

Analysis of the lipid profile of patients submitted to sleeve gastrectomy and Roux-en-Y gastric bypass.

Análise do perfil lipídico de pacientes submetidos à gastrectomia vertical e à derivação gástrica em Y de Roux.

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A B S T R A C T

Objective: to compare the improvements in lipid profile in patients undergoing sleeve gastrectomy (SG) and Roux-en-Y gastric bypass (RYGB). **Methods:** in a mixed cohort study, we evaluated 334 patients undergoing SG and 178 patients undergoing RYGB at the University Hospital of the Federal University of Pernambuco and at the Real Hospital Português de Beneficência, Recife, PE, Brazil. We measured serum levels of total cholesterol, LDL, HDL and triglycerides preoperatively and at three, six, 12 and 24 months follow-up. **Results:** the SG group consisted of 58 men and 276 women. In the group submitted to RYGB, there were 64 men and 114 women. The mean age was 37.2±20.5 years in the SG group and 41.9±11.1 years in the RYGB group. The preoperative mean BMI was 39.4±2.6kg/m² and 42.7±5.8kg/m² for the SG and RYGB groups, respectively. In the preoperative period, 80% of the patients had at least one abnormality in the lipid profile. Two years after surgery, there was improvement in total cholesterol, LDL, HDL and triglycerides in the group submitted to RYGB. In the group submitted to SG, after two years there was improvement in total cholesterol, HDL and triglyceride levels. **Conclusion:** both techniques resulted in improvements in the lipid profile, but the RYGB was more effective.

Keywords: Obesity. Bariatric Surgery. Gastric Bypass. Dyslipidemias.

INTRODUCTION

Atherosclerosis is a chronic disease with a multifactorial etiology, which affects the intimate layer of medium and large caliber arteries, being more common in patients with risk factors such as smoking, hypertension and dyslipidemias. The genesis of atherosclerotic plaque formation begins with aggression to the endothelium and consequent exposure of the intima layer to the deposition of plasma lipoproteins, especially LDL cholesterol¹.

Dyslipidemia is the major risk factor for coronary artery disease. Among obese patients, the estimated prevalence of hypertriglyceridemia is twice as high as in non-obese individuals². In addition, the prevalence of so-called "atherogenic dyslipidemia", characterized by the combination of hypertriglyceridemia with high LDL and low HDL, is more prevalent in obese and overweight patients.

To avoid the risk of manifestations of atherosclerotic disease, the third report of the National Cholesterol Education Program (NCEP) instructs that patients with no other risk factors for coronary heart disease must maintain serum levels of LDL-cholesterol lower than 130mg/dl, total cholesterol less than 200mg/dl, and triglycerides lower than 150mg/dl. The desirable serum HDL cholesterol level should be greater than 50mg/dl for women and greater than 40mg/dl for men³.

Another risk factor for myocardial infarction and peripheral vascular disease is insulin resistance. It is also frequent in obese patients due to the high serum levels of fatty acids released by adipose tissue that decrease liver sensitivity to insulin, stimulating glycogenolysis and gluconeogenesis. As a result, the liver releases more glucose into the bloodstream, perpetuating not only the hepatic insulin resistance, but also the muscular one⁴.

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Insulin resistance is directly related to atherogenic dyslipidemia, typical of obese patients².

Good results from bariatric surgery for the treatment of obesity and comorbidities such as diabetes, insulin resistance, reduction of free fatty acids, and proinflammatory interleukins have been widely demonstrated, especially for Roux-en-Y gastric bypass (RYGB)^{5,6}. For sleeve gastrectomy (SG), despite the good results for weight loss, it is still questioned if this technique would have good results in the control of dyslipidemia in obese patients in the long term.

There are some hypotheses that could justify the improvement of lipid metabolism by SG. It is believed that, in addition to the earlier satiety achieved with the reduction of ghrelin levels, SG causes a reduction in gastric emptying time and in the amount of gastric juice⁷. The arrival of poorly digested food into the small intestine, similar to that of disabsorptive techniques, increases the secretion of GLP-1 by the ileum, which stimulates pancreatic insulin secretion⁸. The improvement of glycemic indices and peripheral resistance to insulin contributes to the improvement of the lipid profile⁹.

