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ORIGINAL

RELAÇÃO ENTRE O NÍVEL DE ADIPONECTINA COM MEDIDAS ANTROPOMÉTRICAS E RESPIRATÓRIAS DE PACIENTES SUBMETIDOS À CIRURGIA DE REVASCULARIZAÇÃO MIOCÁRDICA

RELATIONSHIP BETWEEN ADIPONECTIN LEVEL WITH ANTHROPOMETRIC AND RESPIRATORY MEASURES OF PATIENTS SUBMITTED TO MYOCARDIAL REVASCULARIZATION SURGERY

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RESUMO

Os baixos níveis de adiponectina no plasma tem relação com o aumento da mortalidade em pacientes com doenças cardiovasculares, alterações da função pulmonar, sugerindo ação pró-inflamatória em decorrência da obesidade. Foram avaliados 65 pacientes, submetidos à cirurgia de revascularização do miocárdio. Analisados nível sérico da adiponectina, medidas antropométricas e respiratórias. Verificou-se que 55,8% dos pacientes do sexo masculino e 40% do feminino apresentaram sobrepeso e um IMC médio de 28,10 kg/m². Os maiores índices de sobrepeso foram verificados na faixa etária de 40 a 59 anos (62,5%) e de 60 anos ou mais (47,8%) O teste de comparação de proporção foi significativo para sexo (p=0,004), idade (p<0,001) e IMC (p=0,007). Quanto aos níveis de adiponectina verificou-se maior média no grupo masculino (média = 4,29), entre 40 a 59 anos (média = 4,70), com sobrepeso (média=4,70). Não houve relação entre o nível de adiponectina com as medidas antropométricas e respiratórias de pacientes submetidos à cirurgia de revascularização miocárdica.

Palavras chaves: índice de massa corporal, adiponectina, antropometria, revascularização miocárdica.

ABSTRACT

Low plasma adiponectin levels are associated with increased mortality in patients with cardiovascular disease, changes of pulmonary function, suggesting that pro-inflammatory action as a result of obesity. We evaluated 65 patients submitted to myocardial revascularization surgery. Analyzed serum level of adiponectin, anthropometric and respiratory measures. It was verified that 55.8% of the male patients and 40% of the female patients were overweight and had an average BMI of 28.10 kg / m². The highest rates of overweight were found in the age group of 40-59 years old (62.5%) and 60 or older (47.8%). The proportion-comparison test was significant for gender (p = 0.004), age (p <0.001) and BMI (p = 0.007). Adiponectin levels were higher in the male group (average = 4.29), between 40 and 59 years old (average = 4.70), overweight (average = 4.70). There was no relationship between the level of adiponectin and the anthropometric and respiratory measurements of patients undergoing myocardial revascularization surgery.

Key words: body mass index, adiponectin, anthropometry, myocardial revascularization.

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INTRODUCTION

Overweight and obesity are related to the development of diseases such as hypertension, *Diabetes Mellitus* (DM), dyslipidemia and cardiovascular disease, which are related to the Metabolic Syndrome (MS) [1].

Endocrine disorders in individuals with excess weight have been associated with the accumulation of adipose tissue, the latter being responsible for the production of hormones adipokines[2]. The leptin and adiponectin are two important adipokines that are influenced by the elevation of Body Mass Index (BMI) and can be changed in the presence of pulmonary disease[3].

The ADPN is a biologically active substance, where this adipokine is a hormone synthesized and secreted predominantly by adipocytes. High values of this hormone relate to the protection of the formation of atheromatous plaque and has an inverse relation to body weight[4].

In obese individuals there is an increase in the secretion of pro-inflammatory adipokines and decrease in the production of anti-inflammatory adipokines. These changes in the balance of adipocitocin is a strategic component of the pathogenic metabolism, immune responses, and the lipid metabolism. These are related to cardiovascular diseases [2,5,6].

In addition to the alterations mentioned concerning the levels of cytokines, the accumulation of thoracic and abdominal fat may promote the reduction of total lung compliance, which leads to changes in the respiratory mechanics and influence on changes in forced expiratory volume in 1 second (FEV1) and peak expiratory flow (PEF) [7].

