation. However, alterations in hematocrit and hemoglobin concentrations are late indicators of iron deficiency anemia [7]. Iron deficiency may be identified early through other markers, even with hemoglobin concentrations within the normal range [29].

In our sample, no significant reduction was observed in serum iron levels at the end of the study when compared to the preoperative period. A small increase in these concentrations was observed starting at 6 months following surgery, but it should be noted that, at our center, iron supplementation is offered to all patients with ferritin concentrations below 30 ng/mL to prevent low iron levels. A higher prevalence of iron deficiency was reported in other studies when compared to the results of our sample: Bavaresco et al. [23] and Toh et al. [22] found 12.2 and 15 % of obese subjects with iron deficiency prior to surgery, increasing to 14.6 and 21 %, respectively, 1 year after RYGB. Meanwhile, Flancbaum et al. [20] analyzed 362 patients and found 43.9 % with low concentrations of serum iron in the preoperative period. Two years following surgery, the prevalence of deficiency ranges from 15 to 60 % [30, 31], with long-term persistence [32].

Fertile women have a higher risk of developing iron deficiency anemia, a probability that may be as high as 51 % in the postoperative period due to menstrual bleeding. This finding is significant as fertile women represent more than 80 % of bariatric surgery candidates [7]. In our sample, premenopausal women showed significantly lower levels (p<0.05) in hematocrit and hemoglobin levels prior to surgery as well as in the 12-, 24-, and 36-month periods following surgery. We also recorded lower ferritin levels (p<0.00) in this group in all assessment periods. There were no significant differences in iron levels among premenopausal women.

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Variable	Preoperative	1 month	6 months	12 months	24 months	36 months	d
Weight (kg)	130.7A±27.9	$117.3B\pm 24.3$	95.3C±20.1	84.2D±18.7	$81.1E \pm 18.4$	83.0D±19.1	<0.001
BMI (kg/m <sup>2</sup> )	$48.8A{\pm}9.0$	$43.1B \pm 7.2$	35.6C±6.8	31.5D±6.4	$30.3E \pm 6.1$	$31.0D{\pm}6.3$	<0.001
WC (cm)	$128.6A \pm 22.4$	$120.0A \pm 17.1$	$103.0B \pm 15.9$	96.3C±15.5	92.8C±13.7	93.8C±15.2	<0.001
Hematocrit (%)	$40.1A \pm 2.9$	$39.9AB\pm3.0$	39.4AB±3.0	38.7B±3.5	$38.3B\pm 3.4$	$38.3B\pm4.1$	<0.001
Hemoglobin (g/dL)	$13.3A \pm 1.1$	12.1BC±1.1	13.0B±1.1	12.9BC±1.2	12.7BC±1.3	12.6C±1.5	<0.001
Iron (µg/dL)	$79.1A \pm 29.4$	$60.1B \pm 28.4$	$82.1A \pm 30.1$	$88.3A \pm 34.9$	$95.8A \pm 55.1$	$96.1A \pm 34.4$	<0.001
Ferritin (ng/mL) <sup>a</sup>	94.5AB (49.9–210.7)	178.5A (63.5–298.8)	96.4B (31.5–159.7)	69.6B (32.1–15.0)	35.6C (16.5–106.2)	34.0C (14.1–115.4)	<0.001
Folic Acid (ng/mL) <sup>a</sup>	8.1D (4.9–11.6)	9.6CD (6.0–13.3)	12.5BCD (7.9–16.0)	13.3ABC (8.7–19.6)	13.5AB (10.5–19.2)	14.6A (11.9–20.1)	<0.001
Vitamin B12 (pg/mL) <sup>a</sup>	407.0C (328.0-482.0)	635.0A (467.5–929.0)	459.0BC (350.5–618.0)	511.0B (336.5–859)	426.0BC (326.0–616.5)	450.0BC (350.0–627.5)	<0.001
Albumin (g/dL)	4.2A±0.4	$4.1A{\pm}0.4$	$4.2A\pm0.2$	$4.2A{\pm}0.4$	$4.1\mathrm{A}{\pm}0.3$	$4.1\mathrm{A}{\pm}0.3$	0.259
Glycemia (mg/dL)	$106.0A\pm22.9$	$97.6B{\pm}18.0$	89.5C±11.9	86.2C±10.1	85.8C±8.6	83.5C±8.2	<0.001
Cholesterol (mg/dL)	$204.4A \pm 41.8$	$181.6B \pm 41.3$	$173.8B\pm 29.6$	$175.4B\pm 35.5$	$172.4B\pm 35.5$	$176.7B\pm 34.3$	<0.001
Triglycerides (mg/dL) <sup>a</sup>	132.0A (84.0–183.5)	124.0A (97.5–168.5)	98.0B (78.5–124)	82.0BC (68.0–111.5)	74.0C (57.5–107.5)	75.0C (61.0–106.0)	<0.001
LDL-c (mg/dL)	$126.8A \pm 36.5$	113.1AB±34.1	103.0BC±26.2	$103.4BC \pm 31.4$	95.1C±28.7	$101.1BC \pm 32.1$	<0.001
HDL-c (mg/dL)	47.2C±9.3	$39.9D\pm9.9$	46.6C±7.2	52.1B±11.2	57.4A±12.3	58.7A±11.6	<0.001
Results are expressed as t post hoc Bonferroni's mu BMM body, mose index 10	Results are expressed as the mean $\pm$ SD or median (P25–P75). Mear post hoc Bonferroni's multiple comparisons test, at a significance BMM body mass index <i>WC</i> waist circumference <i>TDL</i> $\alpha$ lowed	25–P75). Mean values follo a significance level of 5 %	1 values followed by different letters significant level of 5 % ty linometein HDL a bigh density linometein	nificantly differ by ANOV	Results are expressed as the mean±SD or median (P25–P75). Mean values followed by different letters significantly differ by ANOVA using the outline of repeated measurements, complemented by post hoc Bonferroni's multiple comparisons test, at a significance level of 5 %	ted measurements, complem	ented by
<sup>a</sup> Median values followed	by different letters significan	ttly differ when using Friedr	nan's nonparametric test, con	uplemented by Friedman's	<sup>a</sup> Median values followed by different letters significantly differ when using Friedman's nonparametric test, complemented by Friedman's multiple comparisons test, at the significance level of 5 %	the significance level of 5 %	

