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ORIGINAL CONTRIBUTIONS

Effects of *Lactobacillus acidophilus* NCFM and *Bifidobacterium lactis* Bi-07 Supplementation on Nutritional and Metabolic Parameters in the Early Postoperative Period after Roux-en-Y Gastric Bypass: a Randomized, Double-Blind, Placebo-Controlled Trial

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Abstract

Studies have suggested that Roux-en-Y gastric bypass (RYGB) causes changes in the intestinal microbiota composition and function due to anatomical and physiological modifications. The role of probiotic supplementation after bariatric procedures remains to be determined.

Purpose The aim of this study was to investigate the effects of *Lactobacillus acidophilus* NCFM and *Bifidobacterium lactis* Bi-07 supplementation on nutritional and metabolic parameters after RYGB.

Materials and Methods This is a randomized, double-blind, placebo-controlled clinical trial. Patients were assigned to receive either a probiotic supplement (FloraVantage®) or placebo for three consecutive months, beginning 7 days after surgery. Anthropometric and biochemical indexes were evaluated in the preoperative period and at the end of the study.

Results Following RYGB, serum 25-OH vitamin D increased in both groups compared to baseline; however, this increase was significant only in the probiotic group ($p = 0.004$). Vitamin B_{12} levels tended to be higher in the probiotic group compared to the placebo group ($p = 0.063$), and triglyceride levels showed a significant reduction in the probiotic group only ($p < 0.001$). In addition, a significant reduction was observed in the anthropometric parameters and glycemic profile ($p < 0.05$) in both groups.

Conclusion Probiotic supplementation after RYGB improves the vitamin and lipid profile.

Keywords Roux-en-Y gastric bypass · Probiotics · Bariatric surgery

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Introduction

The worldwide obesity prevalence has expanded to pandemic proportions and is associated with considerable increases in cardiometabolic risks and morbidity and mortality levels [1–3]. Obesity is the result of a complex interaction between genetic and environmental factors, but many factors and mechanisms associated with its development are still not fully understood [4]. During the last few years, researchers have demonstrated that the intestinal microbiota is a relevant facto; e.g., individuals with obesity have differences in the diversity and richness of their intestinal microflora compared to individuals without overweight. These differences have been shown to contribute to higher energy extraction from the diet and metabolic pathways dysregulation [5].

Bariatric surgery is the most effective and durable treatment for morbid obesity, and Roux-en-Y gastric bypass (RYGB) is the most frequently performed procedure in Brazil [6–8]. The anatomical and physiological changes after RYGB induce a pH and oxygen increase in the intestinal lumen, which can dysregulate the microbiota by impairing the proliferation of microbial species important for maintaining the intestinal barrier and metabolic actions, such *Lactobacillus* and *Bifidobacterium* [9, 10].

Oral probiotics administration can be an effective strategy to achieve intestinal eubiosis and improve surgical results. The literature shows different hypotheses about the mechanisms related to supplementation with probiotics and weight loss, the metabolic profile, and the vitamin level improvements, such as increased expression of genes associated with fatty acid metabolism, insulin sensitivity, the expression of adiponectin and AMPK activation, improved micronutrient absorption, and a strengthened gut barrier [11–15].

Even though the scientific evidence has shown that bariatric surgery causes intestinal microbiota changes and alters metabolic and nutritional parameters [16], few studies have evaluated the effects of probiotic supplementation after RYGB or similar surgical techniques, such as one anastomosis gastric bypass-mini gastric bypass (OAGB-MGB). In the few available studies, *Lactobacillus* and *Bifidobacterium* strain supplementation has been associated with improvements in gastrointestinal symptoms, inflammatory profile, and vitamin levels. Although supplementation might have beneficial effects on metabolic parameters, increase weight loss, and improve body composition, the evidence is scarce and controversial [16–20].

This study was designed to identify the effects of the supplementation of *Lactobacillus acidophilus* NCFM and *Bifidobacterium lactis* Bi-07 on nutritional and metabolic parameters in the early postoperative period after RYGB.

Materials and Methods

This is a randomized, double-blind, placebo-controlled clinical trial conducted with patients undergoing RYGB in a public hospital in Curitiba, Brazil, from April 2018 to January 2019. This study was approved by the Research Ethics Committee of the Pontifical Catholic University of Paraná (PUCPR) (n° 4.252.808) and was registered in the Brazilian Clinical Trials Registry - REBEC (n°RBR-4x3gqp). The inclusion criteria were adult candidates for RYGB, with a body mass index (BMI) of ≥ 35 kg/m^2, who signed the informed consent form and did not use antibiotics 4 weeks prior to the beginning of the study. Patients who were submitted to other surgical techniques or reoperation, as well as those participants who had immediate postsurgical complications, ingested antibiotics during the study period, or had an adherence below 90% in the use of the tablets (inadequate use of the probiotics for more than nine consecutive days), were excluded.

Surgical Methods

All surgical procedures were performed by a single team of surgeons based on the standardization of the surgical procedure, which involves midline laparotomy, 100 cm of alimentary limb (Roux limb), jejuno-jejunal anastomosis 200 cm distal from the Treitz ligament, creation of a gastric pouch with a capacity of approximately 30 mL, antecolic gastrojejunal anastomosis, and a negative intraoperative leak test using methylene blue.