In view of this scenario, the objective of the present study was to evaluate the lipid profile of patients in the postoperative period of bariatric surgery, comparing the effectiveness of RYGB and SG with regard to long-term lipid control.

METHODS

We analyzed the medical records of patients submitted to the RYGB or SG in the period of February 2010 to April 2017, for a total of 512 individuals. The criteria used to indicate surgery were those of the consensus of the National Institutes of Health (NIH), which

determines that patients with BMI greater than 40kg/m² or greater than 35kg/m² associated with severe comorbidities related to obesity may be candidates for surgical treatment¹⁰. We included patients from both genders, aged between 18 and 60 years, undergoing RYGB or SG. We excluded patients presenting with pregnancy, obesity due to psychiatric or endocrinological disorders, chemical dependence, history of cancer treatment, and/or high surgical risk.

We analyzed the following variables: preoperative BMI; type of surgery performed; percentage of excess weight loss; serum total cholesterol, LDL, HDL and triglycerides. Patients with one or more serum lipids above levels considered desirable by the third National Cholesterol Education Program (NCEP) report were considered as having dyslipidemia: total cholesterol= 200mg/dl; LDL= 130mg/dl; triglycerides= 150mg/dl; HDL <50mg/dl for women or <40mg/dl for men³.

The present study was approved by the Ethics in Research Committee of the Health Sciences Center (CCS) of the Hospital das Clínicas of UFPE and by the National Council of Ethics in Research (CONEP) of the Ministry of Health (CAAE: 11258913.3.0000.5208).

We compared the prevalence of dyslipidemias with the Chi-square test for proportion comparison. Furthermore, we evaluated these measures through mean and standard deviation for each study group. In the two-to-two comparison of the lipids means between the preoperative and the other moments, we applied the Student's t-test for paired samples (in case of indication of normality) and the Wilcoxon test (in cases where the variable did not follow a normal distribution). We reached all conclusions considering a level of significance of 5%.

RESULTS

The SG group consisted of 334 patients, 58 males and 276 females. The RYGB group consisted of 178 patients, 64 men and 114 women. The mean age was 37.2 ± 20.5 years in the SG group and 41.9 ± 11.1 years in the RYGB group. The mean preoperative BMI was $39.4 \pm 2.6 \text{ kg/m}^2$ and $42.7 \pm 5.8 \text{ kg/m}^2$ for the SG and RYGB groups, respectively. The percentages of excess weight loss were $49.1 \pm 13.0\%$ (SG) and $43.9 \pm 13.7\%$ (RYGB) at three postoperative months and $81.1 \pm 22.9\%$ (SG) and $88.1 \pm 18.3\%$ (RYGB) at 24 months postoperatively.

In the SG group, prior to surgical intervention, only 17% of women and 19% of men had serum lipid levels considered desirable. In the RYGB group, these values were 5% among women and 17% among men. Thus, throughout the sample, in the preoperative period, 85% of patients had dyslipidemia.

Total Cholesterol

In the SG group, 53% of the patients presented high levels of total cholesterol in the preoperative period. This index fell to 32.5% after 12 months of surgical intervention. In the 24-month evaluation, the percentage of patients with hypercholesterolemia was 36.4%. The mean preoperative total cholesterol was $204.0 \pm 39.0 \text{ mg/dl}$. There was a reduction in the levels of this lipoprotein in all postoperative evaluations. After 24 months, the mean total cholesterol level found was $190.2 \pm 39.9 \text{ mg/dl}$.

In the group submitted to RYGB, 57.3% of the patients had total cholesterol higher than 200 mg/dl before surgery. At the end of 24 months, this percentage was limited to 10.2% of the individuals analyzed. The mean preoperative total cholesterol was $205.4 \pm 40.2 \text{ mg/dl}$. In the postoperative period,

there was a reduction of its levels in relation to the basal ones in all measurements. After 24 months of intervention, the mean total cholesterol found was $155.8 \pm 32.1 \text{ mg/dl}$ - 25% reduction in relation to the preoperative period (Tables 1 and 2).