Associated to these changes occur the mechanical stress on the upper airways, a result of the deposit of adipose tissue around the pharynx. The reduction of lung volumes in obese individuals due to structural changes in the thoracic-abdominal region. Causes diaphragmatic mobility limitation and the costal movement, both of which are essential to the ventilatory mechanics. With this, it will overload the inspiratory muscles, which trigger impairment of ventilation in the lung bases[8].

Studies have shown a correlation between ADPN, morbidity and mortality and pulmonary complications, such as atelectasis, pneumonia, pulmonary thromboembolism. There were reports on the association of plasma ADPN levels with the pulmonary function, suggesting a pro-inflammatory role. Individuals with excess weight, especially with accumulation of visceral fat, joins the hypoadiponectinemia, where the fat accumulation in the Region Thoracic decreases the total lung compliance, taking the individual relationship with predominance of cardiovascular and pulmonary diseases. Studies have reported that low levels of ADPN is a predictor of systemic inflammation, in particular, inland areas[9, 10, 11,12].

In this way, the identification of patients at risk of postoperative pulmonary complications, favors good prognoses and reduction of morbidity and mortality rates.

METHOD

Cross-sectional comparative study with a quantitative approach. Patients were randomly selected: 65 adults aged 42 to 85 years old, submitted to elective surgery for myocardial revascularization. The patients were selected at the Heart Institute of Pernambuco (INCOR-PE) that works in Real Portuguese Hospital of Beneficence in Pernambuco (RHP) located in Recife-PE.

The inclusion criteria were: patients undergoing elective myocardial revascularization surgery, ages 42 to 85, of both genders. The participants form divided into three groups according to the body mass index (BMI): eutrophic, 19.9 kg/m2 < BMI < 24.9 kg/m2, which constituted the control group, individuals with 25 kg / m2 < BMI < 29.9 kg/m2 to be part of the overweight group, individuals with BMI > 30 kg/m2 for the obesity group. There were excluded from the study patients with mental disorders, cognitive deficits and neuromuscular disorders.

Personal data were collected from medical records. The participants were submitted to anthropometric assessment (waist circumference - WC, hip circumference - HC, waist-to-hip ratio - IC and calculation of the BMI).

The participants were also evaluated as to the level of preoperatively adiponective. These ratings occurred in the Immunology Laboratory of Immunopathology Keizo Asami (LIKA - UFPE) using ELISA (Enzyme-linked-immune-sorbent-assay).

The research followed the recommendations proposed by the National Health Council for research involving human beings protocol the ethics of UFPE N 423.305/2014. The participants evaluated signed the informed consent form (ICF).

Statistical analysis

For analysis of the data was built a database in the EPI INFO program, which was exported to the Statistical Package for Social Sciences (SPSS) version 11, where there was performed the analysis. To evaluate the profile of patients evaluated were calculated the percentage frequency and built their distributions of frequencies. To evaluate the laboratory examinations there were calculated the statistics: minimum, maximum, median, average and standard deviation. There were calculated confidence intervals for the average found.

In the comparison of the proportions found was applied the Chi-square test was used for comparison of proportions. The assessment of normality of quantitative variables of the study was applied to the *Kolmogorvo-Smirnov* test and in cases in which the test indicated normality were applied to the t-student test for comparison of averages of PCR and adiponectin, between two groups, and the ANOVA test, comparing the average between three or more groups of interest.

In cases in which the test indicated no normality test was applied, the Mann-Whitney test, the comparison of two groups, and the *Kruskal-Wallis* test, comparing three or more groups. Yet, in order to evaluate the correlation between the variables of interest with the FEV1, PEF, CRP and ADPN was calculated using Pearson's correlation coefficient, in cases in which it was indicated normality of the variables, and the Spearman coefficient, in cases where it was not indicated normality of variable. All conclusions were drawn from considering a significance level of 5%.

RESULTS AND DISCUSSION

Table 1 shows the distribution of the profile of patients. Reveals that the majority were males (67.7%) and are 60 or older (75.0%). On average, patients are 64.4 years old with a

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standard deviation of 10.3 years old. As to BMI, the majority of patients present overweight (50.8%). In addition, notes that the proportion comparison test was significant in all the evaluated factors (p-value = 0.004 for gender, p-value < 0.001 for age and p-value = 0.007 for BMI) indicating that the proportion of male patient, 60 or older and with overweight is significantly higher.

Table 1. Profile of patients about the gender, age and BMI classification.