Randomization and Treatment

The investigators were responsible for the recruitment and randomization. Patient randomization was performed by a systematic 1:1 allocation process, with randomization codes being drawn to distribute the individuals into the placebo or probiotic group. The supplements were provided in similar packaging by a pharmacist who did not otherwise participate in the study. The participants and investigators were blinded to the product identification code. The probiotic used was FloraVantage® (5 billion *Lactobacillus acidophilus* NCFM® Strain, 5 billion *Bifidobacterium lactis Bi-07*®) from Bariatric Advantage (Aliso Viejo, CA, USA) and the placebo was an inert manipulated tablet consisting of starch and 190 mg of lactose. Both were chewable tablets, similar in physical appearance, taste, and color. Patients were instructed to keep the products in places without humidity or sun exposure and to take two of the chewable tablets per day, for 90 days, starting on the seventh postoperative day.

Follow-up Assessments

The first assessment was performed at the first visit, approximately 10 days before surgery. Follow-up assessments were

conducted at approximately 12 weeks postoperatively. According to the hospital's standard protocol, both groups received the same diet orientation and the same multivitamin and protein supplementation prescription. During the intervention period, adherence to the protocol was monitored weekly by phone calls and those who did not follow the protocol or presented with immediate postsurgical complications were excluded. Clinical and anthropometric assessments were performed at both visit times.

Clinical and Anthropometric Assessment

Anthropometric measurements included body weight (kg), height (m), BMI (kg/m^2), waist circumference (cm), percentage of excess weight loss (% EWL), body fat (kg and %), and lean mass (kg). BMI was calculated as body weight (kg)/height squared in meter (m^2), %EWL was calculated using the method described by Deitel et al. [21], and waist circumference was measured around the largest abdominal perimeter between the last rib and the iliac crest [22]. In addition, body composition assessment was performed using tetrapolar impedance analysis, according to the manufacturer's instructions (BIA - 450 Bioimpedance Analyzer, Biodynamics, Seattle, EUA).

Fasting glucose, total plasma cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglyceride levels were measured by a colorimetric enzymatic method (Vitros Fusion 5.1 Chemistry System Analyzer, Ortho Clinical Diagnostics, England, UK). The quantification of glycated hemoglobin (HbA1c) was performed according to the specifications of the HbA1c Reagent Kit (Vitros Chemistry Products; Vitros 5.1, Ortho Clinical Diagnostics, England, UK). The serum concentrations of vitamin B_{12}, folate, 25-hydroxy vitamin D, and fasting insulin were determined using an amplified chemiluminescence method (Vitros 3600, Ortho Clinical Diagnostics, England, UK). Insulin sensitivity (QUICKI) and insulin resistance (HOMA-IR) were estimated using the equations proposed by Katz et al. and Matthews et al., respectively [23, 24].

Clinical and sociodemographic data were collected from a nutritional anamnesis form and medical records. Physical activity practice and alcoholic consumption data were collected according to the World Health Organization's (WHO) criteria [25, 26].

Primary and Secondary Outcomes

The primary outcomes were nutritional status changes, including both the anthropometric data and the serum vitamin levels. Secondary outcomes were metabolic parameter improvements, such as glycemic and lipid markers.

Statistical Analysis

Independent *t* test and chi-square tests of homogeneity were used to verify differences between groups, considering the numerical and categorical variables, respectively. The probiotic effect on each response variable was analyzed and adjusted by age, sex, body mass index, time since diagnosis, and physical activity. Marginal regression models were fitted, and the interaction effect between the group and patient condition (pre or postoperative) was evaluated. A quasi-likelihood approach was used for fitting the regression models, aiming to lead with non-constant variance, non-normality, and correlated (paired) measures taken from each patient. Robust (sandwich) standard errors were calculated to prevent possible model misspecifications. The link function was chosen among two options: identity or logarithmic. In the first case, the effects are additive, whereas under the logarithmic link function, the effects are multiplicative. The best option for each response variable, among these two link functions, was selected based on the quasi AIC [27–30]. The results are presented as differences or the ratio of means. All analyses were performed using the IBM SPSS Statistics version 22.0 software (SPSS, Chicago, IL) and R software version 3.6.1 (GLP, Auckland, New Zealand), considering $P < 0.05$ for statistical significance.

Results

Characteristics of the Participants

From 110 patients initially selected, 9 were not eligible according to the inclusion criteria or refused to participate. Thus, 101 individuals were randomized into the placebo ($n = 50$) or probiotic ($n = 51$) group, and 71 (70.3%) completed the protocol (Fig. 1).

Participants in the placebo and probiotic groups had 99% ± 2.3 and 99% ± 2.4 of adherence to supplementation, respectively ($p = 0.652$). None of the participants reported adverse effects during the intervention.

The baseline demographic, clinical, and anthropometric variables analyzed were similar in both groups, except for age and hypertension, which were significantly higher in the placebo group, and total cholesterol levels, which were higher in the probiotic group (Tables 1 and 2; Figs. 2, 3, and 4).

