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ORIGINAL CONTRIBUTIONS

Metabolic Changes Up to 10 years After Gastric Bypass

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Abstract

Objective The aim of this study was to investigate the lipid and glycemic profiles of patients up to 10 years after Roux-en-Y gastric bypass.

Method A retrospective, longitudinal study was conducted at a multidisciplinary center for the treatment of obesity in the state of São Paulo, Brazil. The study included 150 patients submitted to unbanded laparoscopic Roux-en-Y gastric bypass. The metabolic profile included total cholesterol and fractions, triglycerides, and fasting glucose. The patients were examined before and 3, 6, 12, 24, 48, 72, 96, and 120 months after surgery. Statistical analyses included the generalized estimating equations (GEE) and the Wilcoxon test at a significance level of 5%.

Results All postoperative fasting glucose, total cholesterol, and triglyceride ($p < 0.0001$) test results were significantly lower than the preoperative test results. Low-density lipoprotein cholesterol (LDL-c) differed significantly in all but the 120-month follow-up ($p = 0.0129$). High-density lipoprotein cholesterol (HDL-c) was significantly higher 12, 24, 48, and 72 months after surgery ($p < 0.001$) and also 120 months after surgery ($p = 0.0002$).

Conclusion Gastric bypass promoted the control of metabolic diseases inherent to obesity as long as 10 years after surgery.

Keywords Gastric bypass · Metabolic changes · Lipid profile · Glycemia

Introduction

Morbid obesity is considered a chronic disease with severe metabolic consequences, such as hypertriglyceridemia, hypercholesterolemia, and diabetes, all known risk factors for cardiovascular diseases [1].

Successful bariatric surgery outcomes involve important metabolic changes, all of which have been extensively reported in the literature [2–4]. Many studies have demonstrated the positive metabolic impact of bariatric surgery on patients' lipid profile and blood glucose [5–8].

Gastric bypass promotes hormonal changes that improve or even lead to complete remission of diabetes mellitus type 2 because of the various weight loss mechanisms involved, significant improvement of glucose homeostasis, and higher levels of insulin, glucagon-like peptide-1 (GLP_1), and peptide YY (PYY) [9].

Recent studies [5–9] and meta-analyses [2, 5] have reported that the weight loss secondary to gastric bypass significantly improved patients' lipoprotein profile, with significant reduction of low-density lipoprotein cholesterol (LDL-c) and triglycerides and significant increase of high-density lipoprotein cholesterol (HDL-c).

In a recent meta-analysis, Buchwald et al. [2] reported that 84% of the diabetic patients submitted to gastric bypass were no longer diabetic, and 33.6 to 76.7% of

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dyslipidemic patients were no longer dyslipidemic, despite the difficulties associated with following gastric bypass patients.

In a meta-analysis published in 2016, Heffron et al. [5] discussed the impact of different surgery techniques on serum lipids.

Given the various studies demonstrating the metabolic impact of bariatric surgery and the need of long-term assessment, the objective of the present study was to investigate the lipid and glycemic profiles of patients as long as 10 years after Roux-en-Y gastric bypass.

Method

Description and Characterization of the Study Subjects, Data Collection, and Ethics Approval

The study had a retrospective and longitudinal design. The study population consisted of 150 adults submitted to laparoscopic Roux-en-Y gastric bypass at the obesity service of a private clinic in the state of São Paulo, Brazil, from 2005 to 2015. Data were collected from the patients' medical and nutritional records kept by the institution. The study data, routinely recorded in the medical records, included gender, age, surgery date, surgery technique, blood glucose, total cholesterol, LDL-c, HDL-c, and triglycerides. This study only began after approval of the Research Ethics Committee of the Pontifical Catholic University of Campinas, SP, Brazil, under protocol number 1.132.168.

Inclusion and Exclusion Criteria

The inclusion criteria were as follows: being adult, having undergone only unbanded, laparoscopic vertical gastroplasty and Roux-en-Y gastric bypass and having attended the medical and nutritional follow-ups regularly. The patients submitted to other surgery techniques or who did not attend the medical and nutritional follow-ups regularly in the first year after the Roux-en-Y gastric bypass were excluded.