Rated factor	n	%	p-value[1]
Gender			
Male	44	67,7	0,004
Female	21	32,3	
Age (in years)			
40 - 59	16	25,0	<0,001
60 or older	48	75,0	
Minimum	42		-
Maximum	85		-
Average±Standard deviation	64,4±10,3		-
BMI			
Eutrophic	12	19,0	
Overweight	32	50,8	0,007
Obese	19	30,2	

BMI: Body Mass Index
[1]p-value Chi-square test for comparison of proportion (p-value < 0.05 ratios differ significantly).

As BMI classification, **Table 2** refers to the biomarkers PCR and ADPN, indicates that the group of eutrophic patients, overweight and obese that values have, on average, a CRP level and adiponectin levels higher in the group with overweight; however, the p-value of CRP (p=0.985) and ADPN (p=0.206) there was no statistical relevance.

Table 2. Average values and standard deviation of adiponectin and CRP according to the classification of BMI.

Rated factor	Biomarkers	
	CRP	ADPN
BMI		
Eutrophic	0,37±0,32	2,55±2,31
Overweight	0,62±0,91	4,70±4,06
Obese	0,42±0,40	3,62±3,61
p-value	0,985[1]	0,206[2]

CRP: C-Reactive Protein
[1] p-value of the Kruskal-Wallis test
[2] p-value of the ANOVA test

Table 3 describes the analysis of the correlation coefficients between the anthropometric measures, and respiratory measures with evaluated biomarkers verifies that in the eutrophic group there was no significant correlation between anthropometric measurements, and respiratory measurements with the CRP and ADPN. In the group of patients with overweight was observed significant correlation of CRP with HF and PEF-Pre. Yet, this same group, a significant correlation between ADPN and the IOC.

It was found that from the 65 patients studied, 44 were male (67.7%) and aged 60 or older (75.0%). It was found that 55.8% of male patients and 40% of females were overweight and an average BMI of 28.10 kg/m^2. The highest rates of overweight were observed in the age range of 40 to 59 (62.5%) and 60 or older (47.8%).

The serum levels of adiponectin was observed a higher average in the group of male patients, aged 40 to 59, with overweight and had postoperative complications respiratory complications. In the other parameters evaluated adiponectin showed on average levels are identical.

In the group of females was observed a lower average of FEV1 and PEF, in all periods of the study. Still, the average comparison test was significant (p-value < 0.001) in all comparisons with the group of males indicate that women are significantly lower than the average of the group of males. Regarding age, the group with an average age of 60 or older had an average of FEV1 and PEF less in all moments of analysis; however, the difference was significant only in the PEF of the pre-operative time (p-value = 0.028) and in the PEF of high (p-value = 0.012).

In relation to BMI, the group with overweight presents a higher average of PEF in all evaluated moments. However, the average of FEV1 was higher in the obese group in all moments of analysis. It seems that there was no significant difference in the medium values of FEV1 and PEF between the eutrophic group, overweight and obese, at no time during the study. Soon, we can infer that the classification of the BMI is not a determining factor for the occurrence of changes in the values of FEV1 and PEF.

In obese individuals the adipose tissue (TA) induces the synthesis of molecules with pro-inflammatory action. The hormones secreted by this tissue revolutionized the concepts about its biological function, where there would be only one supplier and storer of energy, but also a dynamic organ and central role in the metabolic regulation (MAFORT et al., 2016).

Hyperinsulinemia and insulin resistance coexist in obesity. Insulin resistance has a connection between the metabolic syndrome and its associated pathologies, where high levels of insulin are required for the maintenance of glucose homeostasis. Where, high levels of insulin promotes oxidative stress, causes the ectopic fat accumulation resulting in atherosclerosis, dyslipidemia, liver steatosis (BŁOGOWSKI et al., 2013)

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Table 3. Correlation coefficient between the anthropometric measurements, respiratory measures with CRP and ADPN, according to BMI.