Table 1 Anthropometric and biochemical characteristics of the sample before and after RYGB

BMI (kg/m <sup>2</sup> )	Preoperative		1 month		6 months		12 months		24 months		36 months	
	n	%	n	%	п	%	n	%	n	%	n	%
Normal (18.5–24.9)	_	_	-	-	2	1.2	22	12.9	27	15.9	28	16.5
Overweight (25-29.9)	_	-	_	_	30	17.6	70	41.2	75	44.1	63	37.1
Class I obesity (30-34.9)	1	0.6	17	10.0	63	37.1	34	20.0	37	21.8	38	22.4
Class II obesity (35-39.9)	23	13.5	44	25.9	30	17.6	30	17.6	22	12.9	28	16.5
Class III obesity (>40)	146	85.9	109	64.1	44	25.9	13	7.6	9	5.3	13	7.6

Table 2 BMI classification before and after RYGB

Results are expressed in number and percentage of patients

In our study, ferritin concentrations showed a significant reduction at 36 months after surgery if compared to the preoperative status, increasing from 5.3 to 23.5 % prevalence of deficiency at the end of the follow-up. Studies have reported between 2 and 24 % of patients with low ferritin levels before surgery [19–22]. Skroubis et al. [33] found low ferritin levels in 38 % of a sample of 79 subjects at 24 months following RYGB, more than twice the value found in our study (15.9 %). In this study, the authors observed a reduction in the number of patients with deficiency, from 44 % at 36 months to 25 % at 60 months postoperatively.

The increase in ferritin concentrations and the reduction in iron levels found in our sample in the first month following surgery indicate inflammatory reaction since ferritin, although an important iron reserve, is an acute-phase protein and an inflammatory marker [34]. However, at 6 months following surgery, reduced ferritin levels and increased serum iron were observed. This continued until the end of the study, in line with the results obtained by Drygalski et al. [35] at 3 months following surgery in a sample of 1,125 patients who showed continuous reductions in ferritin concentrations, from 87.5 ng/mL (95 % CI=75.2–99.7) in the preoperative period to 55.4 ng/mL (95 % CI=42.9–68.0) at the end of the study (24–48 months) and increased levels of serum iron, from 68.4  $\mu$ g/dL (95 % CI=66.8–70.0) in the preoperative period to 82.8  $\mu$ g/dL (95 % CI=76.4–88.7) at the end of the follow-up period. These results indicate reduced inflammation and increased bioavailability of serum iron following surgery.

