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Bariatric surgery and the coronary artery calcium score.

Cirurgia bariátrica e o escore de cálcio coronariano.

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A B S T R A C T

Objective: to investigate the impact of bariatric surgery on the coronary artery calcium score (CACS), and to establish predictors of progression of this score in patients with obesity. **Methods:** prospective study that evaluated 18 obese patients before and after bariatric surgery. All patients were submitted to computed tomography scans and blood tests (total cholesterol, LDL, HDL, triglycerides, fasting plasma glucose, A1C, insulin, serum calcium, C-peptide and C-Reactive Protein) in order to determine CACS and Framingham risk score (FRS). **Results:** the FRS decreased 50% between the pre and postoperative evaluations. The mean CACS increased significantly at the late postoperative period, going from 8.5 to 33.1. HDL levels had also increased between the pre and postoperative periods. All of the other quantitative variables reduced significantly at the postoperative evaluation. When dividing CACS into four degrees, it was observed that 22.2% presented CACS=0 at the postoperative evaluation. The prevalence of mild CACS decreased from 77.8% to 50%, while moderate CACS remained the same (11.1%). Severe CACS increased from 11.1% to 16.7%. Older ages were linked to CACS progression, and this was the only variable that presented statistical association with progression. **Conclusion:** bariatric surgery leads to positive cardiovascular outcomes, apparently regardless of CACS.

Keywords Obesity. Bariatric Surgery. Atherosclerosis. Coronary Artery Disease.

INTRODUCTION

Obesity is a condition associated with the development of risk factors for cardiovascular disease, systemic arterial hypertension (SAH), dyslipidemia, insulin resistance and type-2 diabetes *mellitus* (DM2)[1,2]. Still, some studies have shown that obesity alone is related to increased cardiovascular risk, favoring events such as angina, acute myocardial infarction, heart failure and sudden death[3-5]. This major propensity for cardiovascular disease (CVD) appears to result from the endothelial dysfunction and subclinical inflammation characteristics of obesity[6].

Given this scenario, establishment of an early, non-invasive diagnosis of CVD and its complications is of utmost importance in the population with obesity. A series of clinical scores has been used to estimate the risk of CVD development, Framingham Risk Score (FRS) being one of the most disseminated in clinical practice[7]. This score consists of a multivariate statistical model that takes into account age, gender, smoking, diabetes, hypertension, total cholesterol, HDL and LDL in asymptomatic patients with no previous coronary artery disease (CAD), aiming at the risk of CVD in 10 years.

However, the application of clinical scores alone to predict future cardiovascular risk is limited. Thus, there is a need to incorporate in clinical practice more objective methods that are capable of quantifying the risk of developing CVD. In this context, the coronary arteries calcium score (CCS), measured by computed tomography (CT), appears

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as a useful screening tool, being able to non-invasively detect vascular calcifications *in vivo*[11,12]. CCS has been an independent predictive factor for the occurrence of future cardiovascular events[7].

Bariatric surgery, one of the most effective methods for weight loss, has presented interesting results regarding cardiovascular risk, reducing risk factors and preventing future deleterious events of this nature, as observed in previous studies[13]. This procedure is associated with endothelial improvement and reduction of the subclinical inflammation, present in obesity[14]. Given the reduction of mortality and cardiovascular disease with bariatric surgery, it is to be expected that such patients present with improvement, or at least slower progression, of CCS in the postoperative period[15].

This study aimed to investigate the impact of bariatric surgery on CCS and to establish the predictive factors of this score's progression in obese patients. We also studied the FRS before and after surgery, aiming at more precisely determining the changes in future cardiovascular risk.

METHODS

We conducted a prospective study at the Hospital das Clínicas of the Federal University of Pernambuco during the period between 2014 and 2018. We used CT without intravenous contrast to determine the CCS in the preoperative and late postoperative periods of patients undergoing bariatric surgery, both through Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG).

We selected the sample according to the criteria of the Brazilian Society of Bariatric and Metabolic Surgery (SBCBM): BMI between 30 and 34.9 kg/m^2 associated with at least one severe comorbidity; BMI between 35 and 40 kg/m^2 associated with any comorbidity; or BMI>40kg/m^2 independent of comorbidities.