Methodological Procedures

Surgical Technique

All study patients were submitted to unbanded, laparoscopic vertical gastroplasty and Roux-en-Y gastric bypass [10, 11].

Study Variables

A data collection form created specifically for this study collected the following data: patient identification data, gender, age, surgery date, and the following test results: fasting glucose, total cholesterol, LDL-c, HDL-c, and triglycerides. The data were collected preoperatively and 3, 6, and 12 months after surgery, and 2, 4, 6, 8, and 10 years after surgery. All the laboratory tests described above were requested to all the patients submitted to surgical procedure as part of the assistance protocol and recorded in the patients' medical records. Due to the absence of complete and accurate records and losses to follow-up, the number of patients assessed at each follow-up occasion varied.

The biochemical tests were assessed and interpreted based on internationally recognized and validated parameters. Hence, diabetes mellitus was diagnosed as recommended by the American Society of Diabetes [12] as follows: hypoglycemia (< 70 mg/dl), normal blood glucose level (70–99 mg/dl), diabetes mellitus (≥ 126 mg/dl), and high fasting blood glucose (100–125 mg/dl). Dyslipidemia was diagnosed as recommended by the Brazilian Guidelines for Dyslipidemia and Prevention of Atherosclerosis of 2013, [13] as described below:

	Cholesterol (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	Triglycerides (mg/dl)
Excellent			< 100	
Desirable	< 200	> 60	100–129	< 150
Borderline	200–239		130–159	150–200
High	≥ 240		160–189	200–499
Very high			≥ 190	≥ 500
Low		< 40		

Statistical Analyses

The data were first tabulated in the software Excel[R], and the statistical analyses were performed by the software SAS [14]. The Wilcoxon test [15] assessed related samples and compared the values of the two assessments. Only patients with data for the two compared assessments were included.

The generalized estimating equations [16] (GEEs) analyzed the occurrence of changes in the proportions of biochemical tests over time, given that this method is the most suitable for treating categorical data with measurements repeated over time. The GEEs take into account the correlation between repeated measurements. The analysis used the GENMOD procedure of the SAS statistical package and the command repeated to model the intra-individual covariance structure. The models used the logit function, binomial distribution, and non-structured correlation [16]. The significance level was set at 5% for all statistical tests.

Results

Table 1 shows the total cholesterol, LDL-c, HDL-c, triglyceride, and fasting blood glucose test results, classified according to the reference values.

Preoperatively, 24 (16%) patients had high total cholesterol. LDL-c was high or very high in 18 (13.96%) patients, HDL-c was low in 33 (24.63%) patients, and triglycerides were high in 27 (19.28%) patients (Table 1).

The preoperative fasting blood glucose of 35 (23.97%) patients was high, and 16 (10.96%) patients had diabetes mellitus (Table 1).

Six months after the surgery, 63 (91.30%), 45 (68.18%), and 61 (95.3%) patients had desirable total cholesterol level, excellent LDL-c level, and desirable triglyceride level, respectively. HDL-c was normal in 51 (77.3%) patients, and blood glucose was normal in 65 (87.80%) patients (Table 1).

Twenty-four months after gastric bypass, 88 (83.0%), 66 (66.0%), and 97 (94.1%) patients had desirable total cholesterol level, excellent LDL-c level, and desirable triglyceride level, respectively. HDL-c was normal in 101 (98.1%) patients, and blood glucose was normal in 98 (89.09%) patients (Table 1).

In the 72-, 96-, and 120-month follow-ups, 55 (83.30%), 40 (83.30%), and 33 (82.50%) patients, respectively, had desirable total cholesterol level; 40 (62.50%), 26 (57.80%), and 23 (57.50%) patients, respectively, had excellent LDL-c level; 61 (93.85%), 43 (91.4%), and 37 (92.50%) patients, respectively, had normal HDL-c level; 57 (91.94%), 43 (89.50%), and 34 (85.00%) patients, respectively, had desirable triglyceride level; and 59 (86.76%), 36 (76.69%), and 32 (78.05%) patients, respectively, had normal fasting blood glucose level (Table 1).

