ORIGINAL ARTICLE

ASSOCIATION OF C-REACTIVE PROTEIN WITH CARDIOVASCULAR RISK FACTORS, LUNG FUNCTION AND QUALITY OF LIFE IN YOUNG ADULTS

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Highlight: Increased inflammatory response is associated with obesity; Increased inflammatory response affects lung function; Psychological, functional and vitality quality of life were higher in young adults with moderate cardiovascular risk.

PRE-PROOF

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ASSOCIATION OF C-REACTIVE PROTEIN WITH CARDIOVASCULAR RISK FACTORS, LUNG FUNCTION AND QUALITY OF LIFE IN YOUNG ADULTS

ABSTRACT

Objective: To associate ultrasensitive C-reactive protein (US-CRP) with cardiovascular risk factors, lung function and quality of life. *Methods*: Body mass index (BMI), waist circumference (WC), haemodynamic parameters, blood sampling for US-CRP, spirometry (peak expiratory flow - PEF; forced expiratory volume in one second - FEV_1) and individualised application of the Short Form-36 (SF-36) health-related quality of life (HRQoL) questionnaire. *Results:* Of the 100 young adults studied, BMI and WC were higher in those at high risk. PEF and FEV_1/FVC ratio were higher in low-risk young adults. Mental health, functional capacity and vitality (VT) were higher in young people at lower cardiovascular risk. Of the overweight/obese young adults, 87.5% were at moderate and high risk (p=0.044), and of those with WC above the predicted level, 86.7% were at moderate and high risk (p=0.002). Among young adults with HRQoL above P(50), 43.5%, 50%, and 45.7% were at low cardiovascular risk for functional capacity, general health, and vitality, respectively. US-CRP was positively correlated with BMI (p=0.044), whereas PEF (p=0.046) and FEV_1/FVC ratio (p=0.002) were inversely correlated. *Conclusions:* US-CRP was associated with BMI and WC, lung function and HRQoL, especially with respect to physical aspects. Obesity control should be emphasized, and regular physical activity and proper nutrition may help, including reducing the chronic inflammatory response.

Keywords: inflammation; obesity; abdominal obesity; pulmonary function test; quality of life

INTRODUCTION

Currently, the increasing prevalence of overweight has become a global public health challenge.[1, 2] Obesity is a chronic disease in which the accumulation of adipose tissue leads to consequences such as an increase in cardiovascular and metabolic disease, disability and mortality, and is associated with low levels of physical activity.[3, 4] The most commonly used markers of obesity are body mass index (BMI) and waist circumference (WC), the latter being used as a marker of abdominal obesity.[4]

Obesity is an important cause of cardiovascular disease (CVD), and several factors have been studied to elucidate the relationship between the two conditions.[5] Among them, C-reactive protein (CRP) has been shown to be an influential predictor of CVD, as adipose tissue can influence the secretion of pro-inflammatory cytokines, and when these enter the systemic circulation and reach the liver, they stimulate the release of CRP.[6] Thus, a low chronic inflammatory response is a common aspect of obese individuals.[7]

In addition, the accumulation of fat in the body causes changes in respiratory physiology, affecting various parameters of lung function, such as reduced diaphragmatic mobility and costal movement.[8] The association between obesity and reduced lung function is related to low levels of physical activity and poorer quality of life (QoL) in obese individuals.[4, 9] There is also an association between elevated CRP, obesity and the presence of restrictive ventilatory disorders.[10] The overlap of these conditions leads to impairment in aspects related to QoL, both physical (activities of daily living and vitality) and mental health.[3]

In summary, it is suggested that elevated CRP is a current risk factor, is associated with obesity, leads to a low chronic inflammatory response, and that this condition may affect lung function and have consequences for HRQoL, especially aspects related to activities of daily living and vitality. The literature on the relationship between CRP and lung function and HRQoL is still in its infancy. The literature that has been found is based on adult samples, whereas the present study is based on young people. If CRP levels are high in young people, there is likely to be obesity and, as a result, impaired lung function and quality of life. If these conditions persist into adulthood, there is a risk of developing metabolic and cardiovascular disease and restrictive ventilatory disorders. The aim of this study was to investigate the association of ultrasensitive C-reactive protein (US-CRP) with cardiovascular risk factors, lung function and quality of life.