The prevalence of hypercholesterolemia in the preoperative period did not differ significantly between the techniques. However, in all subsequent evaluations, this prevalence was significantly higher in the SG group.

LDL Cholesterol

About 42.1% of patients submitted to SG presented $\text{LDL} = 130 \text{ mg/dl}$ preoperatively, with a mean of $124.6 \pm 34.9 \text{ mg/dl}$. There was a reduction in LDL cholesterol levels after three and 12 months of surgery - mean $110.8 \pm 32.7 \text{ mg/dl}$ at 12 months.

In the RYGB group, 40.8% of patients had elevated LDL before surgery, with a mean of $121.1 \pm 31.6 \text{ mg/dl}$. In the postoperative period, there was a reduction in serum LDL levels in all measurements. After 24 months of intervention, mean LDL was $84.3 \pm 25.3 \text{ mg/dl}$, which was therefore lower than the preoperative levels. Only 7% of subjects remained with $\text{LDL} = 130 \text{ mg/dl}$ 24 months after surgery (Tables 1 and 2).

In the preoperative evaluation, there was no significant difference between the prevalence of elevated LDL levels between the two techniques. However, in subsequent evaluations, the prevalence was significantly higher in the SG group.

HDL Cholesterol

Of the women submitted to SG, 52.2% had $\text{HDL} = 50 \text{ mg/dl}$ preoperatively, with a mean of $50.6 \pm 11.7 \text{ mg/dl}$. There was improvement in HDL serum levels at three, 12 and 24 months of follow-up. Nevertheless, 28.9% of women

Table 1. Analysis of serum lipid levels in the pre and postoperative periods (3, 6, 12 and 24 months after surgery).

Lipids	Preop	3 Months	6 Months	12 Months	24 Months
	SG	SG	SG	SG	SG
	RYGB	RYGB	RYGB	RYGB	RYGB
	p	p	p	p ¹	p
Total cholesterol (mg/dl)	204.0±39.0	186.2±38.2	187.6±29.4	183.2±35.2	190.2±39.9
	205.4±40.2	158.8±34.6	154.8±35.2	155.6±30.4	155.8±32.1
	0.706 ¹	<0.001 ¹	<0.001 ¹	<0.001	<0.001 ¹
LDL cholesterol (mg/dl)	124.6±34.9	118.7±37.0	118.6±33.2	110.8±32.7	113.1±37.9
	121.1±31.6	95.9±28.9	88.5±22.9	86.9±24.4	84.3±25.3
	0.264 ¹	<0.001 ¹	<0.001 ¹	<0.001	<0.001 ¹
HDL Cholesterol (mg/dl) Women	50.6±11.7	49.0±12.4	51.3±13.4	56.4±12.1	59.3±15.2
	48.6±12.9	44.2±13.3	50.5±14.1	54.4±12.5	61.2±13.9
	0.035 ²	0.001 ²	0.742 ¹	0.281	0.561 ¹
HDL Cholesterol (mg/dl) Men	41.9±10.4	44.3±12.6	50.4±9.2	57.4±9.7	50.2±10.0
	42.9±9.3	36.5±7.5	44.3±9.3	47.6±9.6	52.5±8.2
	0.594 ¹	0.001 ¹	0.052 ¹	0.004	0.614 ¹
Triglycerides (mg/dl)	153.1±92.6	96.9±35.1	94.2±37.9	78.3±28.3	91.9±51.0
	191.3±173.6	115.1±52.8	95.8±32.9	81.8±30.6	72.0±24.2
	0.001 ²	<0.001 ²	0.435 ²	0.620	0.075 ²

¹Student's t-test for paired samples (if p-value <0.05, the means of the two types of treatment differ significantly);

²Mann-Whitney test (if p-value <0.05, the measured distributions differ between the treatments types).

