

## ORIGINAL MANUSCRIPT

## Continuous or Interval Training and Inflammatory Response in Obese Women

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### Abstract

**Background:** Recent studies have shown probable benefits of high intensity, predominantly anaerobic activities in fat oxidation capacity. However, the effect of predominantly anaerobic exercise in reducing obesity and inflammatory condition is still little known.

**Objectives:** To assess the effects of aerobic vs. anaerobic training on the levels of C-reactive protein (CRP) in women with central obesity, and the association of CRP levels with body composition.

**Methods:** Randomized clinical trial with a population composed of adult, sedentary women with central obesity, enrolled at the Teaching-Care Outpatient Facility of Escola Bahiana de Medicina e Saúde Pública. A group of 19 women was randomly divided into two groups: Continuous training (CT - intensity at 20% of the ventilatory threshold - VT) or Interval Training (IT - 2-minute stimulus at 120% of VT and 2-minute recovery at 80% of VT) for 10 weeks, twice a week, 20-40-minute sessions. A medical and physical, laboratory and cardiopulmonary assessment was carried out before and after the intervention.

**Results:** Median CRP levels were, respectively, before and after training: CT: 2.2mg/L (0.6-4.1mg/L) vs. 2.1mg/L (0.8-5.5mg/L) p=0.75; IT: 3.9mg/L (0.7-8.6mg/L) vs. 3.2mg/L (1.2-5.7mg/L) p=0.90. There was no significant difference when comparing the delta ( $\Delta$ ) CRP levels between groups, p=0.49. There was no association between CRP levels and other pre-intervention variables.

**Conclusion:** Low-volume exercise programs, regardless of their intensity, do not change CRP levels in women with central obesity.

**Keywords:** Abdominal obesity; Exercise; C-reactive protein

### Introduction

Atherosclerosis is a progressive disease characterized by lesions with accumulation of lipids and fibrous elements in the tunica intima (inner layer) of vessels called atheroma<sup>1</sup>. Atherosclerosis causes the reduction or obstruction of the vascular lumen, which can result in ischemia in the heart, brain or extremities (heart attack), and are the main cause of increase in the number of deaths from cardiovascular disease (CVD) in developed countries<sup>2,3</sup>.

The atherosclerosis process has long been associated with obesity, based only on high cholesterol levels. Although hypercholesterolemia plays an important role in this process, it is known that the process associating obesity to the atherogenic process is more complex, and systemic inflammation is a major factor in the progression of the disease<sup>4</sup>.

Over the latest decades, adipose tissue has been considered an endocrine organ capable of secreting substances that can act on the adipocytes themselves and

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physiologically modifying the operation of other tissues<sup>5</sup>. The accumulation of adipose tissue causes acute phase cytokines to increase, raising directly or indirectly the production of factors that relate to the inflammatory condition<sup>6</sup>. Yet there remains no consensus on the role of all these molecules in atherosclerosis, but some of them are known to be associated with vascular attack process and the consequent formation of obstructive plaques<sup>7</sup>. However, some authors have demonstrated an association between C-reactive protein (CRP) and the early stages of atherosclerotic plaque formation<sup>8-10</sup>.

Regular physical exercises are an important factor for the prevention and treatment of obesity<sup>11</sup>. Low-intensity and long-duration, predominantly aerobic exercises, known as continuous training (CT), are recommended for better development of cardiorespiratory fitness and weight loss<sup>12,13</sup>. However, studies have shown the likely benefits of high-intensity, predominantly anaerobic activities, better known as interval or intermittent training (IT), in fat oxidation capacity and bodyweight control<sup>14-16</sup>.

However, the effect of predominantly anaerobic exercise in reducing obesity and inflammatory condition is still little known<sup>17</sup>. This study aims, therefore, to assess aerobic vs. anaerobic training effects on the levels of C-reactive protein (CRP) in women with central obesity, and the association of CRP levels with body composition.

## Methods

Randomized clinical trial with a population composed of adult, sedentary women with central obesity, enrolled at the Teaching-Care Outpatient Facility of Escola Bahiana de Medicina e Saúde Pública, or who participated in extension activities promoted by Escola Bahiana de Medicina e Saúde Pública, from 2009 to 2010, at Paróquia Nossa Senhora de Brotas.