METHODS

This is an analytical, cross-sectional study carried out with young people enrolled in a higher education course in the field of health at a university. The study was carried out between August 2018 and February 2019, with 180 students enrolled from the first to the tenth semester. Regularly enrolled young people aged 18 and over were included, while those with chronic co-morbidities (heart disease, chronic lung disease) and cognitive impairment registered with the course secretary were excluded. The sample was recruited by convenience and power was calculated using G*Power 3.1 software in post-hoc mode, considering the analysis performed (correlation of continuous variables), an effect size (ρH1) of 0.3, a significance level of 5%, and a power of 92%.

The study was approved by the Human Research Ethics Committee of the Evangelical University of Goiás (CEP-UNIEVANGÉLICA), following the guidelines of Resolution 466/2012 of the National Health Council (CNS), according to opinion number 2.989.854/2018. All participants signed an informed consent form (ICF). The young adults were approached by the researchers during class, with the permission and schedule of the teacher in the class at the time. The stages and assessments were explained by reading the ICF orally and then giving it to the young people to read again and sign. This was followed by an explanation of the blood collection procedures, which were scheduled according to the participant's availability. On the same day, the QoL questionnaire was administered, and anthropometric and haemodynamic measurements were taken. The lung function test was performed on a different day because of the need for preparation: no coffee on the day of the test, no physical activity in the previous 24 hours, and no smoking in the previous 2 hours. The tests were carried out at the university, specifically in the multidisciplinary laboratory of the physiotherapy course.

Sociodemographic data were collected using an identification form with information on sex, alcohol and smoking history, physical activity and current medication.

BMI (kg/m2) was calculated by dividing body mass (kg) (Filizola digital scale, model 2096 PP, São Paulo, Brazil) by height (m) squared (Sanny stadiometer, São Paulo, Brazil). The cut-off points for eutrophic and overweight/obese subjects were ≤ 24.99 kg/m² and ≥ 25 kg/m², respectively.[11] WC was measured using an inextensible anthropometric tape (Teklife, model TL200, São Paulo, Brazil) positioned at the midpoint between the upper iliac crest and the last costal arch at the end of expiration at rest. The reference values to characterise WC as within the predicted range were less than 94 cm for men and 80 cm for women.[12]

Systemic blood pressure was measured with the young adults sitting for five minutes at rest. Measurements were taken one minute apart, and the first measurement was discarded.[13] A semi-automatic device (OMRON, model HEM 705CP, Kyoto, Japan) was used to measure systolic blood pressure (SBP) and diastolic blood pressure (DBP). The reference values for normal SBP and DBP were less than 120 x 80 mmHg.

A blood sample was taken for US-CRP measurement (5 mL taken to analyse 1 mL of serum). The method of analysis was immunoturbidimetric and classified as low (< 1mg/dL), intermediate (1 - 3 mg/dL) and high (> 3 mg/dL) cardiovascular risk.[14]

Spirometry was performed using a portable device (brand Mir, model MiniSpir, Rome, Italy) with specific disposable filters and mouthpieces. The participant performed the test in a seated position with the head in a neutral position and attached to a nose clip. Acceptability and reproducibility criteria were based on the American Thoracic Society/European Respiratory Society standard.[15] Manoeuvres performed with 1) maximal inspiration before the test, 2) satisfactory start of expiration, 3) evidence of maximal effort, 4) test duration of at least 6 seconds, 5) plateau in the last second and 6) absence of cough, leak, obstruction, Valsalva manoeuvre and glottis closure were accepted. The parameters analysed were peak expiratory flow (PEF), forced expiratory volume in one second (FEV_1), forced vital capacity (FVC) and FEV_1/FVC ratio. For reproducibility, two manoeuvres were considered if the difference in PEF was < 0.5 L and FEV_1 if the difference between manoeuvres was < 0.15 L. The results were interpreted according to the values predicted for the Brazilian population.[16]

HRQoL was assessed using the Short Form-36 (SF-36) questionnaire.17 The questionnaire has a multi-item scale that includes: functional capacity (10 items), limitations due to physical health problems (4 items), limitations due to mental/emotional health problems (3 items), social functioning (2 items), emotional well-being (5 items), pain (2 items), vitality (4 items), and perception of general health (5 items). Scores range from 0 to 100, with lower scores corresponding to poorer HRQoL and higher scores reflecting better QoL.[17]

The results are presented as mean, standard deviation, frequencies, percentages, and variation (Δ) between means. Normality of the data was tested using the Kolomogorov-Smirnov test. Comparisons between groups were made using the one-way ANOVA test with post hoc for variables with a normal distribution and the Kruskal-Wallis test with Dunn's post hoc for variables with an asymmetric distribution. The chi-squared test was used to test the association between categorical variables, and the SF-36 domains were classified according to percentiles (P50). The correlation between continuous variables was assessed using Pearson's coefficient (normal distribution) and Spearman's coefficient (asymmetric distribution). The p-value used was < 0.05

and the data were analyzed using the Statistical Package for Social Science (SPSS, IBM, version 23.0, Armonk, NY) software.