Regarding folic acid, the low intake of foods that are sources of this vitamin and the lack of adherence to

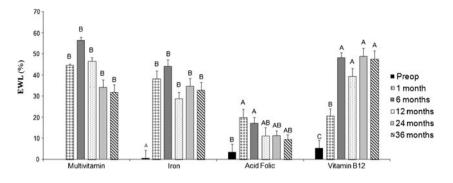
Table 3 Alterations in biochemical parameters before and after RYGB

Variable		Preoperative		1 month		6 months		12 months		24 months		36 months	
	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE	
Low hematocrit ( $^{\wedge}_{\bigcirc}$ <40 %; $\stackrel{\bigcirc}{_{\rightarrow}}$ <38 %)	20.0	6.9	29.4	6.4	31.8	6.3	32.9	6.3	44.7	5.7	43.5	5.8	< 0.001
Low hemoglobin ( $\sqrt[n]{<13}$ g/dL; $\stackrel{\bigcirc}{_{+}}<12$ g/dL)	6.5	7.4	20.6	6.8	21.8	6.8	18.8	6.9	34.1	6.2	33.5	6.3	< 0.001
Low iron ( $\sqrt[7]{<49}$ µg/dL; $\stackrel{\circ}{_+}$ <37 µg/dL)	5.9	7.5	17.1	7.0	5.9	7.5	1.2	7.7	8.8	7.3	8.2	7.3	< 0.001
Low ferritin (♂<22 ng/mL; ♀<10 ng/mL)	5.3	7.5	2.4	7.7	4.1	7.5	4.1	7.5	15.9	7.0	23.5	6.7	< 0.001
Low folic acid (<2.8 ng/mL)	6.5	7.4	2.9	7.5	4.7	7.5	1.2	7.7	1.8	7.7	0.6	7.7	0.009
Low vitamin B12 (<211 pg/mL)	2.9	7.5	1.2	7.7	3.5	7.5	3.5	7.5	5.3	7.5	7.1	7.4	0.036
Low albumin (<3.5 g/dL)	1.2	7.7	4.7	7.5	0.6	7.7	2.9	7.5	1.8	7.7	5.9	7.5	0.020
High glycemia (≥100, ≤125 mg/dL)	34.1	6.2	31.2	6.4	12.4	7.2	6.5	7.4	3.5	7.5	3.5	7.5	< 0.001
High glycemia (≥126 mg/dL)	14.7	7.1	6.5	7.4	1.8	7.7	-	_	1.8	7.7	-	_	< 0.001
High cholesterol (>200 mg/dL)	54.7	5.2	26.5	6.6	18.2	6.9	17.6	7.0	19.4	6.9	19.4	6.9	< 0.001
High triglycerides (>150 mg/dL)		6.0	39.4	6.0	10.6	7.3	11.2	7.2	10.0	7.3	6.5	7.4	< 0.001
High LDL-c (>100 mg/dL)		3.4	60.0	4.9	55.3	5.1	45.3	5.7	39.4	6.0	41.2	5.9	< 0.001
Low HDL-c ( $\Im$ <35 mg/dL; $\Im$ <45 mg/dL)		6.3	64.1	4.6	32.9	6.3	17.6	7.0	12.9	7.1	8.2	7.3	< 0.001

Results are expressed in percentage of patients and standard error of proportion. Reference values according to the laboratory of Hospital São Lucas PUCRS

LDL-c low-density lipoprotein, HDL-c high-density lipoprotein, SE standard error of proportion

Fig. 5 Percentage distribution of supplement use before and after RYGB. Percentages followed by *different letters* significantly differ, for each assessment period, by ANOVA using the outline of repeated measurements, complemented by the Bonferroni multiple comparisons test, at a significance level of 5 %



supplementation are considered the main causes of deficiency [7]. Folate absorption occurs mainly in the jejunum, but it may occur across the small intestine, and then, malabsorption is not considered the main reason of folic acid deficiency [18]. In the preoperative period, the prevalence of folic acid deficiency ranges from 0 to 24 % [21, 22, 36]. Madan et al. [36] reported deficiency in 15 % of patients 6 months following surgery, dropping to 11 % one year following surgery. On the other hand, Skroubis et al. [33] did not find folic acid deficiency in any of the 79 patients submitted to RYGB whose laboratory tests were analyzed before surgery and annually, for 5 years, following surgery.

Our study showed a gradual and significant increase in folic acid concentrations along the follow-up period, from 8.1 to 15.6 ng/mL, combined with a reduction in the number of patients with deficiency, from 6.5 % before surgery to 0.6 % at 36 months following RYGB. This was also reported by Brolin et al. [37] in a sample of 348 patients where the authors found a significant increase from  $5.5\pm3.4$  ng/dL before surgery to 9.2±5.2 ng/dL at assessment in the 36th month or later. In this study, patients who regularly took multivitamins showed a 31 % prevalence of folic acid deficiency versus a 52 % prevalence in those patients who did not take supplements. The results obtained in our sample can be explained by the regular use of multivitamins that contain folic acid in the postoperative period as well as the specific supplement offered according to the results of routine laboratory tests. In Brazil, since 2004, flours have to be fortified with iron and folic acid; every 100 g of wheat flour and corn flour should contain 4.2 mg iron and 150 mg folic acid [38]. According to the ASMBS, folic acid deficiency is preventable with 800 µg/day and corrected with 1,000 mg/day. However, concentrations above 1,000 mg/day should not be offered as they can mask a possible deficiency of vitamin B12 [7].