Primary Outcomes

After 90 days of intervention, significant reductions were observed in the anthropometric parameters (weight, BMI, WC, body fat) in comparison to the baseline values ($p < 0.05$) in both groups (Table 2). Serum 25-OH vitamin D increased in both groups compared to baseline; however, this increase was

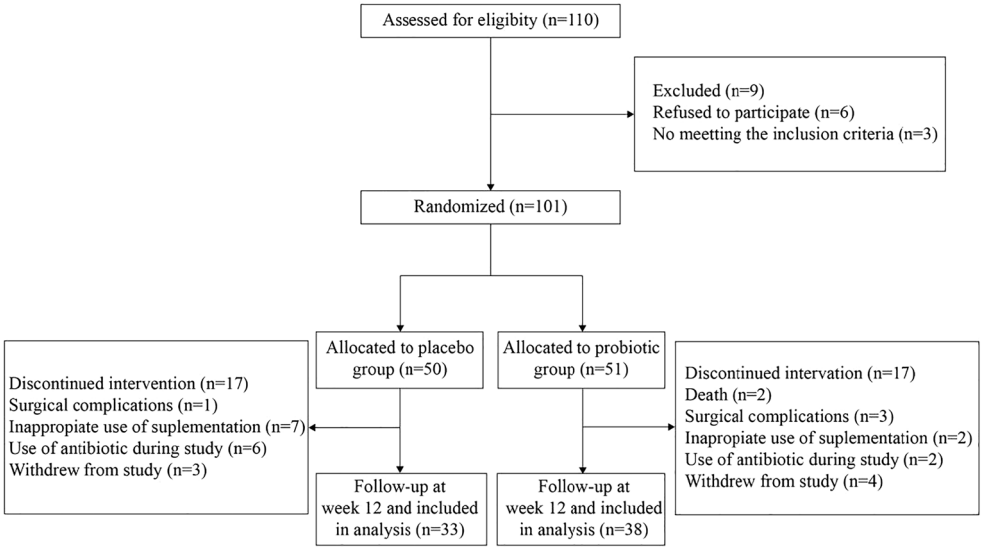


Fig. 1 The study consort flowchart

significant only in the probiotic group ($p = 0.004$). Vitamin B_{12} levels tended to be significantly higher in the probiotic group than in the placebo group ($p = 0.063$) (Fig. 2). The remaining anthropometric and nutritional variables were similar in both groups.

Secondary Outcomes

As shown in Figs. 3 and 4, statistically significant improvements in FBS, HbA1c, insulin, HOMA-IR, QUICKI, total cholesterol, HDL, and LDL were observed in both groups

Table 1 Clinical and demographic baseline characteristic

	Placebo group	Probiotic group	*p* value[a]
Age (years)*	43.80±10.40	37.10±11.10	0.010
Sex			
Male[#]	5 (15.20)	4 (10.50)	0.740
Female[#]	28 (84.80)	34 (89.50)	
Obesity diagnosis time (years)			
<5 years[#]	2 (6.10)	5 (13.20)	0.510
5–9 years[#]	9 (27.30)	6 (15.8)	
10–19 years[#]	12 (36.40)	17 (44.70)	
≥20 years[#]	10 (30.30)	10 (26.30)	
Physical activity[#]	16 (48.50)	20 (52.70)	0.670
Current smokers[#]	1 (3.00)	0 (0.00)	0.460
Drinking alcohol[#]	4 (12.10)	8 (21.10)	0.370
Previous comorbidities			
Arterial hypertension[#]	21 (63.60)	11 (28.90)	0.010
Diabetes type 2[#]	7 (21.20)	6 (15.80)	0.760
Dyslipidemia[#]	18 (54.40)	27 (71.10)	0.210
Hepatic steatosis[#]	25 (75.80)	26 (68.40)	0.600
Medications used			
Metformin[#]	6 (18.20)	6 (15.80)	1.000
Other oral hypoglycemic agents[#]	8 (24.20)	7 (18.40)	0.580
Proton pump inhibitors[#]	4 (12.10)	1 (2.60)	0.160
Dyslipidemia drugs[#]	3 (9.10)	3 (7.90)	1.000

*Values are represented by mean ± SD

[#] Values are represented by *n* (%)

[a] Between-group at the baseline, based on independent *t* test

Table 2 Anthropometric measurements at the baseline and after 12 weeks of supplementation

	Placebo group	Probiotic group	p_a	p_c
Weight (kg)				
Baseline*	120.36 (2.93)	122.24 (3.318)		0.550
12 weeks*	96.22 (2.68)	99.626 (2.76)		
p_b	<0.001	<0.001		
Change (95% CI)	0.79 (0.75; 0.84)	0.81 (0.76; 0.86)	0.647	
BMI (kg/m^2)				
Baseline*	44.31 (0.75)	43.95 (0.76)		0.630
12 weeks*	35.94 (0.73)	36.06 (0.66)		
p_a	< 0.001	< 0.001		
Change (95% CI)	0.80 (0.77; 0.83)	0.82 (0.78; 0.85)	0.461	
EWL (%)				
Baseline*	NA	NA		NA
12 weeks*	50.87 (12.73)	47.94 (9.96)	0.290	
p_a	NA	NA		
WC (cm)				
Baseline*	134.13 (2.55)	130.85 (2.47)		0.240
12 weeks*	114.99 (2.28)	115.93 (1.96)		
p_a	<0.001	<0.001		
Change (95% CI)	0.85 (0.82; 0.89)	0.88 (0.84; 0.92)	0.290	
Body Fat (kg)				
Baseline*	55.42 (2.73)	55.95 (2.75)		0.820
12 weeks*	35.81 (2.22)	37.14 (1.84)		
p_a	< 0.001	< 0.001		
Change (95% CI)	0.64 (0.58; 0.71)	0.66 (0.59; 0.74)	0.726	
Body Fat (%)				
Baseline*	46.71 (1.33)	46.18 (1.22)		0.720
12 weeks*	37.02 (1.65)	36.95 (1.24)		
p_a	< 0.001	< 0.001		
Change (95% CI)	− 9.65 (− 12.56; − 6.73)	− 9.22 (− 11.90; − 6.54)	0.836	
Lean body mass (kg)				
Baseline*	63.22 (1.87)	65.23 (1.81)		0.350
12 weeks*	59.60 (1.71)	62.52 (1.81)		
p_a	0.090	0.166		
Change (95% CI)	0.94 (0.88; 1.00)	0.95 (0.90; 1.01)	0.719	