RESULTS

The characterisation of the sample is described in Table 1. Most of the young adults were female (82%), without a history of alcoholism (51%) or smoking (79%) and without regular physical activity (62%). The most common medication used was contraceptives (17%).

Table 1 - Characterization of the sample of young adults who took part in the study (n = 100)

Variables	**Mean (SD)**
Age (years)	20,90±2,37
Mass (kg)	62,04±11,16
Height (cm)	166,26±08,04
	n (%)
Sex	
Women	82 (82)
Male	18 (18)
Ethylism	49 (49)
Smoking	21 (21)
Physical activity	37 (37)
Medicines in use	
Anxiolytics/antidepressants	10 (10)
Contraceptives	17 (17)
Analgesia/anti-inflammatory	3 (3)
Vitamins and minerals	4 (4)
Neurological	4 (4)
Intestinal disorders	5 (5)
Others	5 (5)

Source: Prepared by the authors (2023).

With regard to anthropometric data, young adults at high cardiovascular risk had higher BMI (low risk: Δ= +3.78 kg/m², p< 0.001; moderate risk: Δ= +2.77 kg/m², p= 0.011) and WC (low risk: Δ= +6.90cm, p= 0.001; moderate risk: Δ= +5.53cm, p= 0.019) (Table 2).

About lung function, young adults at moderate cardiovascular risk had a higher PEF compared to those at low (Δ= +1.74 L/s, p< 0.001) and high risk (Δ= +1.10 L/s, p= 0.013). In addition, young adults classified as low risk according to CRP had a higher FEV_1/FVC ratio compared to those at moderate (Δ= +0.06, p= 0.021) and high risk (Δ= +0.04, p= 0.037).

In terms of perceived quality of life, young people at moderate cardiovascular risk had a higher mental health score than those at high cardiovascular risk (Δ= +13.85, p= 0.037). In terms of functional capacity, young people at moderate risk had high scores compared with young people at low (Δ= +7.36, p= 0.041) and high (Δ= +8.65, p= 0.007) risk. Finally, participants at low cardiovascular risk had higher scores in the vitality domain compared to those at moderate risk (Δ= +5.93, p= 0.007).

Table 2 - Comparison of anthropometric measurements, hemodynamic parameters, pulmonary function and quality of life according to CRP (n = 100)

Variables	CRP < 1 mg/dL (n = 48)	CRP 1 – 3 mg/dL (n = 26)	CRP > 3 mg/dL (n = 26)	p*
Anthropometric measurements				
BMI (kg/m²)	21.18±2.60	22.19±3.13	24,96±4,55	<0,001
WC (cm)	69,75±6,70	71,12±7,72	76,65±7,83	0,001
Hemodynamic parameters				
SBP (mmHg)	106,23±11,56	105,73±14,29	107,04±10,61	0,925
DBP (mmHg)	69,83±7,09	71,50±9,05	73,96±7,59	0,097
Pulmonary function				
PEF (L/s)	6.16±1.97	4.42±1.51	5.52±1.51	0.001

FEV_1 (L)	3.07±0.71	2.93±0.68	3.08±0.70	0.435
FVC (L)	3.25±0.77	3.30±0.72	3.38±0.78	0.774
FEV_1/FVC ratio	0.95±0.09	0.89±0.13	0.91±0.10	0.027
Domains of the SF-36				
Mental health	56.08±20.77	59.08±17.32	45.23±20.70	0.030
Functional capacity	80.52±18.63	87.88±17.95	79.23±12.94	0.021
Physical limitations	64.58±36.41	61.54±33.34	67.31±33.74	0.778
Emotional limitation	42.36±41.11	44.87±37.64	43.59±41.92	0.930
Social aspects	62.80±25.56	44.87±37.64	43.59±41.92	0.349
Pain	59.10±24.72	63.31±23.73	60.31±15.24	0.655
General state of health	53.25±13.87	57.23±15.54	48.58±13.49	0.071
Vitality	45.42±22.12	51.35±18.03	36.54±17.76	0.026

Legend: BMI: body mass index; WC: waist circumference; SBP: systolic blood pressure; DBP: diastolic blood pressure; PEF: peak expiratory flow; FEV_1: forced expiratory volume in the first second; FVC: forced vital capacity. *Data for $p < 0.05$.