This study was approved by the Research Ethics Committee of Escola Bahiana de Medicina e Saúde Pública, under no. 26/2007. All women who participated in the study signed an Informed Consent Form.

Forty-seven sedentary women, all with abdominal obesity, were randomly sampled from the outpatient facility of Escola Bahiana de Medicina. They volunteered for the study to carry out either of the two physical training programs: continuous training (CT) and interval training (IT) for 10 weeks.

Of these, 28 women were excluded: 16 for not completing the exercise protocol, 11 for missing the last assessment and 1 for her extreme values. Therefore, 19 women completed the study.

Inclusion criteria were: waist circumference  $\geq 80$  cm<sup>18</sup> and being sedentary at baseline. Exclusion criteria were: ischemic heart disease history, diabetes, pulmonary or musculoskeletal disease, inflammation, or use of vasoactive drugs, oral hypoglycemic agents, insulin, glucocorticoids, antipsychotics or hormone replacement therapies.

All participants underwent medical and physical, laboratory and cardiopulmonary assessment before and after the intervention.

## Cardiorespiratory fitness assessment

Participants completed continuous training in a treadmill in order to obtain peak oxygen volume ( $VO_2$ ). The initial treadmill speed was set at 3 km.h<sup>-1</sup>, and then increased by 0.5 km h<sup>-1</sup> or 1 km h<sup>-1</sup> every 2 minutes until voluntary fatigue. Metabolic data [minute volume (MV), oxygen uptake ( $VO_2$ ) and carbon dioxide production ( $VCO_2$ )] were collected during the protocol, using open circuit spirometry (VO2000-Medical Graphics®, St Paul, MN, USA) and heart activity was assessed using electrocardiography (Marquette Max-1 electrocardiographic recorder, Marquette, WI, USA). The  $VO_2$  peak was the highest oxygen uptake reached during the test. The ventilatory threshold (VT) was identified at the level of physical exertion in which the MV/ $VO_2$  ratio reached its minimum value before progressive increases without increases in MV/ $VCO_2$ . When this method did not provide VT, the V-Slope method was used for confirmation. VT was determined independently by two different examiners.

## Intervention

Participants were randomly assigned to either of the following interventions: CT – Continuous training: 10 weeks of continuous supervised exercise, twice a week, with intensity 20% below the speed of their VT. IT – interval training 10 weeks of moderate-high intensity, interval supervised exercise, twice a week, with stimulus intensity and recovery at 20% of the speed above and below VT, respectively, with a stimulus/recovery ratio

### ABBREVIATIONS AND ACRONYMS

- *BMI* – body mass index
- *CRP* – C-reactive protein
- *CT* – continuous training
- *CVD* – cardiovascular disease
- *IT* – interval training
- *VT* – ventilatory threshold
- *WC* – waist circumference

of 2:2 minutes. Those women who did not reach VT, 20% of the speed above and below the maximum speed developed was used during the assessment of cardiorespiratory fitness<sup>19</sup>.

All exercise sessions were supervised by a member of the research team, who monitored the perceived exertion rate. During the first and second weeks, the exercise session was 20 minutes in duration, and during the subsequent eight weeks, the exercise session lasted 40 minutes.

### Clinical and laboratory tests

The participants submitted a detailed medical history and underwent physical examination. Blood samples were collected from a peripheral vein for measurement of ultra-sensitive C-reactive protein. CRP was determined using the nephelometry method before and after the training protocol (two days after the last session) and reported in mg/L.

An inelastic tape was used to measure the waist circumference (WC) (lower measure between the last rib and the iliac crest) and hip circumference (maximum circumference of the gluteal area). For height to be measured, a calibrated vertical stadiometer (professional stadiometer Sanny, São Paulo, Brazil) was used, and body weight was measured using a calibrated scale (PL200, Filizola, São Paulo, Brazil).