BMI body mass index, *EWL (%)* percentage excess weight loss, *WC* waist circumference

*Values are represented by mean (SE)

[a] Between-group at the baseline, based on independent *t* test

[b] Time effect for each group based on the fitted regression model

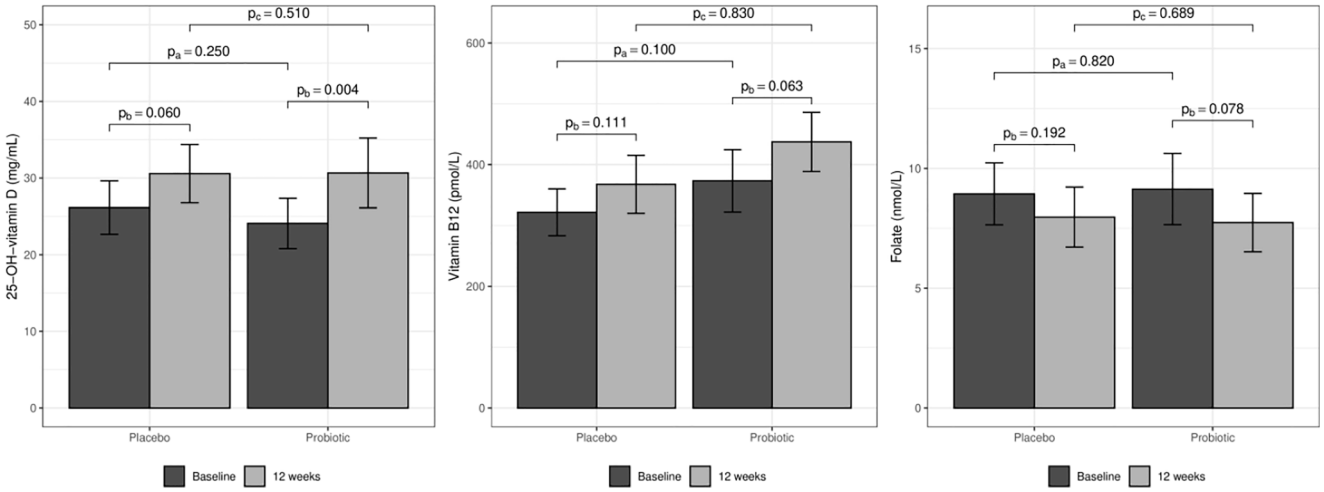
[c] Interaction effect based on the fitted regression model

regardless of the use of probiotics. However, triglyceride levels showed a significant reduction in the probiotic group only ($p < 0.001$).

Discussion

This is the first randomized, double-blind, and placebo-controlled study to test the effect of supplementation with *Lactobacillus acidophilus* NCFM combined with *Bifidobacterium lactis* Bi-07 on nutritional and metabolic parameters 3 months after RYGB.

The results of the present study showed significant improvements of anthropometric and metabolic parameters in both groups after RYGB, consistent with other clinical trials, confirming that bariatric surgery is a very effective therapy for weight loss management and metabolic improvement in morbidly obese individuals [31–34]. However, there was a



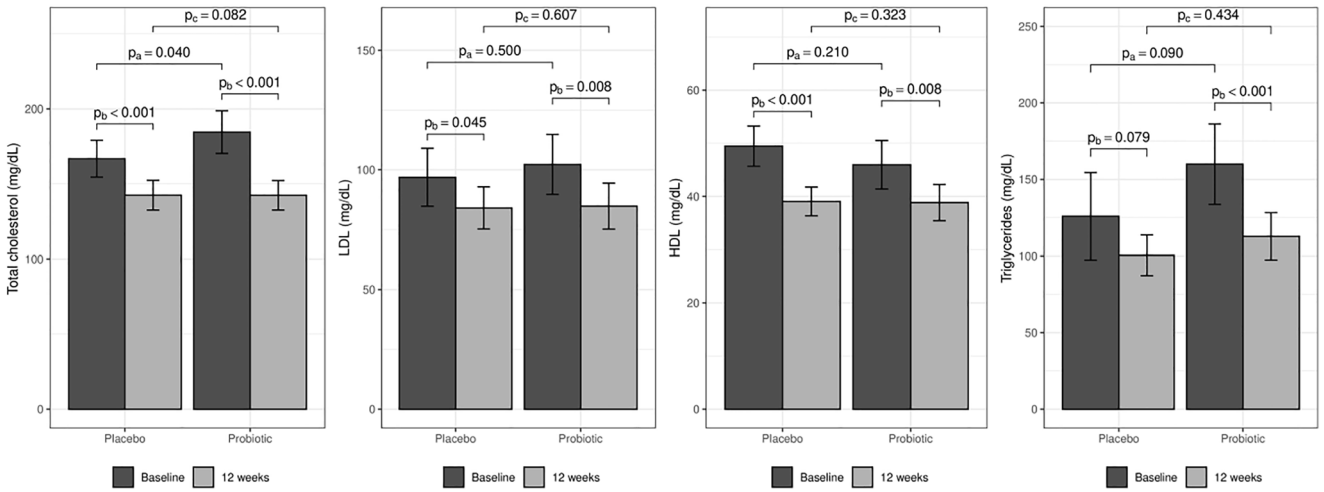
[a]Between-group at the baseline, based on independent t-test
[b]Time effect for each group based on the fitted regression model
[c] Interaction effect based on the fitted regression model

Fig. 2 Vitamin levels of patients in the probiotic and placebo group over the supplementation period. Values are represented by mean (SE)

significant improvement in the serum concentrations of 25-OH vitamin D and triglycerides and a trend for increased serum vitamin B_{12} levels in the probiotic group only.

