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ADIPOSITY, METABOLIC PARAMETERS AND C-REACTIVE PROTEIN IN PATIENTS AT CARDIOVASCULAR RISK

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ABSTRACT

Background: Several studies have shown that C-reactive protein is positively associated with the body mass index (BMI) and waist circumference (WC), but the association of the concentration of C reactive protein with lipid and glycemic profile is still controversial. This study aimed to determine high-sensitive C-reactive protein (hs-CRP) concentrations in patients undergoing angiography and its correlation with BMI, WC and biochemical parameters. Ninety-seven patients attended the Unit of Cardiac Surgery and Hemodynamics located at University Hospital of the University of Marília (UNIMAR) participated in the study. Anthropometric (weight and height for calculation of BMI and WC) and biochemical parameters (hs-CRP, glycaemia, total cholesterol, LDL-c, HDL-c, and triglycerides) were collected. Pearson test was used to evaluate the correlation between the data and the significance level adopted was 5% ($p < 0.05$). The patients had a mean age of 55 ± 12.04 years, and 55.32% were men and 44.68% women. The mean values of hs-CRP were 0.40 ± 0.42 mg/dL. hs-CRP correlated positively with BMI ($p < 0.008$) and WC ($p < 0.018$) but not with other variables such as blood glucose ($p = 0.118$), total cholesterol ($p = 0.559$), LDL-c ($p = 0.8180$, HDL-c ($p = 0.417$) and triglycerides ($p = 0.590$). Body composition, characterized by increased body adiposity according to BMI and WC were the main factors related to high concentrations of hs-CRP in the patients underwent coronary arteriography.

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INTRODUCTION

Cardiovascular diseases (CVD) lead mortality rates in developed countries, and in the last decade scientific research has been increasing, reporting sufficiently demonstrative evidence about C-reactive protein (CRP) as a predictor of these pathologies (Tarzia *et al.,* 2017; Cerda *et al.,* 2017; Agostinis *et al.,* 2015).

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The prevalence of obesity is increasing worldwide, and it is associated with low-grade inflammation. In America, there has been an increase in obesity regardless of the socioeconomic situation of the country. In Brazil, it is considered a public health problem with a prevalence of 14.8% of the population (Malta *et al.,* 2016). Chronic mild inflammation of adipose tissue releases cytokines such as tumor necrosis factor (TNF-alpha), C-reactive protein and interleukin-6. This last one is responsible for signaling the synthesis of CRP in the liver (Premanath *et al.,* 2016). The activation of the low-intensity inflammatory process, characterized by the increase of inflammatory and oxidative biomarkers, may contribute to the onset of endothelial lesions, increasing cardiovascular risk

(Derosa and Maffioli, 2016; Hung *et al.,* 2017). The body mass index (BMI) and waist circumference are the most common methods to classify obesity and may be related to CVD due to several aspects such as the release of inflammatory biomarkers. Inflammatory processes are the main factor that could be useful in stratifying the risks inherent to obesity (Buchan *et al.,* 2017; Mastroeni *et al.,* 2017; Mirhafez *et al.,* 2016). High sensitivity-CRP (hs-CRP) has been linked to overweight, obesity and atherosclerotic disease, however, in individuals with a diagnosis of previous heart disease, this relationship was barely studied. Therefore, studies are necessary to evaluate these relationships in individuals of this group. This study aimed to determine the levels of hs-CRP in patients undergoing angiography and its correlation with BMI, waist circumference (WC) and biochemical parameters.

MATERIALS AND METHODS

Group of patients and Ethics

This project has included 100 patients (55 men and 45 women varying in age from 36 to 68 years) undergoing coronary arteriography, and it was conducted at the Hemodynamic Laboratory of the University Hospital in the city of Marilia, of São Paulo, Brazil. After reading and signing an informed consent form, height and weight were measured to calculate the body mass index (BMI), waist circumference (WC) and blood pressure (BP). This project was approved by the Ethics Committee of the University of Marilia (UNIMAR) under protocol number 449. The experimental protocol was in accordance with the *Ethical Standards of the Institutional Ethics Committee and the Helsinki Declaration* of 1975 (revised in 2008). Participation in the study did not cause discomfort to the participants and did not imply in health risks during data collection. If the participant at any time felt embarrassed could give up participating in the research.