Table 2. Prevalence of dyslipidemias in the pre and postoperative periods (3, 6, 12 and 24 months after surgery).

Lipids	Preop	3 Months	6 Months	12 Months	24 Months
	SG	SG	SG	SG	SG
	RYGB	RYGB	RYGB	RYGB	RYGB
	p ¹	p ¹	p ¹	p ¹	p ¹
Total cholesterol	177 (53.0%)	66 (34.4%)	31 (32.6%)	41 (32.5%)	16 (36.4%)
	102 (57.3%)	14 (10.3%)	5 (6.2%)	11 (10.9%)	6 (10.2%)
	0.361	<0.001	<0.001	<0.001	<0.001
LDL cholesterol	136 (42.1%)	65 (34.2%)	33 (35.1%)	34 (27.0%)	12 (27.3%)
	69 (40.8%)	15 (11.3%)	2 (2.6%)	5 (5.0%)	4 (7.0%)
	0.785	<0.001	<0.001	<0.001	0.006
HDL CholesterolWomen	144 (52.2%)	99 (60.7%)	38 (45.8%)	38 (33.6%)	11 (28.9%)
	72 (63.7%)	64 (73.6%)	24 (54.5%)	28 (38.9%)	10 (23.8%)
	0.038	0.043	0.347	0.466	0.602
HDL CholesterolMen	24 (51.1%)	12 (44.4%)	1 (8.3%)	0 (0.0%)	0 (0.0%)
	23 (37.1%)	33 (70.2%)	11 (30.6%)	7 (24.1%)	1 (6.3%)
	0.145	0.029	0.248	-	-
Triglycerides	121 (36.4%)	16 (8.4%)	11 (11.7%)	1 (0.8%)	5 (11.6%)
	89 (50.0%)	19 (14.2%)	8 (9.9%)	2 (2.0%)	0 (0.0%)
	0.003	0.097	0.699	0.845	-

¹Chi-square test for proportion comparison (if p-value <0.05, the proportions differ significantly); - the test could not be applied because some frequencies were equal to zero.

persisted with low levels of HDL at 24 months postoperatively. As for men, 51.1% presented baseline HDL=40mg/dl, with an average of 41.9 ± 10.4 mg/dl. The averages found at six, 12 and 24 months of follow-up were higher than baseline. After 24 months of surgery, the mean HDL cholesterol found was 50.2 ± 10 mg/dl.

In the RYGB group, 63.7% of the women had low HDL before surgery, with an average of 48.6 ± 12.9 mg/dl. In the postoperative period, there was a reduction in HDL cholesterol at three months of follow-up, but with increase at 12 and 24 months. After 24 months of intervention, mean HDL was 61.2 ± 13.9 mg/dl, which is therefore better than the preoperative level, with a percentage increase of 25.9%. HDL remained low in 23.8% of women 24 months after surgery.

Of the men submitted to the RYGB, 37.1% had baseline HDL less than 40mg/dl, with an average of 42.9 ± 9.3 mg/dl. After 24 months, 6.3% of the men still had low levels of this lipoprotein. We also observed that after three months of surgery there was worsening of the serum HDL level, with a mean of 36.5 ± 7.5 mg/dl (Tables 1 and 2).

Triglycerides

In the SG group, 36.4% of the subjects had hypertriglyceridemia in the preoperative period, with a mean of 153.1 ± 92.6 mg/dl. Postoperatively, there was reduction during the entire follow-up period. The 24-months postoperative mean was 81.1 ± 22.9 mg/dl. Only 11.6% of the individuals evaluated two years after surgery persisted with hypertriglyceridemia.

In the RYGB group, 50% of the subjects had hypertriglyceridemia before surgery, with an average of 191.3 ± 173.0 mg/dl.

There was reduction in the mean serum triglycerides in all postoperative measurements. After 24 months of follow-up, all patients had normal triglyceride levels (Tables 1 and 2).

In the preoperative period, the prevalence of hypertriglyceridemia was significantly higher in the SG group. However, in the evaluations during the postoperative follow-up, there was no significant difference between the techniques.