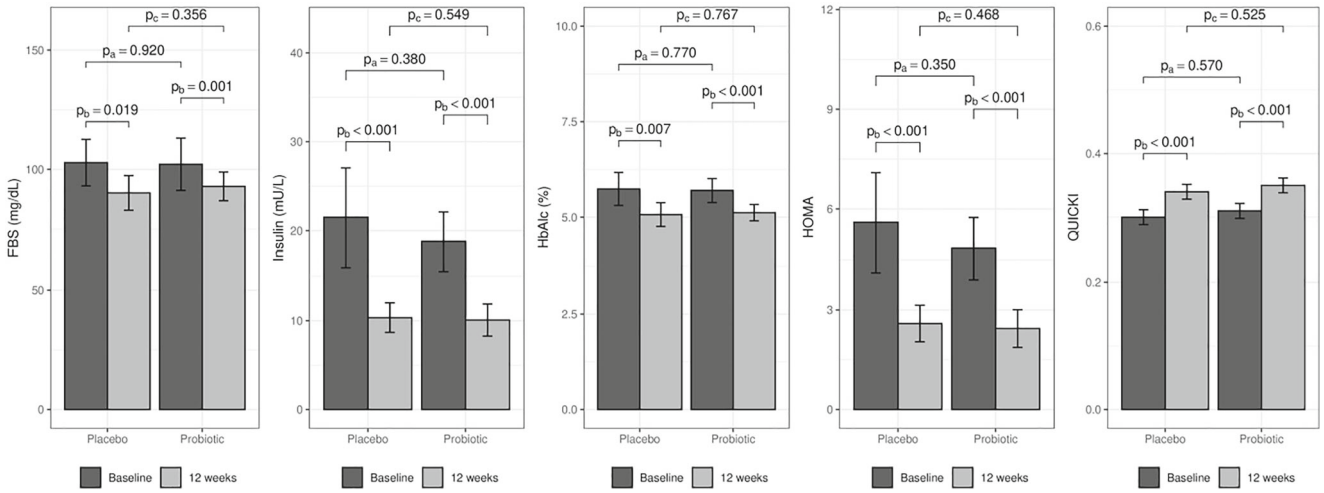
After RYGB, patients lose an average of 50–80% of their excess body weight, and they generally experience long-term comorbidity remission [35]. Dietary restriction, poor nutrient absorption, reduced ghrelin levels, and microbiota modifications all play important roles in the significant weight loss after surgery [36, 37]. In addition, the literature shows different mechanistic hypotheses related to probiotic supplementation and weight loss, such as increased expression of genes associated with fatty acid metabolism, resensitization to insulin, increased production of adiponectin, and AMPK activation [38, 39]. Karbashian et al. [19] showed a significant reduction in postoperative body weight and %EWL in patients who received *Lactobacillus* and *Bifidobacteria* supplementation. However, it is important to emphasize that in that study, probiotic supplementation began 4 weeks before OAGB-MGB and was continued for 12 weeks after the surgery. However, in agreement with our study, Woodard et al. [17] showed no statistically significant difference in %EWL after daily *Lactobacillus* species supplementation for 6 months after RYGB.

Microbiota-produced vitamins can contribute to serum vitamin levels, particularly vitamin B_{12}. However, after bariatric surgery, changes in the intestinal microbiota can modify the



[a]Between-group at the baseline, based on independent t-test
[b]Time effect for each group based on the fitted regression model
[c] Interaction effect based on the fitted regression model

Fig. 3 Lipid profile of patients in the probiotic and placebo group over supplementation period. *LDL* low-density lipoprotein cholesterol, *HDL* high-density lipoprotein cholesterol. Values are represented by mean (SE)



[a]Between-group at the baseline, based on independent t-test
[b]Time effect for each group based on the fitted regression model
[c] Interaction effect based on the fitted regression model

Fig. 4 Glycemic profile of patients in the probiotic and placebo group over the supplementation period. *FBS* fasting blood sugar, *HbAlc* glycated hemoglobin, *HOMA-IR* homeostasis model assessment of insulin resistance, *QUICKI* quantitative insulin check index. Values are represented by mean (SE)

microbial functional capacity, especially during the first 3 months after surgery [40]. Intestinal bacterial overgrowth, preoperative vitamin deficiency, and nonadherence to the use of multivitamin supplements may contribute to worsening serum vitamin B concentrations in the postoperative period [41].

Lactobacillus and *Bifidobacteria* supplementation may be an appropriate strategy to improve the status of vitamin B_{12} through intestinal microbiota modulation [14, 42]. Although supplementation did not present significant differences between the groups in this study, there was a tendency toward increased serum B_{12} concentration in the group supplemented with probiotics. Another study conducted with patients after RYGB who were supplemented with *Lactobacillus* species for 6 months has reported significantly higher postoperative vitamin B_{12} levels in the probiotic supplemented group [17].