The study included patients with obesity classes II and III, of both genders, with age between 18 and 75 years, who presented positive CCS in the preoperative evaluation. We excluded from the sample the patients who experienced CAD, including angina, myocardial infarction and coronary revascularization. We also excluded patients with negative CCS in the preoperative evaluation and those who refused undergoing the CT scan.

All patients underwent preoperative evaluation, when they were questioned about the presence of cardiovascular risk factors, such as hypertension, hypercholesterolemia, smoking, and medication use. Blood samples were collected after a 12-hour fast to analyze the biochemical variables, including total cholesterol, HDL, LDL, triglycerides, fasting glucose, glycosylated hemoglobin (A1C), insulin, serum calcium, C-peptide, and C-reactive protein (CRP). We repeated these exams in the late postoperative period, aiming to determine the patients' FRS.

We defined hypertension as systolic pressure >130mmHg or diastolic pressure >80mmHg, and diabetes, as fasting blood glucose >6.5%, or use of antidiabetic drugs. We considered hypercholesterolemia as total cholesterol >200mg/dl or the use of lipid-lowering medications, and hypertriglyceridemia, as triglycerides >150mg/dl.

All patients underwent CT for CCS determination. We obtained 48 contiguous slices, with intervals of 3mm, starting 1cm below the carina and progressing in the caudal direction, aiming at covering the entire coronary tree. Image acquisition occurred between 60% and 80% of the electrocardiographic R-R interval. Images were interpreted by an experienced radiologist, using the Agatson method to calculate the CCS.

We defined a coronary calcium focus as the presence of three or more pixels with more than 130 Hounsfield units. Total CCS was calculated by summing the score of each of the three main epicardial coronary arteries (left anterior descending, circumflex and right coronary arteries). We stratified the CCS results in four categories (0: absent; 0.1-99: mild; 100-400: moderate; >400: severe).

We carried out the evaluations in two different moments, before and after (late postoperative) and compared them.

The study was approved by the Ethics in Research Committee of the Health Sciences Center of the Federal University of Pernambuco (CEP/CCS/UFPE), according to Resolution nº 196/96 of the National Health Council, under CAAE protocol number 00895712.5.0000.5208.

We expressed the results through absolute frequencies and percentages for the categorical variables, and mean, median, standard deviation and 25th and 75th percentiles for the quantitative variables. We applied the Shapiro-Wilk test for the normality of the distribution. We compared the pre and postoperative evaluations with the T-test for paired samples when the distribution displayed normality, and the Wilcoxon test otherwise. We used the Fischer's exact test, the Mann-Whitney test, Student's t-test for equal variances, and the Student's test for different variances to analyze the categorical variables. To assess whether distributions showed the same variance, we applied the Levene test (F-test). The level of significance was set at 0.05.

RESULTS

We recruited 202 patients, all candidates for bariatric surgery, at our center. Of these, we included only 18 in the study. Ten underwent RYGB, and eight, SG. The sample was composed of 55.6% men and 44.4% women. The average age was 55.3 years, ranging from 31 to 71. The mean postoperative follow-up time was 2.2 years, ranging from 1.5 to 4.0. As for comorbidities, 83.3% had DM2, 83.3% SAH, and 38.9%, hypercholesterolemia.

Table 1 shows the clinical and laboratory variables. BMI, calcium, insulin, C-peptide, fasting glycemia, A1C, total cholesterol, LDL and triglycerides had a statistically significant decrease in the postoperative period. The mean values of HDL and CCS displayed a statistically significant increase in the postoperative evaluation.

In the FRS evaluation, that calculates the risk of cardiovascular development in 10 years, we observed a significant reduction of the average score, from 6% in the preoperative period to 3% in the late postoperative period (p<0.001) (Figure 1).