Anthropometric Measurements	Eutrophic		Overweight		Obesity	
	CRP	ADPN	CRP	ADPN	CRP	ADPN
RCQ	0,430 (0,163[1])	0,118 (0,716)	0,186 (0,307[2])	0,023 (0,902)	-0,209 (0,391[1])	-0,101 (0,680)
IC	0,451 (0,142[1])	0,257 (0,420)	0,367 (0,039[2])	-0,268 (0,137)	-0,401 (0,089[1])	-0,214 (0,379)
IOC	0,423 (0,171[1])	0,211 (08,511)	0,319 (0,075[2])	-0,354 (0,047)	-0,282 (0,242[2])	0,058 (0,814)
Respiratory measurements						
VEF1 – Pre	-0,101 (0,755[1])	-0,030 (0,927[1])	-0,062 (0,737[2])	0,080 (0,663[2])	0,053 (0,830[1])	0,385 (0,104[1]
PEF – Pre	-0,256 (0,422[1])	-0,184 (0,568[1])	-0,441 (0,011[2])	0,104 (0,571[2])	-0,147 (0,548[1])	0,153 (0,530[1])
VEF1 – Rec	-0,308 (0,357[1])	-0,488 (0,128[1])	-0,003 (0,989[2])	0,52 (0,790[2])	-0,124 (0,624[1])	0,151 (0,550[1])
PEF – Rec	-0,340 (0,307[1])	-0,501 (0,116[1])	0,001 (0,996[2])	0,133 (0,491[2])	-0,383 (0,116[1])	-0,032 (0,899[1])
VEF1 – Post	-0,163 (0,632[1])	-0,350 (0,291[1])	-0,084 (0,666[2])	0,230 (0,229[2])	-0,042 (0,869[1])	0,301 (0,226[1])
PEF – Post	-0,289 (0,388[1])	-0,306 (-0,361[1])	-0,142 (0,462[2])	0,306 (0,106[2])	-0,036 (0,888[1])	0,363 (0,138[1])

WHR: relationship waist hip; IC: index of taper; IOC: central obesity index; PCR: C-reactive Protein; Serum Level of adiponectin ADPN:; FEV1-forced Expiratory Volume in 1: second Pre operative; PEF-Peak expiratory flow pre: pre surgery; FEV1-Rec: Forced Expiratory Volume in 1 second surgical recovery; PEF-Peak expiratory flow Rec: surgical recovery; FEV1-Post: Forced Expiratory Volume in 1 second discharge; PEF-Peak expiratory flow post: hospital [1] p-value of the Pearson correlation test; [2] p-value of the Spearman correlation test.

The adipose tissue produces cytokines involved in the inflammatory process, the so-called pro-inflammatory adipokines, among these there is also the release of tumor necrosis factor-alpha (TNF-alpha) and interleukin 6 (IL-6). The adipokines produce inflammatory responses in several chronic inflammatory diseases [15].

Adiponectin is an anti-inflammatory adipocin, when you're in low plasma concentration acts on inflammatory characteristic expression in patients with obesity, type 2 diabetes and coronary disease. However, the normal concentration of ADPN favors changes in the phenotype of macrophages from pro-inflammatory to anti-inflammatory. Therefore, there are studies that reported adiponectin as an adipocin that has functions: anti-inflammatory, anti-atherogenic, and cardio protector (SATO et al., 2014).

Assad et al., the concentration of ADPN is reduced in obesity, where it is possible to observe the turgency of adipocytes that induce hypoxia, consequently, cell necrosis and inflammatory process induction [16]. The inflammation attracts macrophages that stimulate the production of signaling molecules TNF-α and IL-6. Thus, necrotic adipocytes may offer overweight. In the present study, it was reported profile of patients submitted to myocardial revascularization with 50.8% (p=0.007) overweight. For Sousa et. al., cardiac surgery related to anthropometric measurements 45.1% with overweight and 20.6% obesity [17]. Johnson et al., analyzing mobi-mortality in the postoperative period described the profile of patients with overweight 44% and 23% obese [18].

ADPN and its receptors are expressed in various cells of the lung. Thus, this anti-inflammatory adipokine acts in pulmonary protection; however, the elevation of the level of ADPN is not sufficient to remove the impairment of pulmonary function in obstructive respiratory pathologies. In addition, the adiponectin deficiency exacerbates the production of pro-inflammatory cytokines. These; however, are involved in the inflammatory process, in turn, lead to the increase of local inflammatory expression that evokes systemic responses to search for patients with acute coronary syndromes and the levels of CRP and ADPN, verified high serum levels of CRP ($p<0.05$). In relation ADPN and CRP entered in high serum level of CRP is related to low values (ADPN $p<0,001$) [12,16,19].