Vitamin B12 requires more attention after RYGB. It needs hydrochloric acid and the intrinsic factor produced by the gastric mucosa to be absorbed in the intestinal tract by the epithelial cells of the terminal ileum, where both processes are affected by the bypass [18]. The low intake of meat due to intolerance following surgery [27] is a factor that favors vitamin B12 deficiency; studies have reported that meat intake may significantly increase folic acid and vitamin B12 levels following surgery and should be widely encouraged [32]. Candidates for surgery have shown a prevalence of 0-13 % of vitamin B12 deficiency [20-22, 33, 36]. Madan et al. [36] found, 12 months following surgery, only 3 % of patients with abnormal levels for vitamin B12, similar to the result obtained in our sample. At 36 months, vitamin B12 deficiency range from 8 to 37 %, depending on the surgery technique [3, 24, 33]. In the long term, Skroubis et al. [33] observed a reduced prevalence, from 33 % at 48 months to 25 % at 60 months postoperative. Our study did not indicate any significant alteration in vitamin B12 levels before surgery when compared to the end of the follow-up despite a small increase in the number of patients with deficiency at 12 months following surgery, from 3.5 to 7.1 %. Other studies have demonstrated an increase in the prevalence of vitamin B12 one year following surgery [30, 37, 39] since before this period, body reserves are enough for the daily requirements of  $2-3 \mu g/$ day [2]. At our center, vitamin B12 supplementation starts at levels below 400 pg/mL. According to Brolin et al. [37], the use of multivitamins alone is not enough to prevent vitamin B12 deficiency following surgery.

Nowadays, postoperative vitamin and mineral supplementation creates many controversies regarding the frequency of replacement and quantity to be replaced as the bioavailability of vitamins and minerals following bariatric surgery has not been clarified. Colossi et al. [40] suggest that multivitamin supplementation should start 30 days following surgery and continue over the patient's lifetime. According to Gasteyger et al. [6], the use of multivitamins alone is, however, not enough to prevent nutritional deficiencies following RYGB as it does not fulfill the amount required of each specific micronutrient. All patients analyzed received vitamin and mineral supplements according to the levels described in each parameter evaluated.

Current evidence attests to the association of weight loss with reduced risk factors for developing comorbidities and with improved health conditions [41–46]. Prior to surgery, 34.1 % of subjects presented with impaired glucose tolerance (pre-diabetes), declining to 3.5 % three years after RYGB. Our study also showed, at the end of the follow-up period, type 2 DM (DM2) remission and a significant improvement in lipid profiles: recommended lipid levels were observed in 80.6 % of the patients for total cholesterol, 93.5 % for triglycerides, 58.8 % for LDL-c, and 91.7 % for HDL-c, similar to results found in the literature mentioned above.

Despite the weight regain observed in our sample 36 months following surgery, glycemia and lipid fractions remained unaltered. Buchwald et al. [43] examined in a meta-analysis the impact of bariatric surgery on DM2 and found that the clinical and laboratory manifestations of type 2 diabetes are resolved or improved in the greater majority of patients after bariatric surgery. Also, the proportion of patients with diabetes resolution or improvement was fairly constant at time points <2 years and 2 years or more after bariatric surgery. In another study with morbid and diabetic obese patients, the bypass effectively controlled DM2, a condition that persisted for more than 5 years following surgery [44].

The gastric bypass procedure was effective for weight reduction, glycemic control, and lipid profile improvement. Nutritional deficiencies observed in this study are expected following surgery and agree with data reported in the literature. The study attests to the importance of biochemical assessment and regular and long-term follow-up in these patients, as well as the effective use of vitamin and mineral supplements, in both the preoperative and postoperative periods to prevent or correct nutritional deficiencies and to avoid possible complications.

There were important limitations when carrying out this study since data were not prospectively collected and not aimed for the ends of this study. These limitations are inherent to any retrospective study.

**Conflict of Interest Statement** Blume, Boni, Casagrande, Rizzolli, Padoin, and Mottin declare that they have no conflicts of interest.

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