DISCUSSION

Since dyslipidemia and obesity are related to the development of atherosclerosis and increased risk of myocardial infarction, the improvement of serum lipid levels may reduce the incidence of coronary events. Studies have shown that insulin resistance and increased adipose tissue found in obese individuals are associated with increased oxidative stress due to the higher production of free oxygen radicals. These contribute to atherogenesis, since they induce LDL oxidation. Gastroplasty, by reducing excess weight, induces reduction of oxidative stress and has a cardioprotective effect¹¹.

A study by Julve *et al.* also showed benefits of gastroplasty for the treatment of dyslipidemias and reduction of cardiovascular risk. In their research, the authors found increased hepatic expression of the PON-1 gene in obese subjects submitted to RYGB. This gene encodes the enzyme serum paraoxonase, which contributes to the antioxidative and antiatherogenic activity of HDL¹².

In the present study, we observed that in the SG group there was a significant improvement in total cholesterol levels, although more discrete than in the RYGB group. There was a percentage reduction of total cholesterol of 8.7% after three months and of 6.7% after 24 months of postoperative follow-up.

These results were better than those found in a study by Ruiz-Tovar *et al.*, in which there was no statistical significance in the comparison between total and LDL cholesterol in the preoperative period and after 12 months of follow-up after SG¹³.

In the current study, as for RYGB, the reduction of serum total cholesterol levels was 23% at three months and 24% at 24 months of follow-up. There was also a reduction of LDL of 21% and 30%, also at three and 24 months, respectively. These findings are similar to those found by Jamal *et al.*, who evaluated 248 patients submitted to the same surgical technique, with a six-year follow-up and a 27% reduction in total cholesterol and 40% in LDL cholesterol¹⁴.

Zlabek *et al.*, evaluating patients submitted to RYGB, found a reduction of total cholesterol of 12.5% after one year and of 7.5% after two years of surgery¹⁵. These results, as well as the ones found in this study, where the SG was less effective than the RYGB for reduction of serum lipids, support the hypothesis that the malabsorption is associated with greater control of dyslipidemia. Other studies have already shown that there is an association between decreased absorption area and reduced intestinal absorption of cholesterol¹⁶.

In a research on cholesterol metabolism in patients undergoing gastroplasty, Benetti *et al.* found that in the disabsorptive techniques there was a decrease in cholesterol absorption, implying a reduction in serum LDL levels. This reduction is due to the lower reabsorption of cholesterol and bile salts by the intestine. As compensation, there was an increase in hepatic cholesterol catabolism, which contributed to the maintenance of lower serum LDL levels. These changes were not found in the group of patients treated with restrictive technique through an adjustable gastric band¹⁷.

Regarding LDL, the percentage reduction we found in the SG group was 5% at three months and 10% at 24 months. Benaiges *et al.*, evaluating 51 patients submitted to SG, found a statistically significant difference between the LDL preoperative mean and that of 12 months after surgery. However, the percentage reduction of LDL was also low, being around 5%¹⁸. Regarding the HDL levels 12 months after SG, they found a percentage increase of 33% of this lipoprotein. At the same follow-up time, Tovar *et al.* found a 28% increase in HDL¹³.

In the present study, we observed that in the first postoperative measurement, there was a fall in HDL among women submitted to SG, and between men and women submitted to RYGB. This drop in HDL levels coincided with the period of faster weight loss. After this initial phase, there was a significant increase in HDL in both the female and male groups submitted to the RYGB at 24 months, an increase of 22.3% for men and 25.9% for women. In the SG group, there was a more discrete increase (17.2%) in HDL after a 24-month follow-up for women. In the male subgroup, the percentage increase in HDL was 19.8%.

Zvintzou *et al.* also describe a decline in serum HDL levels in the observation of patients undergoing gastroplasty through a disabsorptive technique. The authors found that, despite the initial fall in HDL, there was a qualitative improvement in this lipoprotein levels, with increased expression of HDL rich in apolipoprotein A-1 (Apo A-1), which have anti-oxidant action, and reduction of expression of HDL with apolipoprotein E (Apo E), which has a hyperlipidemic action. For the authors, this initial HDL decrease represents a period of conversion of Apo E-rich HDL into Apo A-1-rich HDL¹⁹.