The Wilcoxon test for related samples (Table 2) compared total cholesterol, LDL-c, HDL-c, triglycerides, and blood glucose over time. Only patients with these test results in the two compared occasions were included. The test results 12, 24, 48, 72, 96, and 120 months after the surgery were compared with those before surgery.

Blood glucose, total cholesterol, and triglycerides ($p < 0.0001$) in all postoperative follow-ups were significantly lower than the respective preoperative values (Table 2). LDL-c had also decreased significantly in all but the 120-month follow-up ($p = 0.0129$). HDL-c was significantly higher 12, 24, 48, and 72 months after surgery, with $p < 0.001$, and 120 months after surgery, with $p = 0.0002$ (Table 2).

Discussion

Gastric bypass is a surgery technique with proven metabolic effects [2, 4–7, 10]. The metabolic concept was incorporated to bariatric surgery some years ago given the importance that the procedure gained in the treatment of chronic diseases, such as diabetes, hypertension, and dyslipidemia [17].

The main focus of this retrospective, longitudinal study was to assess the lipid and blood glucose profiles on different occasions up to 10 years after surgery and compare the test results with the preoperative test results and thereby verify whether those profiles indeed improve after gastric bypass. The exams concerning metabolic profile were routinely requested to all patients who had undergone gastric bypass, had medical and nutritional follow-up, and had been registered in the medical records. The data studied were collected from the records previously described. The loss of the follow-up and the absence of complete data records were the main limiting factor of this study. The loss of the follow-ups refers to patients who did not return within the period set by the team; it explains the decrease in the sample size for some analyses throughout the period. Another limiting factor of this study was the incomplete records of all the laboratory tests; it also explains the different data outcome at each follow-up occasion. It is important to point out that all the patients with medical and nutritional follow-up were periodically requested to carry out laboratory tests although the results were not properly registered in the medical records by the team responsible for them. This fact, along the 10-year follow-up, explains the different findings in the laboratory tests at each follow-up occasion.

Blume et al. [18] assessed the nutritional profile of patients after Roux-en-Y gastric bypass and found that total cholesterol, LDL-c, triglyceride, and blood glucose levels decreased and that HDL-c increased. The present study found similar results for total cholesterol, LDL-c, HDL-c, blood glucose, and triglycerides. In all study periods, the lipid profile and fasting blood glucose were significantly lower, and HDL-c was significantly higher than preoperatively.

In a recent meta-analysis on changes in the lipid profile of bariatric surgery patients, Heffron et al. [5] found, as the primary outcome, that blood lipid levels changed from the beginning until 1 year after surgery, evidenced by significant decreases in the levels of total cholesterol, LDL-c, and triglycerides and a significant increase in the level of HDL-c ($p < 0.00001$), demonstrating the importance of the surgery technique for the metabolic benefits. Gastric bypass achieved better metabolic outcomes than other techniques. All patients in the present study sample had undergone gastric bypass.

An important differential of the present study was the assessment of biochemical parameters over a 10-year follow-up period with clinical outcome and important results regarding the lipid and blood glucose profiles of the study sample. These profiles are considered significant markers of cardiovascular risk.

The mechanisms involved in the improvement of the lipid and blood glucose profiles after gastric bypass are complex and include, in addition to the dietary changes associated with

Table 1 Prevalence of hypercholesterolemia, hypertriglyceridemia, and diabetes mellitus in patients up to 10 years after Roux-en-Y gastric bypass