In this study, the probiotic group showed a significant increase in vitamin D levels, corroborating the findings of Karbashian et al. [19]. This increase in vitamin D levels is expected after rapid weight loss due to the release of vitamin D from adipose tissue [43]. Also, recent studies have demonstrated that vitamin D status is associated with the intestinal microbiota composition and that probiotic treatment could increase 7-dehydrocholesterol synthesis and vitamin D receptor (VDR) expression and activity [44, 45].

Our results showed that probiotic supplementation after RYGB is effective in reducing triglycerides levels. Additionally, in absolute numbers, the average reduction of total cholesterol was almost 18 mg/dl (8.3%) greater in the probiotic group than in the placebo group. Several clinical trials have reported a total cholesterol level reduction without changes in the HDL and triglycerides levels in patients with hypercholesterolemia supplemented with probiotics [46–51]. Those studies included both lean and overweight patients, which may have contributed to the different findings with regard to the triglyceride levels. Although the mechanism of action is not well-known, it seems possible that the decrease in triglyceride levels may be due to the upregulation of apolipoprotein A-V (ApoA-V), bile acid receptor (FXR), and PPAR alpha expression in the plasma [46]. Some studies have suggested that probiotic supplementation produces a cholesterol-lowering effect through multiple mechanisms, including increased salt hydrolase expression by lactic acid bacteria, intracellular cholesterol transfer to the cellular surface, cholesterol precipitation by deconjugated bile salt hydrolysate, ferulic acid (FA) synthesis, which can inhibit enzymes involved in endogenous cholesterol production, and higher levels of production of short-chain fatty acids (SCFAs) that can block hepatic cholesterol synthesis [13, 52–55].

Despite evidence that changes in the intestinal microbiota and the use of probiotics can improve glycemic parameters in animal models and in humans, especially those with type 2 diabetes (T2D) [56], in the present study, the glucose profile and the insulin index did not show any significant improvement after probiotic supplementation. Another study that investigated the effects of probiotics on the glycemic profile after OAGB-MGB also found no significant differences between the control and probiotic groups [19]. These controversial results can be explained by study heterogeneity and many confounding factors, such as the use of drugs, individuality of the intestinal microbiota, BMI, type of surgical procedure, and specific strain effects.

The strengths of our study are the design (randomized, double-blind, placebo-controlled), the use of probiotics and placebo developed for this specific supplementation period

(both being chewable and palatable), and the high adherence achieved with the use of probiotics or placebo (over 99% supplementation adherence).

The main limitation of this study is the lack of an intestinal microbiota composition analysis. Randomization, use of the same surgical technique, a standardized diet and multivitamin supplementation, and weekly contact between researchers and participants to monitor their adherence to the research protocol were strategies used to minimize interindividual variability.

In conclusion, anthropometric and metabolic improvements were observed in both groups after RYGB. However, only the probiotic group showed significant improvements in serum 25-OH vitamin D and triglyceride levels. Additional studies, including a longer probiotic supplementation time, are needed to confirm these positive results.

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Compliance with Ethical Standards

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

Ethical Approval This study was approved by the Research Ethics Committee of the Pontifical Catholic University of Paraná (PUCPR) (n° 4.252.808) and was registered in the Brazilian Clinical Trials Registry - REBEC (n°RBR-4x3gqp). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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

Disclaimer CAPES had no influence on the writing, submission, or any other part of research formulation.