Anthropometric and Biochemical parameters

The anthropometric data collected were weight, height, and WC (Gibson, 2005). The BMI was calculated by weight (kg) divided by height (m) performed with a digital anthropometric scale (Sanny®), with capacity for 200 kg, duly calibrated, a fixed stadiometer (Alturaexata®), fixed in a flat location and consisting of a metric scale of 150 cm. Blood samples were collected by venipuncture to determine levels of high-sensitive C-reactive protein, glycaemia, total cholesterol (TC), LDL-c, HDL-c and triglycerides (TG).

Statistical analysis

Statistical analysis was performed using the Bioestat 5.0 program, and the Pearson test was used to evaluate the correlation between the data. The comparisons of the parametric data were made by Student's test and the non-parametric by the Mann Whitney test. The significance level adopted was 5% ($p < 0.05$).

RESULTS

One hundred patients with a mean age of 56 ± 12.01 years participated in the study (55.32% were men, and 44.68% were women). Table 1 shows the characteristics of the sample in relation to the anthropometric and biochemical data presented as a mean, median and standard deviation. Significant differences were found only for weight, height and HDL-c levels when comparing men and women. hs-CRP correlated positively with BMI and WC (Figure1). Glycaemia, triglycerides, total cholesterol, LDL-c, and HDL-c, did not present significant correlation with hs-CRP (Table 2). Results for anthropometric data show that the mean of the BMI was 27.93 ± 4.34 kg/m^2. The distribution of the nutritional diagnosis showed that 26.59% were eutrophic and 73.41% were overweight (48.94% were overweight, and 24.47% were obese). When patients were divided according to the BMI, there was a significant difference only for triglycerides (Table 3). The evaluation of WC showed that 24.47% presented the measure considered adequate and 75.53% presented values above the recommended (women > 80 cm and men > 94 cm are considered inadequate). There was no significant difference in biochemical parameters when patients were divided according to WC (Table 3).

DISCUSSION

Our results show that hs-CRP is positively correlated with BMI and WC in patients underwent arteriography. Obesity, especially the central adiposity, is related to inflammation due to the production of adipokines that stimulate the hepatocytes to synthesize acute phase inflammatory proteins such as CRP. When highly stimulated, hepatocytes produce high levels of this protein, leading to a low-intensity inflammatory process, which may induce a local immune-response with an increase in inflammatory biomarkers, and oxidative chemical species (Buchan *et al.,* 2017; Hajsadeghi *et al.,* 2015; Costa *et al.,* 2013). It is noteworthy to say that our patients underwent arteriography present high median values for glycaemia and triglycerides levels. These parameters are related to diabetes, metabolic syndrome and CVD (Barbalho *et al.,* 2016a). Intolerance to glucose may be associated with obesity and inflammation and production of reactive compounds that may lead to the oxidative stress. These compounds may be the advanced glycation ends that may activate macrophages and lead to the production of IL-6. As a result, LDL-c may be oxidized contributing to the oxidative stress and inflammation, which increase the possibility to originate atherogenic plaques. Furthermore, many other complex biochemical processes may link or give synergism among CVD and insulin resistance, chronic inflammation and oxidative stress.

Insulin is involved in the uptake of free fatty acids in the muscles and the adipose. The insulin resistance leads to an augment in the levels of these acids delivered to liver increasing VLDL-c and the exchange of triglycerides to cholesterol ester from HDL-c and LDL-c. As a result, there is the higher catabolic rate of HDL-c and conversion of LDL-c to small density LDL-c that is easily oxidized and may penetrate the arterial wall and induce a macrophage answer inducing to the beginning of the formation of atherosclerotic plaques (Wang *et al.,* 2017; Barbalho *et al.,* 2016b; Mokta *et al.,* 2017). The development of CVD is also related to low-grade inflammation, so CRP concentrations have been defined as a risk factor in adults. Cardiovascular risk has also been studied in obese children associated with CRP, evidencing that the sooner their dosage, the faster the diagnosis and the better the treatment and prevention (Meshkani *et al.,* 2009; Barbalho *et al.,* 2016b; Mansour *et al.,* 2016). Also, CRP also presented significance in the elderly, presenting high levels in patients with a higher risk of mortality related to CVD (Puzianowska-Kuźnicka *et al.,* 2016).