Time	Preoperative		3 months		6 months		12 months		24 months		48 months		72 months		96 months		120 months	
Tests	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%
	Total cholesterol* ($p < 0.0001$)																	
Desirable	86	57.33	71	83.53	63	91.30	100	90.09	88	83.02	70	76.92	55	83.33	40	83.33	33	82.50
Borderline	40	26.67	11	12.94	5	7.25	11	9.91	15	14.15	16	17.58	10	15.15	6	12.50	7	17.50
High	24	16.0	3	3.53	1	1.45	–	–	3	2.83	5	5.49	1	1.52	2	4.17	–	–
Total	150		85		69		111		106		91		66		48		40	
	LDL-cholesterol* ($p < 0.0001$)																	
Excellent	34	26.36	46	58.97	45	68.18	73	69.52	66	66.0	60	67.42	40	62.5	26	57.78	23	57.5
Desirable	47	36.43	16	20.51	16	24.24	24	22.86	22	22.0	17	19.10	13	20.31	15	33.33	14	35.0
Borderline	30	23.26	11	14.10	4	6.06	8	7.62	11	11.0	9	10.11	10	15.63	3	6.67	2	5.00
High	9	6.98	3	3.85	1	1.52	–	–	1	1.0	2	2.25	1	1.56	1	2.22	1	2.5
Very high	9	6.98	2	2.56	–	–	–	–	–	–	1	1.12	–	–	–			
Total	129		78		66		105		100		89		64		45		40	
	HDL-cholesterol* ($p < 0.0001$)																	
Low	33	24.63	25	32.47	15	22.72	9	8.49	2	1.94	1	1.11	4	6.15	4	8.51	3	7.5
Normal	101	75.37	52	67.53	51	77.28	97	91.51	101	98.05	89	98.89	61	93.85	43	91.49	37	92.5
Total	134		77		66		106		103		90		65		47		40	
	Triglycerides* ($p < 0.0001$)																	
Desirable	79	56.43	69	87.34	61	95.31	101	92.66	97	94.17	78	90.7	57	91.94	43	89.58	34	85.0
Borderline	34	24.29	5	6.33	2	3.13	6	5.5	5	4.85	6	6.98	3	4.84	3	6.25	5	12.5
High	26	18.57	5	6.33	1	1.56	2	1.83	1	0.97	2	2.33	2	3.23	2	4.17	1	2.5
Very high	1	0.71	–	–	–	–												
Total	140		79		64		109		103		86		62		48		40	
	Blood glucose* ($p < 0.0001$)																	
HG	1	0.68	7	7.22	3	4.05	5	4.39	1	0.91	2	2.04	2	2.94	1	2.13	1	2.44
Normal	94	64.38	80	82.47	65	87.84	107	93.86	98	89.09	89	90.82	59	86.76	36	76.6	32	78.05
HFG	35	23.97	9	9.28	5	6.76	2	1.75	11	10.0	5	5.10	5	7.35	9	19.15	7	17.07
DM	16	10.96	1	1.03	1	1.35		–	–	–	2	2.04	2	2.94	1	2.13	1	2.44
Total	146		90		74		114		110		98		68		47		41	

Values expressed as *N* and percentage. *HG* hypoglycemia, *HFG* high fasting glucose, *DM* diabetes mellitus

*Generalized estimating equations (GEE), including all patients who had been tested on each study occasion

Table 2 Total cholesterol, LDL-c, HDL-c, triglycerides, and blood glucose of patients compared on different occasions up to 10 years after Roux-en-Y gastric bypass

Time		Preop 12 months	Preop 24 months	Preop 48 months	Preop 72 months	Preop 96 months	Preop 120 months	*p* value**
Tests								
		N = 98	*N* = 95	*N* = 80	*N* = 60	*N* = 38	*N* = 34	
Total cholesterol (mg/dl)	Preop months	203.4 (± 41) 163 (± 27.9) *N* = 83	202.5 (± 44) 168.6 (± 29.8) *N* = 81	199.4 (± 40.1) 178.2 (± 32.6) *N* = 67	202.6 (± 36.5) 177.2 (± 25.5) *N* = 51	202.4 (± 40.9) 175.4 (± 31.2) *N* = 30	202.0 (± 32.2) 171.8 (± 25.1) *N* = 24 ***	$p < 0.0001$
LDL-cholesterol	Preop months	127.6 (± 39.6) 88.2 (± 25.1) *N* = 85	126.4 (± 39.4) 90.2 (± 28.6) *N* = 84	124.3 (± 34.7) 96.2 (± 30.5) *N* = 71	126.3 (± 35.7) 95.2 (± 25.6) *N* = 52	128.2 (± 38.6) 93.3 (± 30.8) *N* = 32	122.1 (± 29.9) 101.4 (± 24.3) *N* = 26****	$p < 0.0001$
HDL-cholesterol	Preop months	48.7(± 13.0) 56.8 (± 13.2) *N* = 88	49.4 (± 12.7) 61.1 (± 14.5) *N* = 87	48.4 (± 11.2) 64.2 (± 12.9) *N* = 71	46.7 (± 11.3) 62.5 (± 14.5) *N* = 53	47.0 (± 11.2) 58.9 (± 11.6) *N* = 35	46.8 (± 10.7) 56.7 (± 11.9) *N* = 32	$p < 0.0001$
Triglycerides	Preop months	159 (± 76.2) 92.1 (± 36.4) *N* = 99	152.0(± 80.0) 7.3 (34.6) *N* = 97	158.9 (± 86.9) 94.7 (± 42.7) *N* = 86	162.9 (± 116.4) 93.8 (± 41.1) *N* = 59	155.6 (± 81.2) 95.3 (± 50.9) *N* = 37	177.8(± 129.6) 103 (± 63.3) *N* = 31	$p < 0.0001$
Blood glucose	Preop months	99.2 (± 23.6) 83.7 (± 8.3)	103.9 (± 30.3) 85.9 (± 10)	101.9 (± 29.6) 85.8 (± 12.8)	107.6 (± 36.0) 89.4 (± 15.9)	112.9 (± 41.9) 92.6 (± 16.9)	116.3 (± 46.0) 93.5 (± 16.2)	< 0.0001