References

1. Gonzalez AB De, Phil D, Hartge P, Sc D, Cerhan JR, Ph D, et al. NIH Public Access. 2011;363:2211–9.
2. Lee WJ, Almulaifi A. Recent advances in bariatric/metabolic surgery: appraisal of clinical evidence. J Biomed Res. 2015;29:98–104.
3. Tsatsoulis A, Paschou SA. Metabolically healthy obesity: criteria, epidemiology, controversies, and consequences. Curr Obes Rep. 2020;9:109–20.
4. Hruby A, Hu FB. The epidemiology of obesity: a big picture. Pharmacoeconomics. 2015;33:673–89.
5. Mazloom K, Siddiqi I, Covasa M. Probiotics: how effective are they in the fight against obesity? Nutrients. 2019;11:1–24.
6. English WJ, Williams DB. Metabolic and bariatric surgery: an effective treatment option for obesity and cardiovascular disease. Prog Cardiovasc Dis. Elsevier Inc; 2018;61:253–69. Available from: https://doi.org/10.1016/j.pcad.2018.06.003.
7. Himpens J, Ramos A, Welbourn R, Dixon J, Frcp F, Kinsman ER, et al. The IFSO global registry report 2018. 4th ed. Oxfordshire: Dendrite Clinical Systems Ltd.; 2018. Available from: https://www.ifso.com/pdf/4th-ifso-global-registry-report-last-2018.pdf.
8. Sociedade Brasileira de Cirurgia Bariátrica e Metabólica (SBCBM). Cirurgia Bariátrica: Técnicas cirúrgicas. 2017. Available from: https://www.sbcbm.org.br/tecnicas-cirurgicas-bariatrica/
9. Bernardeau M, Vernoux JP, Henri-Dubernet S, et al. Safety assessment of dairy microorganisms: the Lactobacillus genus. Int J Food Microbiol. 2008;126:278–85.
10. Russell DA, Ross RP, Fitzgerald GF, et al. Metabolic activities and probiotic potential of bifidobacteria. Int J Food Microbiol. 2011;149:88–105.
11. Falcinelli S, Rodiles A, Hatef A, et al. Influence of probiotics administration on gut microbiota core a review on the effects on appetite control, glucose, and lipid metabolism. J Clin Gastroenterol. 2018;52:S50–6.
12. Kobyliak N, Conte C, Cammarota G, Haley AP, Styriak I, Gaspar L, et al. Probiotics in prevention and treatment of obesity: a critical view. Nutr Metab; 2016;13. Available from: https://doi.org/10.1186/s12986-016-0067-0.
13. Kumar M, Nagpal R, Kumar R, et al. Cholesterol-lowering probiotics as potential biotherapeutics for metabolic diseases. Exp Diabetes Res. 2012;2012:1–14.
14. Leblanc JG, Laiño JE, del Valle MJ, et al. B-group vitamin production by lactic acid bacteria - current knowledge and potential applications. J Appl Microbiol. 2011;111:1297–309.
15. Lee ES, Song EJ, Do NY, et al. Probiotics in human health and disease: from nutribiotics to pharmabiotics. J Microbiol. 2018;56:773–82.
16. Fernandes R, Beserra BTS, Mocellin MC, et al. Effects of prebiotic and synbiotic supplementation on inflammatory markers and anthropometric indices after Roux-en-Y gastric bypass. J Clin Gastroenterol. 2016;50:208–17.
17. Woodard GA, Encarnacion B, Downey JR, et al. Probiotics improve outcomes after roux-en-Y gastric bypass surgery: a prospective randomized trial. J Gastrointest Surg. 2009;13:1198–204.
18. Wagner NRF, Ramos MRZ, de Oliveira Carlos L, da Cruz MRR, Taconeli CA, Filho AJB, et al. Effects of probiotics supplementation on gastrointestinal symptoms and SIBO after Roux-en-Y gastric bypass: a prospective, randomized, double-blind, placebo-controlled trial. Obes Surg. 2020.
19. Karbaschian Z, Mokhtari Z, Pazouki A, et al. Probiotic supplementation in morbid obese patients undergoing one anastomosis gastric bypass-mini gastric bypass (OAGB-MGB) surgery: a randomized, double-blind, placebo-controlled, Clinical Trial. Obes Surg. 2018;28:2874–85.
20. Mokhtari Z, Karbaschian Z, Pazouki A, et al. The effects of probiotic supplements on blood markers of endotoxin and lipid peroxidation in patients undergoing gastric bypass surgery; a randomized, double-blind, placebo-controlled, clinical trial with 13 months follow-up. Obes Surg. 2019;29:1248–58.
21. Deitel M, Gawdat K, Melissas J. Reporting weight loss. Obes Surg. 2007;17:1275.
22. Associação Brasileira para o Estudo da Obesidade e Síndrome Metabólica (ABESO). Diretrizes Brasileiras de Obesidade [Internet]. São Paulo; 2016. Available from: https://abeso.org.br/wp-content/uploads/2019/12/Diretrizes-Download-Diretrizes-Brasileiras-de-Obesidade-2016.pdf.
23. Katz A, Nambi SS, Mather K, et al. Quantitative insulin sensitivity check index: a simple, accurate method for assessing insulin sensitivity in humans. J Clin Endocrinol Metab. 2000;85:2402–10.
24. Matthews DR, Hosker JP, Rudenski AS, et al. Homeostasis model assessment: insulin resistance and β-cell function from fasting