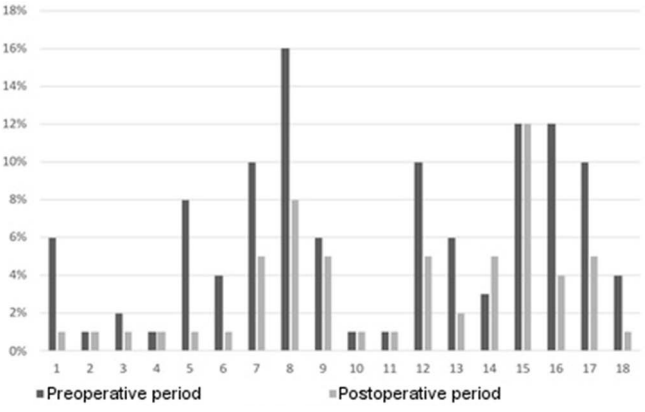

Figure 1. *Framingham risk score before bariatric surgery.*

Table 2 shows the CCS evaluation in the pre and postoperative periods. In the initial evaluation, the majority of patients (77.8%) were stratified as mild risk, none as absent risk, and the rest as moderate (11.1%) or severe (11.1%) risk. In the postoperative evaluation, half of the patients were stratified as light risk, 22.2% as absent risk, 11.1% as moderate risk and the remaining 16.7% as severe risk. There was no statistically significant difference (p=0.414) between the pre and postoperative evaluations, though.

Table 3 shows the relation of CCS progression with variables age, gender, type of surgery and follow-up time. No variable, except for age, showed statistical significance in the comparison between those patients who progressed and those who did not. Age was more advanced in the group that progressed in CCS (p=0.034).

Table 4 presents an analysis of the clinical and laboratory parameters according to CCS progression. There was no statistically significant association between the CCS progression and the parameters evaluated.

Table 1. *Clinical and laboratory parameters in the pre and postoperative periods of bariatric surgery.*

Parameters	Preoperative	Postoperative	p-value
BMI*	42.56±4.66	28.18±3.37	$p^{(1)}<0.001$
CCS**	8.50	33.10	$p^{(2)}=0.002$
Calcium	9.67±0.66	9.14±0.53	$p^{(1)}=0.010$
CRP***	3.40±5.12	2.46±5.91	$p^{(1)}=0.095$
Insulin	29.19±20.18	6.14±2.54	$p^{(1)}<0.001$
C-peptide	4.68±2.12	1.97±0.54	$p^{(1)}<0.001$
FG	132.17±46.74	93.50±27.18	$p^{(2)}<0.001$
A1C##	6.89±1.31	5.54±0.61	$p^{(1)}<0.001$
Total cholesterol	196.94±38.40	157.89±32.88	$p^{(1)}=0.001$
LDL	113.78±28.18	91.22±25.81	$p^{(1)}=0.009$
HDL	42.55±8.65	51.02±11.09	$p^{(1)}=0.001$
Triglycerides	217.17±118.26	96.67±31.05	$p^{(1)}<0.001$

(1) Student's t-test; (2) Wilcoxon test; BMI: body mass index; CCS**: coronary calcium score; CRP**: C-reactive protein; FG#: fasting blood glucose; A1C##: glycosylated hemoglobin.*

Table 2. *Evaluation of coronary calcium score (CCS) in the pre and postoperative periods of bariatric surgery.*

CCS*	Preoperative n (%)	Postoperative n (%)	p-value(1)
Total	18	18	
Absent	-	4 (22.2)	
Light	14 (77.8)	9 (50.0)	0.414
Moderate	2 (11.1)	2 (11.1)	
Severe	2 (11.1)	3 (16.7)	

(1) Wilcoxon test; CCS: coronary calcium score.*

Table 3. *Progression of coronary calcium score according to age, gender, type of surgery and time of postoperative follow-up.*

	CCS* Progression		
	Yes n (%)	No n (%)	p-value
Total	13 (72.2)	5 (27.8)	p(1)0.034
Age (years)	58.46±8.30	47.20±11.58	
Gender			
Male	8 (80.0)	2 (20.0)	p(2)=0.608
Female	5 (62.5)	3 (37.5)	
Procedure			
RYGB**	7 (70.0)	3 (30.0)	p(2)=1,000
SG***	6 (75.0)	2 (25.0)	
Follow-up time			
Up to 2 years	8 (66.7)	4 (33.3)	p(2)=0.615
More than 2 years	5 (83.3)	1 (16.7)	