**Wilcoxon test for related samples. Only patients who were tested on the two compared occasions were included. The values are expressed as mean and standard deviation

***LDL-c was not significant in the 120-month follow-up

****Significant HDL-c change in the 120-month follow-up ($p = 0.0002$)

weight loss, lower glycemic load, higher insulin sensitivity, and higher incretin action. While assessing recent advances in bariatric and metabolic surgery, Albaugh et al. [19] found that the mechanisms responsible for the beneficial metabolic effects of Roux-en-Y gastric bypass surgery changed in the last 10 to 15 years. Although related to issues of restriction and malabsorption, current studies are focusing on the neurohormonal system and changes in biliary acids and intestinal microbiota, an area that is intensively being studied in the expanding field of bariatric and metabolic surgery.

Even with the limitation inherent to retrospective studies as they do not allow the investigation of other variables, the present results show a significant decrease of the comorbidities associated with morbid obesity and their control over as much as a 10-year period.

Mehaffey et al. [6] found very a significant decrease of the comorbidities associated with obesity in a 10-year follow-up. The present study found a similar result in its 10-year follow-up.

Recently, Laguna et al. [20] found that even weight regain did not worsen patients' lipid fractions 6 years after surgery. The present study could not relate the assessed parameters with weight regain, but HDL-c had increased significantly, and LDL-c, total cholesterol, triglycerides, and blood glucose had decreased significantly in the long-term follow-ups.

In a 2-year follow-up, Griffo et al. [21] found that LDL-c decreases only after gastric bypass, demonstrating the importance of this surgery technique for the metabolic results.

A prospective, observational, and descriptive study [22] of 150 gastric bypass patients followed for 2 years found that surgery improved their lipid profile and promoted important health benefits.

Lost to follow-up is a reality among gastric bypass patients, having been reported by many long-term studies [2–4]. This difficulty was also found in the present study as only 26.6% of the patients were still being followed 10 years after the surgery. Since the losses to follow-up occurred over a 10-year period, the Wilcoxon test considered only patients who had been assessed in the two follow-ups being compared.

A recent review [23] on clinical biomarker changes after gastric bypass found that the expression of genes associated with metabolic homeostasis seems to change after bariatric procedures, making epigenetics an important area for future studies.

The limitations of the present study refer primarily to the limitations of retrospective studies and the difficulties related to the long-term follow-up of bariatric patients. Presenting all the biochemical test results of all patients on all study occasions was not possible as the present study collected pre-existing data that had been recorded in the medical and nutritional records of the study institution.

Conclusion

The 10-year follow-up of patients submitted to gastric bypass showed that the metabolic diseases inherent to obesity remained under control.

Statement of Authorship All authors contributed equally to data collection and analysis and manuscript writing and review.

Compliance with Ethical Standards

Conflicts of Interest The authors declare that they have no conflicts of interest.

Ethical Approval 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 Does not apply. For this type of study, formal consent is not required.

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