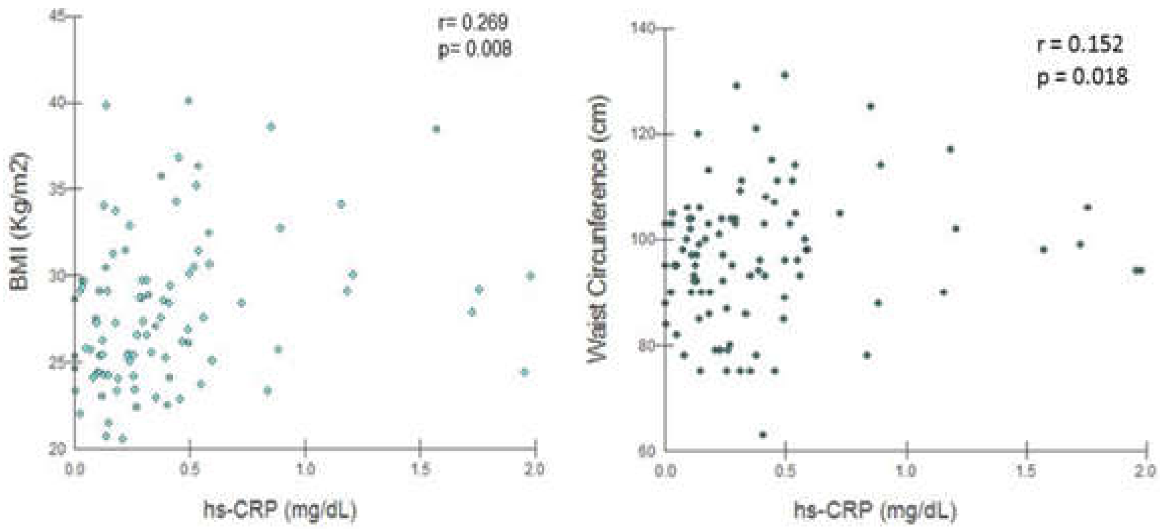

Figure 1. Correlation between hs-CRP and body mass index (BMI) and Waist Circumference

Table 1. Mean, median and standard deviation of the anthropometric and biochemical parameters

Parameters	Media±DP Male n=52	Median	Media±DP Female n=42	Median	Media±DP Total n=94	*p*
Weight	82.85±16.28	80.5	70.05±9.44	69.5	77.13±15.02	<0.0001*
Stature	1.72±0.07	1.72	1.59±0.05	1.59	1.66±0.09	<0.0001**
BMI	28.02±4.54	27.56	27.80±4.14	27.15	27.93±4.34	0.387**
WC	98.34±12.10	98.0	95.02±13.48	94.5	96.86±12.77	0.105**
Glucose	116.28±36.13	105	118.47±40.14	110	117.26±37.78	0.390**
TGC	134.92±66.47	117.5	128.47±65.36	116	132.04±65.70	0.319**
TC	178.22±43.17	176	182.19±44.50	186	180.03±43.58	0.334**
LDL-c	110.07±37.10	106.2	106.42±41.42	105.9	108.45±38.90	0.329**
HDL-c	41.23±8.55	40.5	50.05±13.07	47.5	45.17±11.61	0.0003*
hs-CRP	0.36±0.38	0.26	0.46±0.47	0.32	0.40±0.42	0.305*

BMI: Body Mass Index (Kg/m^2); WC: Waist circumference (cm); TGC: triglycerides (mg/dL); TC: Total cholesterol (mg/dL); HDL-c: High density lipoprotein (mg/dL); LDL-c: Low density lipoprotein (mg/dL); hs-CRP: high sensitivity C reactive protein (mg/dL).*Mann Whitney. ** T-Student.

Table 2. Correlation between hs-PCR and biochemical parameters

Parameters	Glycaemia	TGC	TC	LDL-c	HDL-c
hs-PCR	r = -0.162 *p* = 0.118	r = -0.056 *p* = 0.590	r = -0.061 *p* = 0.559	r = -0.024 *p* = 0.818	r = -0.08 *p* = 0.417

TGC: triglycerides; TC: Total cholesterol; HDL-c: High density lipoprotein; LDL-c: Low density lipoprotein; hs-CRP: high sensitivity C reactive protein.