(1) Mann-Whitney test; (2) Fisher's test; CCS: coronary calcium score; RYGB**: Roux-en-Y gastric bypass; SG***: sleeve gastrectomy.*

Table 4. *Evaluation of anthropometric and biochemical parameters, according to the progression or not of coronary calcium.*

		CCS Progression*		
		Yes	No	p-value
BMI**	Preop	41.5±4.8	45.3±3.0	p(1)=0.068
	Postop	27.6±3.3	29.6±3.5	p(1)=0.257
	Difference	13.86	15.73	p(1)=0.301
A1C***	Preop	6.8±1.4	7.1±1.3	p(1)=0.553
	Postop	5.6±0.7	5.3±0.4	p(1)=0.347
	Difference	1.18	1.82	p(1)=0.333
Total cholesterol	Preop	192.8±39.4	207.6±37.7	p(1)=0.522
	Postop	160.5±33.0	151.2±35.4	p(1)=0.730
	Difference	32.38	56.40	p(1)=0.257
LDL	Preop	108.2±26.7	128.2±29.5	p(1)=0.218
	Postop	91.4±27.9	90.8±22.1	p(1)=0.961
	Difference	16.85	37.40	p(1)=0.200
HDL	Preop	43.0±9.0	41.4±8.7	p(1)=0.693
	Postop	52.5±11.7	47.1±9.4	p(1)=0.459
	Difference	9.54	5,68	p(1)=0.374
Triglycerides	Preop	228.4±133.8	188.0±65.0	p(1)=0.693
	Postop	98.5±35.2	91.8±18.3	p(1)=0.921
	Difference	129.85	96.20	p(1)=0.767
CRP#	Preop	3.72±5.89	2.58±2.52	p(1)=0.522
	Postop	2.71±6.81	1.80±2.93	p(1)=0.961
	Difference	1.01	0.77	p(1)=0.882

(1) Mann-Whitney test; CCS: coronary calcium score; BMI**: body mass index; A1C***: glycosylated hemoglobin; CRP#: C-reactive protein.*

DISCUSSION

Bariatric surgery significantly reduces the occurrence of cardiovascular events[3,16,17]. Adams *et al*. showed, in a retrospective study, that long-term mortality was significantly lower in the group submitted to bariatric surgery than the obese group, with a 56% reduction in the prevalence of CAD[18].

Batsis *et al*. used the FRS and the PROCAM score to assess the risk of developing cardiovascular diseases in 197 patients submitted to RYGB, comparing with a control group of 163 subjects from the Rochester Epidemiology Project[19]. The FRS decreased more in the post-RYGB group (from 7% to 3.5%, p<0.001) than in the control group (7.1% to 6.5%, p=0.13)[19]. Vogel *et al*., also using the FRS, found a reduction in the risk of developing cardiovascular diseases in 10 years in 39% in Men and 25% in Women[20].

In the present study, there was a 50% reduction in the FRS, decreasing from 6% in the preoperative period to 3% in the late postoperative period. The results are in agreement with those reported by Batsis *et al*.[19]. However, our study provides an assessment with longer follow-up.

Priester *et al*. compared the CCS of patients submitted to RYGB (test group) with a control group composed of obese individuals[21]. Using this methodology, they found CCS=0 in 72% of the test group and only 49% in the control group. They also observed that the test group displayed a lower average CCS compared the control one (30±109 x 103±325).

We found 22.2% of CCS=0 in the postoperative period. This is important for strengthening the hypothesis that bariatric surgery reduces patients' CCS, since there was no preoperative case of CCS=0. On the other hand, there was progression of the mean CCS in the postoperative period (from 8.5 to 33.1, p=0.002), despite improvements in all comorbidities and in FRS. This is intriguing, given that the literature has already demonstrated that bariatric surgery reduces cardiovascular risk, and that CCS progression itself is considered a factor of future cardiovascular disease and mortality[18,22]. Similarly, other studies have shown that the use of statins do not halt CCS progression either, yet such drugs contribute to reduce patients' cardiovascular risk in the long term[23].