Source: Prepared by the authors (2023).

There was a significant association between CRP and BMI ($p < 0.001$) and WC ($p = 0.002$). Of the overweight/obese young adults, 87.5% were at moderate and high risk, and of those with WC above the predicted level, 86.7% had CRP ≥ 1 mg/dL (moderate and high risk). Among young people with HRQoL above P(50), 43.5%, 50% and 45.7% were at low cardiovascular risk for functional capacity, general health and vitality, respectively.

Table 3 - Association of anthropometric variables, hemodynamic parameters, pulmonary function and quality of life according to CRP (n=100)

	CRP			
Variáveis	**< 1 mg/dL** (n = 48) n (%)	**1 – 3 mg/dL** (n = 26) n (%)	**> 3 mg/dL** (n = 26) n (%)	**p***
BMI (kg/m^2)				
Eutrophic	45 (59.2)	20 (26.3)	11 (14.5)	< 0.001
Overweight/Obesity	03 (12.5)	06 (25.0)	15 (62.5)	
WC (cm)				
On schedule	46 (54.1)	22 (25.9)	17 (20.0)	0.002
Above expectations	02 (13.3)	04 (26.7)	09 (60.0)	
SBP (mmHg)				
Normotensive	48 (49.0)	24 (24.5)	26 (26.5)	0.064
Hypertensive	00 (00.0)	02 (100.00)	00 (0.00)	
DBP (mmHg)				
Normotensive	47 (50.0)	23 (24.5)	24 (25.5)	0.226
Hypertensive	01 (16.7)	03 (50.0)	02 (33.3)	
FEV_1 (L)				
On schedule	12 (41.4)	08 (27.6)	09 (31.0)	0.667
Below expectations	36 (50.7)	18 (25.4)	17 (23.9)	
FVC (L)				
On schedule	15 (40.5)	12 (32.4)	10 (27.0)	0.441
Below expectations	33 (52.4)	14 (22.2)	16 (25.4)	
FEV_1/FVC ratio				
On schedule	46 (50.5)	21 (23.1)	24 (26.4)	0.115
Below expectations	02 (22.2)	05 (55.6)	02 (22.2)	
Mental health				

> P (50)	21 (47.7)	15 (34.1)	08 (18.2)	0.148
< P (50)	27 (48.2)	11 (19.6)	18 (32.1)	
Functional capacity				
> P (50)	20 (43.5)	18 (39.1)	08 (17.4)	0.015
< P (50)	28 (51.9)	08 (14.8)	18 (33.3)	
Physical limitations				
> P (50)	19 (54.3)	07 (20.0)	09 (25.7)	0.551
< P (50)	29 (44.6)	19 (29.2)	17 (26.2)	
Emotional limitation				
> P (50)	18 (43.9)	10 (24.4)	13 (31.7)	0.554
< P (50)	30 (50.8)	16 (27.1)	13 (22.0)	
Social aspects				
> P (50)	23 (48.9)	14 (29.8)	10 (21.3)	0.531
< P (50)	25 (47.2)	12 (22.6)	16 (30.2)	
Pain				
> P (50)	18 (45.0)	12 (30.0)	10 (25.0)	0.755
< P (50)	30 (50.0)	14 (23.3)	16 (26.7)	
General state of health				
> P (50)	25 (50.0)	17 (34.0)	08 (16.0)	0.041
< P (50)	23 (46.0)	09 (18.0)	18 (36.0)	
Vitality				
> P (50)	21 (45.7)	17 (37.0)	08 (17.4)	0.040
< P (50)	27 (50.0)	09 (16.7)	18 (33.3)	

Legend: BMI: body mass index; WC: waist circumference; SBP: systolic blood pressure; DBP: diastolic blood pressure; PEF: peak expiratory flow; FEV_1: forced expiratory volume in the first second; FVC: forced vital capacity; P: percentile. *Data for $p < 0.05$.
Source: Prepared by the authors (2023).

CRP had a positive correlation with BMI ($p = 0.044$), while PEF ($p = 0.046$) and the FEV_1/FVC ratio ($p = 0.002$) showed an inversely proportional correlation.

Table 4 - Correlation between CRP and anthropometric and pulmonary function measurements (n=100).