The occurrence of obstruction of the airways in humans, may be associated with the levels of ADPN. Hayashikawa et al., reported that low levels of total serum ADPN in obesity may contribute to the predominance of smooth muscles in the airways[7]. However Wei et al., we observed that metabolic and cardiovascular diseases are associated with respiratory disorders[5]. As a result of research, the serum levels of ADPN were significant (p=0.003) related to the FEV1 not related to obesity.

The measurement of lung volumes can be useful to evaluate and detect the risk of death due to cardiovascular and

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respiratory diseases. The FEV1 is a strong indicator of lung function. Thus, the analysis of pulmonary function in individuals with cardiovascular and respiratory impairment, which demonstrates the connection between the pulmonary dysfunction and the aspect of chronic inflammation[5, 7,19] .

There is evidence of the association between the decrease in forced expiratory volume in 1st second (FEV1) and mortality due to cardiovascular diseases (CVD). In this way, it was found that low values of FEV1 are considered as independent risk factor for premature deaths by CVD [20]. In obese individuals the reduction of serum concentration of ADPN is related to obesity, and consequently with the CVD [21].

The surgical procedure leads to tissue exposure, the aggressors, factors such as the trauma exercised by surgical manipulation, extra corporeal circulation (CPB) and also contact with anesthetic substances. As a consequence, leads to impairment of the homeostatic balance of the body. The patients showed a decrease of functionality of respiratory functions, in the course of the postoperative period with a slight improvement in the hospital, independent of the classification of BMI. In agreement with the literature changes in lung function occurs in a large proportion of patients after open heart surgery what is in agreement with the data presented in this study[22,23].

Patients with obstructive diseases and their association between serum levels of ADPN and pulmonary function, are related to levels of ADPN with inversely proporcionaios values for FEV1. This result shows the ADPN has anti-inflammatory properties, and that the decrease in the levels of ADPN relates to reduced ability of protection against the development of obstructive pulmonary diseases[12,15]. However, Miller et al. demonstrated that the deficiency of adiponectin levels in rats in the process of inflamatrio induced by tobacco caused the increase of emphysema. Thus, evidence-that the pro-inflammatory effects of adiponectin levels[24].

The excess weight can compromise the thoracic mobility and the diaphragm, as a result, promote changes in ventilatory function. One way to evaluate the obstruction of the upper airways is through the measurement of peak of expiratory flow (PEF), being considered a direct indicator of obstruction[25]. Research promoted by Sarawasthi et al., demonstrated that the PEF was significantly lower in obese men than in non-obese patients; however, there was no difference between the respective groups in women.

Among the measures of FEV1 and PEF in relation to BMI, the group of overweight patients showed higher average PEF, while in obese patients the mean FEV1 was higher. The classification of the BMI was not a determinant factor for the occurrence of changes in the values of FEV1 and PEF. However, showed that there was no significant difference between the values obtained and provided to the respiratory measures between the eutrophic and obese groups[2,8].

It is known that the increase in the stiffness of the chest, as a result of age, resulting in the loss of the elastic recoil of the lungs and significant decrease in respiratory muscle strength. In this way, can lead to a progressive reduction of pulmonary function in the elderly, which is confirmed by the lowest mean FEV1 and PEF found in patients above 60. [25,26]

The parameters of pulmonary function impairment of respiratory parameters (FEV1 and PEF) in the immediate postoperative period, both in individuals with overweight and obese, there was minimal reduction in lung volumes, coming of normality, when compared to predicted values. Patients with heart disease often have respiratory changes. The associated comorbidities, the loss of respiratory muscle strength, the instability of the chest, the inflammatory process triggered by external factors, such as the CEC, directly affect the individual's lung capacity during this period[27].

The limitations of the study are found in the associated comorbidities in the population studied, the variability of the surgical procedure and the complications of intra and postoperative. In this way, the findings of this study, have suffered interference. On the other hand, the short period of hospitalization resulted in the low variability of values of ADPN. And also, the process of pain after cardiac surgery may have resulted in the thoracic instability. Thus, the results obtained may have suffered interference. Moreover, this work spanned only two phases of the process, pre and post surgery, missing, the intraoperative.

CONCLUSION

There was no correlation between the level of ADPN, BMI, anthropometric and respiratory measurements of patients who underwent myocardial revascularization surgery.

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