Julve *et al.*, though not having found significant changes in serum levels of HDL in patients in the pre and postoperative period of RYGB, also found qualitative changes of these lipoproteins. Postoperatively, there was an increase in the expression of HDL-2, a HDL subtype with a higher cholesterol content, which has a greater cardioprotective effect¹².

Regarding the dosages of triglycerides in the present study, there was a significant reduction after RYGB during the entire follow-up period. After 24 months, the reduction in triglyceride levels was 62%. Nguyen *et al.*, following a cohort of 95 patients submitted to the same surgical technique, observed a similar percentage reduction (63%) of triglycerides in the follow-up of 12 months²⁰. A systematic review with 29 studies on RYGB also reported a similar value (60.5%)²¹.

There was also a reduction in serum triglyceride levels in the SG group. This percentage reduction was 40% at 24 months postoperative follow-up. Strain *et al.* also found a reduction in triglycerides in a cohort one year after SG: preoperative mean was 128.7±66.7mg/dl, and after one year, it dropped to 97.1±43.5mg/dl. However, after five years of surgery, the mean value found was 119.8±68.2, even lower than in

the preoperative period, but showing a tendency to increase triglycerides in the long term²².

It is noteworthy that in the present study, we found a similar percentage of weight loss between the two study groups. These percentages were 81.1±22.9% in the SG group and 88.1±18.3% in the RYGB group. These results show that SG was effective for weight loss, reaching levels similar to RYGB. However, the percentage of weight loss did not seem to be the only factor involved in the control of dyslipidemias, since SG produced inferior results in the treatment of this comorbidity.

The results of the present study showed that RYGB is markedly more effective than SG in improving patients' lipid profile. The latter technique, although significantly lowering the percentage of patients with undesirable levels of triglycerides and total cholesterol, showed a trend of lipoprotein elevation with two years of follow-up. In addition, SG restored HDL cholesterol in females more effectively than in males.

Thus, the authors conclude that Rou-en-Y gastric bypass leads to a better control of the lipid profile than the sleeve gastrectomy, and should be considered when planning the treatment of a patient with difficulty to control dyslipidemia.

R E S U M O

Objetivo: comparar as melhorias no perfil lipídico de pacientes submetidos à gastrectomia vertical (GV) e à derivação gástrica em Y de Roux (DGYR). **Metódodos:** estudo de coorte misto, em que foram avaliados 334 pacientes submetidos à GV e 178 pacientes submetidos à DGYR no Hospital das Clínicas da Universidade Federal de Pernambuco e no Real Hospital Português de Beneficência, Recife, PE, Brasil. Foram realizadas dosagens séricas de colesterol total, LDL, HDL e triglicérideos no pré-operatório e com três, seis, 12 e 24 meses de seguimento. **Resultados:** o grupo submetido à GV foi composto por 58 homens e 276 mulheres. No grupo submetido à DGYR, foram analisados 64 homens e 114 mulheres. A média de idade foi de 37,2±20,5 anos no grupo da GV e de 41,9±11,1 anos no grupo da DGYR. O IMC médio pré-operatório foi de 39,4±2,6kg/m² e 42,7±5,8kg/m², para o grupo da GV e da DGYR, respectivamente. No pré-operatório, 80% dos pacientes tinha, no mínimo, uma anormalidade no perfil lipídico. Dois anos após a cirurgia houve melhora do colesterol total, LDL, HDL e triglicérideos no grupo submetido à DGYR. No grupo submetido à GV, após dois anos houve melhora dos níveis de colesterol total, HDL e triglicérideos, apenas. **Conclusão:** ambas as técnicas resultaram em melhorias no perfil lipídico, porém a DGYR foi mais efetiva.

Descritores: Obesidade. Cirurgia Bariátrica. Derivação Gástrica. Dislipidemias.

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