When analyzing the sample according to CCS progression, we found that age was the only measure related to the score progression. In patients with CCS progression, ages were more advanced compared with the group in which there was no progression (58.46 x 47.2 years, p=0.034). Similarly, other studies have pointed out that CCS tends to progress with the patient's age, and that this phenomenon is more intense in men[12,24]. In the present study, however, we did not find a statistically significant difference between genders.

In contrast with our results, Gadelha *et al*. observed a direct relation between DM2 and SAH and CCS progression[22]. DM2, SAH and dyslipidemia are classic cardiovascular factors and are related to a higher propensity for cardiovascular disease development. this context, it is a plausible to infer that obese patients, showing the aforementioned comorbidities, would display a worse progression of CCS. In our sample, we had no statistically significant relationship between comorbidities and CCS progression.

Regarding the type of surgery performed, we also could not find a statistically significant difference in the progression of CCS between individuals submitted to RYGB or SG. Both techniques presented similar results as to CCS Progression during patients postoperative follow-up.

There has been evaluation of the impact of bariatric surgery on CCS through cross-sectional studies[21]. The present study appears to be the first prospective, cohort study to analyze the effects of bariatric surgery on coronary calcium. This methodology renders the data analysis more reliable, since a comparison is made between the initial evaluations, prior to surgery, and the final evaluation, in the late postoperative period.

The greatest limitation of this work was the sample size. Our sample was reduced because among the 202 patients who were candidates for surgery, only 18 had preoperative positive CCS. Another important limitation was the absence of a control group with obese individuals under clinical treatment only. If we had used a control group, we could rate how effective bariatric surgery is in relation to clinical treatment in reducing the risk of future cardiovascular events.

There was an increase in the mean coronary calcium in the late postoperative period compared with the preoperative one. The single variable that was statistically significant with the progression of the coronary calcium score was patients' age. The mean Framingham risk score was reduced by 50% between the pre and the late postoperative periods.

Taking into consideration the results of this study, the authors conclude that bariatric surgery provides positive cardiovascular outcomes - as evidenced by the reduction in the Framingham score - independently of the coronary calcium score. However, future prospective studies with larger samples and long-term follow-up are needed to obtain more robust conclusions about the mechanisms by which bariatric surgery leads to a reduction in the occurrence of coronary artery disease.

RESUMO

Objetivo: *investigar o impacto da cirurgia bariátrica no escore de cálcio coronariano (ECC) e estabelecer fatores preditivos de progressão desse escore em pacientes obesos.* **Métodos:** *estudo prospectivo de 18 pacientes obesos antes e depois da cirurgia bariátrica. Todos os pacientes foram submetidos à tomografia computadorizada e a exames laboratoriais com dosagens sanguíneas de colesterol total, LDL, HDL, triglicerídeos, glicose de jejum, A1C, insulina, cálcio sérico, peptídeo C e proteína C-reativa, para determinar o ECC e o escore de risco de Framingham (ERF).* **Resultados:** *o ERF reduziu 50% entre as avaliações pré e pós-operatórias. O ECC médio aumentou significativamente no período pós-operatório, aumentando de 8,5 para 33,1. Os níveis de HDL também aumentaram no pós-operatório. Todas as outras variáveis quantitativas reduziram significativamente no pós-operatório. Ao estratificar o ECC em quatro categorias, foi observado que 22,2% da amostra apresentou ECC=0 no pós-operatório. A prevalência de ECC leve reduziu de 77,8% para 50%, enquanto que ECC moderado permaneceu igual no pré e no pós-operatório (11,1%). ECC grave aumentou de 11,1% para 16,7%. Idade avançada foi associada à progressão do ECC, e essa foi a única variável que apresentou correlação estatística com a progressão do ECC.* **Conclusão:** *cirurgia bariátrica produz desfechos cardiovasculares positivos, que, aparentemente, ocorrem de forma independente do ECC.*

Descritores: *Obesidade. Cirurgia Bariátrica. Aterosclerose. Doença da Artéria Coronariana.*

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