Variáveis	**CRP (mg/dL)**	
	r	**p***
BMI (kg/m²)	0.202	0.044
PEF (L/s)	-0.200	0.046
FEV_1/FVC ratio	-0.302	0.002

Legend: BMI: body mass index; PEF: peak expiratory flow; FEV_1: forced expiratory volume in the first second; FVC: forced vital capacity. *Data for $p < 0.05$.

Source: Prepared by the authors (2023).

DISCUSSION

The main findings of the study were that obesity, BMI and WC were higher in young adults with CRP> 3 mg/dL, while PEF and FEV_1/FVC ratio were higher in young adults with low cardiovascular risk. In terms of quality of life, scores were higher for mental health, functional capacity and vitality, with the first two domains being higher in young people with CRP between 1 and 3 mg/dL, and the third domain being higher in young people with low-risk CRP. Most of the young adults who were obese were at moderate and high cardiovascular risk. CRP was positively correlated with BMI, while PEF and FEV_1/FVC ratio were negatively correlated.

Young adults with CRP > 3 mg/dL had higher body mass index, BMI and WC, and total CRP levels were directly correlated with BMI. These results are supported by the literature, as in young people CRP is closely associated with anthropometric indicators, BMI and WC.[18, 19] This is justified because obesity is signaled by an inflammatory state in which there is an increase in adipose tissue together with a decrease in adiponectin. Associated with this process, adipose tissue is taken over by inflammatory cytokines, leading to local inflammation and consequently to systemic inflammation, defined by a marked increase in inflammatory markers such as CRP.[18, 20]

In terms of lung function, PEF and FEV_1/FVC ratio were higher and inversely related in students with low-risk CRP. Consistent with these findings, a greater decline in FEV_1 has been reported in individuals with higher baseline CRP in young adults in their 20s.[10, 21] In addition, it has been shown that lung function suffers with increased inflammation.[22] However, in the study by Ahmadi-Abhari et al.[23] a significant association between CRP and lung function was found only in older individuals, as CRP is a marker of an age-related pro-inflammatory process, but may have high concentrations in young people depending on their health-related factors. According to this theory, chronic inflammation increases telomere shortening, which in turn leads to senescence of the alveolar and endothelial cells of the lung. In addition, endothelial dysfunction induced by systemic inflammation can lead to pulmonary vascular infiltration and lung tissue damage.[23]

Scores were higher in the domains of mental health, functional capacity, and vitality, with the first two domains being higher in young people with CRP between 1 and 3 mg/dL, whereas the third domain was higher in low-risk participants. Taking into account the questions of the QoL questionnaire (SF-36), it can be concluded that a decline in general health already has an impact on QoL. Consistent with these findings, the study by Cho et al.[24] states that the higher the plasma concentration of CRP, the greater the fatigue, independent of risk factors such as BMI, depressive symptoms, sleep quality, pain and physical activity. Fatigued individuals may be less physically active, and low physical activity may lead to an increase in CRP levels. This is because physical and psychological stressors activate the peripheral immune system and trigger an inflammatory response with the release of pro-inflammatory cytokines and acute phase proteins.[25] It is worth noting that the level of physical activity was not the subject of this study but should be considered in future studies.

The following limitations should be noted. Firstly, it was not possible to establish a cause-and-effect relationship because of the cross-sectional nature of the study. In addition, there was low adherence among young people, but the sampling power, based on the type of data analysis carried out, was sufficient to generalize the results to the population studied. Secondly, many young adults were unable to reach the six-second value for the forced expiratory maneuver, but this was minimized by the ATS guidance using estimates. In terms of strengths, the study is innovative in relating CRP to HRQoL, as it was conducted in young people who theoretically would not have elevated blood CRP due to the direct relationship with age (young adults rarely have elevated CRP), and the study of the relationship between CRP and lung function parameters is important, as airway obstruction leads to greater inflammation and consequently higher CRP concentrations.

CONCLUSION

It can therefore be concluded that there is a directly proportional relationship between CRP and BMI, whereas the relationship between CRP and lung function is inversely proportional. The HRQoL assessment showed higher scores in mental health and functional capacity in young people with CRP between 1 and 3 mg/dL, and in vitality in young people with low cardiovascular risk. However, further studies are needed to clarify the mechanical and physiological effects of CRP on lung function. In this sense, it is important to control obesity to reduce the inflammatory response, and to this end, regular physical activity and an adequate diet can help to reduce the chronic inflammatory response.

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