Table 3. Comparison between the biochemical parameters, BMI and Waist Circumference

Parameters	BMI < $25Kg/m^2$ n=25	BMI ≥ $25Kg/m^2$ n=69	*p-value*
Glycaemia (mg/dL)	109.12±29.22	120.21±40.22	0.1744*
TGC (mg/dL)	112.88±70.41	138.98±63.01	0.0444**
TC (mg/dL)	175.12±39.42	181.81±45.13	0.2568**
LDL-c (mg/dL)	106.34±33.82	109.21±40.78	0,3776**
HDL-c (mg/dL)	46.20±8.67	44.79±12.54	0,1223*
hs-CRP (mg/dL)	0.29±0.39	0.44±0.43	0,0694**
Parameters	Normal Waist Circumference n=23	High Waist Circumference n=71	*p-value*
Glycaemia (mg/dL)	109.69±23.91	119.72±41.14	0.357*
TGC (mg/dL)	120.43±76.66	135.80±61.88	0.166**
TC (mg/dL)	173.91±37.35	182.01±45.48	0.221**
LDL-c (mg/dL)	103.69±33.85	109.99±40.49	0.251**
HDL-c (mg/dL)	46.13±7.76	44.86±12.64	0.124*
hs-CRP (mg/dL)	0.29±0.18	0.44±0.47	0.281*

BMI: Body Mass Index; TGC: triglycerides; TC: Total cholesterol; HDL-c: High density lipoprotein; LDL-c: Low density lipoprotein; hs-CRP: high sensitivity C reactive protein. *Mann Whitney. ** T-Student.

The relationship with arterial vascular inflammation makes CRP a subclinical marker associated with atherosclerosis and assists in the early detection of macrovascular disease (Lachine *et al.,* 2016). Furthermore, CRP show a relationship with unstable and stable angina (Leite) *et al.,* 2015), which proved to be a predictor of aortic stenosis and valve stenosis (Katsiki *et al.,* 2017), confirming its relationship as a biomarker of cardiovascular risk. There are several controversial relationships when analyzing anthropometric measures. Pardina, *et al..*. (2016), in a study with patients undergoing bariatric surgery, showed that the higher the weight loss, the lower the serum levels of CRP. In another study by Rohani *et al.* (2016), the weight loss that culminated in lower anthropometric measurements was not related to a decrease in CRP levels. Patients with various components of the metabolic syndrome (MS) practicing moderate intensity exercise for a short period of 12 weeks showed a significant decrease in WC and BMI, also correlated with a decrease in CRP (Rouhani *et al.,* 2016) Lin *et al.* (2017) found that hsCRP were much higher in obese women than in obese men.

There is a consensus in the literature that the inflammatory processes play a major role in the beginning and progression of atherosclerosis and its complications. The vascular vulnerability and progression of atherosclerosis through different pathways may include modifications on the endothelial nitric oxide bioactivity. These modifications may include down-regulation of transcription of the synthase of nitric oxide), overexpression of plasminogen activator inhibitor 1, increased expression of focal adhesion molecules, oxidation of LDL-c, and association with the release of IL- 1β, IL-6, and TNF- α by activated monocytes (Asgari *et al.,* 2016; Joris *et al.,* 2017; Schmidt *et al.,* 2015). Once hs-CRP is a not expensive and an easy-to-measure inflammatory marker and BMI and WC are also non-invasive and non-expensive parameters, we may say that the association of these variables could be an important tool to help physicians in predicting other complications in patients underwent arteriography. Furthermore, these variables could interfere in the therapeutic approaches that may reduce the risk factors in these patients in order to seek a better quality life and extend life expectancy.

Conclusion

Our study showed that in patients underwent coronary arteriography, the body composition, characterized by increased body adiposity according to BMI and WC, were the main factors correlated to high concentrations of hs-CRP in patients underwent arteriography. This indicates that the control of body weight and waist circumference is indispensable to improve quality of life and life expectancy in this kind of patient once it is associated to several other risk factors that increase the morbidity and mortality and management of this condition requires continuous attention.

Compliance with ethical standards

Disclosure of potential conflicts of interest: We did not have funding support for this research. Authors declare no conflict of interests.

Research involving Human Participants: This project was approved by the under protocol number 449. All procedures performed in this study were in accordance with the ethical standards of the Ethics Committee of the University of Marilia (UNIMAR) – Sao Paulo – Brazil.

The experimental protocol was in accordance with the Ethical Standards of the Institutional Ethics Committee and the Helsinki Declaration of 1975 (revised in 2008).

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

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