plasma glucose and insulin concentrations in man. Diabetologia. 1985;28:412–9.
25. World Health Organization. Physical Activity. 2018. Available from: https://www.who.int/news-room/fact-sheets/detail/physical-activity.
26. World Health Organization. Global Status Report on Alcohol 2004. 2004. Available from: https://www.who.int/substance_abuse/publications/globalstatusreportalcoholchapters/en/.
27. Halekoh U, Højsgaard S, Yan J. The R package geepack for generalized estimating equations. J Stat Softw. 2006;15:1–11.
28. Yan J, Fine J. Estimating equations for association structures. Stat Med. 2004;23:859–74.
29. Lenth R. Emmeans: Estimated Marginal Means, aka Least-Squares Means. 2018. Available from: https://cran.r-project.org/package=emmeans.
30. R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing. 2018. Available from: https://www.r-project.org/.
31. Adams TD, Davidson LE, Litwin SE, et al. Weight and metabolic outcomes 12 years after gastric bypass. N Engl J Med. 2017;377:1143–55.
32. Halperin F, Ding SA, Simonson DC, et al. Roux-en-Y gastric bypass surgery or lifestyle with intensive medical management in patients with type 2 diabetes: feasibility and 1-year results of a randomized clinical trial. JAMA Surg. 2014;149:716–26.
33. Schauer PR, Bhatt DL, Kirwan JP, et al. Bariatric surgery versus intensive medical therapy for diabetes - 5-year outcomes. N Engl J Med. 2017;376:641–51.
34. Adams TD, Pendleton RC, Strong MB, et al. Health outcomes of gastric bypass patients compared to nonsurgical, nonintervened severely obese. Obesity. 2010;18:121–30.
35. Cummings DE, Overduin J, Foster-Schubert KE. Gastric bypass for obesity: mechanisms of weight loss and diabetes resolution. J Clin Endocrinol Metab. 2004;89:2608–15.
36. Ionut V, Bergman RN. Mechanisms responsible for excess weight loss after bariatric surgery. J Diabetes Sci Technol. 2011;5:1263–82.
37. Ulker I, Yildiran H. The effects of bariatric surgery on gut microbiota in patients with obesity: a review of the literature. Biosci Microbiota Food Health. 2019;38:3–9.
38. Kim SW, Park KY, Kim B, Kim E, Hyun CK. Lactobacillus rhamnosus GG improves insulin sensitivity and reduces adiposity in high-fat diet-fed mice through enhancement of adiponectin production. Biochem Biophys Res Commun. 2013;431:258–63. Available from: https://doi.org/10.1016/j.bbrc.2012.12.121.
39. Rouxinol-Dias AL, Pinto AR, Janeiro C, Rodrigues D, Moreira M, Dias J, et al. Probiotics for the control of obesity - its effect on weight change. Porto Biomed J. PBJ-Associação Porto Biomedical/Porto Biomedical Society; 2016;1:12–24. Available from: https://doi.org/10.1016/j.pbj.2016.03.005.
40. Ciobârcă DCAF, Copăescu C, Miere DCG. Bariatric surgery in obesity : effects on gut microbiota and micronutrient status. Nutrients. 2020;12:235.
41. Patel JJ, Mundi MS, Hurt RT, et al. Micronutrient deficiencies after bariatric surgery: an emphasis on vitamins and trace minerals. Nutr Clin Pract. 2017;32:471–80.
42. Castañeda Guillot C. Probiotics: an update. Rev Cubana Pediatr. Sociedade Brasileira de Pediatria; 2018;90:286–98. Available from: https://doi.org/10.1016/j.jpedp.2014.08.006.
43. Mason C, Xiao L, Imayama I, et al. Effects of weight loss on serum vitamin D in postmenopausal women. Am J Clin Nutr. 2011;94:95–103.
44. Shang M, Sun J. Vitamin D/VDR, probiotics, and gastrointestinal diseases. Curr Med Chem. 2016;24:876–87.
45. Jones ML, Martoni CJ, Prakash S. Oral supplementation with probiotic L. reuteri NCIMB 30242 increases mean circulating 25-hydroxyvitamin D: a post hoc analysis of a randomized controlled trial. J Clin Endocrinol Metab. 2013;98:2944–51.
46. Mo R, Zhang X, Yang Y. Effect of probiotics on lipid profiles in hypercholesterolaemic adults: a meta-analysis of randomized controlled trials. Med Clin (Barc). Elsevier España, S.L.U.; 2019;152:473–81. Available from: https://doi.org/10.1016/j.medcli.2018.09.007.
47. Fuentes MC, Lajo T, Carrión JM, et al. Cholesterol-lowering efficacy of Lactobacillus plantarum CECT 7527, 7528 and 7529 in hypercholesterolaemic adults. Br J Nutr. 2013;109:1866–72.
48. Choi ID, Kim SH, Jeong JW, et al. Triglyceride-lowering effects of two probiotics, Lactobacillus plantarum KY1032 and Lactobacillus curvatus HY7601, in a rat model of high-fat diet-induced hypertriglyceridemia. J Microbiol Biotechnol. 2015;26:483–7.
49. Tonucci LB, Olbrich dos Santos KM, Licursi de Oliveira L, Rocha Ribeiro SM, Duarte Martino HS. Clinical application of probiotics in type 2 diabetes mellitus: a randomized, double-blind, placebo-controlled study. Clin Nutr. Elsevier Ltd; 2017;36:85–92. Available from: https://doi.org/10.1016/j.clnu.2015.11.011.
50. Pourrajab B, Fatahi S, Dehnad A, Kord Varkaneh H, Shidfar F. The impact of probiotic yogurt consumption on lipid profiles in subjects with mild to moderate hypercholesterolemia: a systematic review and meta-analysis of randomized controlled trials. Nutr Metab Cardiovasc Dis. The societies SID, SISA and SINU and the Department of Clinical Medicine and Surgery at Federico II University in Italy; 2020;30:11–22. Available from: https://doi.org/10.1016/j.numecd.2019.10.001
51. Jiang J, Wu C, Zhang C, Zhao J, Yu L, Zhang H, et al. Effects of probiotic supplementation on cardiovascular risk factors in hypercholesterolemia: a systematic review and meta-analysis of randomized clinical trial. J Funct Foods. Elsevier; 2020;74:104177. Available from: https://doi.org/10.1016/j.jff.2020.104177
52. Klaver FAM, Van der Meer R. The assumed assimilation of cholesterol by lactobacilli and Bifidobacterium bifidum is due to their bile salt-deconjugating activity. Appl Environ Microbiol. 1993;59:1120–4.
53. Xie N, Cui Y, Yin YN, Zhao X, Yang JW, Wang ZG, et al. Effects of two Lactobacillus strains on lipid metabolism and intestinal microflora in rats fed a high-cholesterol diet. BMC Complement Altern Med. BioMed Central Ltd; 2011;11:53. Available from: http://www.biomedcentral.com/1472-6882/11/53.
54. Kimoto H, Ohmomo S, Okamoto T. Cholesterol removal from media by lactococci. J Dairy Sci. Elsevier; 2002;85:3182–8.
55. Tomaro-Duchesneau C, Jones ML, Shah D, et al. Cholesterol assimilation by Lactobacillus probiotic bacteria: an in vitro investigation. Biomed Res Int. 2014;2014:1–9.
56. Yao K, Zeng L, He Q, et al. Effect of probiotics on glucose and lipid metabolism in type 2 diabetes mellitus: a meta-analysis of 12 randomized controlled trials. Med Sci Monit. 2017;23:3044–30453.

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