Body composition was measured using a bioelectrical impedance analyzer (Omron HBF-306®, Omron, Bannockburn, Illinois, USA), and the equation used to determine the percentage of body fat included: gender, age, and physical activity, included in a measurement model of the equipment. Participants were instructed to avoid physical activities and alcoholic beverages throughout the intervention period and advised to drink 2 liters of water in 24 hours before the measurements.

### Statistical analysis

This study was conducted in a convenience sample, whose sample size calculation had been made for a main study with another outcome variable. Although being a convenience sample, it accords with the sample size of other studies<sup>20-23</sup>. In the main study, a minimum number of nine individuals was estimated in each group.

The distribution of variables was verified using Shapiro-Wilk and Kolmogorov-Smirnov tests, and visual analysis of the normal curve. Wilcoxon Signed Rank test was used

to identify whether the effect of each intervention was significant on subclinical inflammation markers (CRP). The Mann Whitney test was used to compare deltas between the groups. After dividing baseline PCR values, the McNemar test was used to compare the proportion of participants with CRP value above the median before and after exercise, regardless of the protocol. Paired t-test was used to assess the body mass index (BMI) changes and WC within the group. To investigate the association between CRP and anthropometric and cardiorespiratory fitness, the Spearman correlation test was used. All statistical analyzes were performed using the SPSS 15.0 software (SPSS, Chicago, IL, USA). Statistical significance was set at  $p \leq 0.05$ .

### Results

Nineteen sedentary women with increased WC completed the training protocol. Baseline characteristics were similar between groups, with differences observed in age, WC and BMI (Table 1).

There was no significant difference in the CRP levels neither within the groups, nor when comparing delta ( $\Delta$ ) CRP levels between groups,  $p=0.49$  (Table 2).

No reduction was observed in the percentage of women with CRP levels above the median baseline values after the completion of either exercise protocol ( $p=0.62$ ).

No positive association was observed between CRP and anthropometric and cardiorespiratory fitness variables before intervention (Table 3).

There was no significant correlation between Delta PCR and Delta BMI in the study population ( $\rho=-0.04$ ,  $p=0.87$ ).

In the analysis of anthropometric variables, both groups had a decrease in the WC (IT of  $91.0 \pm 9.0$  cm to  $88.0 \pm 10.0$  cm;  $\Delta = -2 \pm 3$  cm,  $p=0.03$ ; CT of  $102.0 \pm 9.0$  cm to  $99.0 \pm 8.0$  cm,  $\Delta = -3 \pm 3$  cm,  $p=0.04$ ). Only the IT group showed significant reduction in weight (from  $71.8 \pm 13.0$  kg to  $70.6 \pm 13.0$  kg,  $\Delta = -1 \pm 1$  kg,  $p=0.01$ ), and in BMI (from  $28.0 \pm 6.0$  kg/m<sup>2</sup> to  $28.0 \pm 1.0$  kg/m<sup>2</sup>,  $\Delta = 0.4 \pm 0.4$  kg/m<sup>2</sup>,  $p=0.01$ ). The CT group has not shown the same reductions (weight from  $84.6 \pm 11.0$  kg to  $84.3 \pm 10.0$  kg,  $\Delta = -0.2 \pm 0.9$  kg,  $p=0.53$ ; and BMI from  $34.3 \pm 6.0$  kg/m<sup>2</sup> to  $34.2 \pm 6.0$  kg/m<sup>2</sup>,  $\Delta = -0.1 \pm 0.3$  kg/m<sup>2</sup>,  $p=0.52$ ).

**Table 1**  
Clinical and anthropometric characteristics of the study population (n=19)

| Variables                                       | CT<br>(n=8)  | IT<br>(n=11) | P    |
|---|--------------|--------------|------|
| Age (in years)                                  | 41.0 ± 12.0  | 52.0 ± 9.0   | 0.07 |
| Weight (kg)                                     | 84.6 ± 11.0  | 71.8 ± 13.0  | 0.08 |
| Height (cm)                                     | 157.0 ± 4.0  | 157.0 ± 6.0  | 0.88 |
| Waist circumference (cm)                        | 102.0 ± 9.0  | 91.0 ± 9.0   | 0.03 |
| Hip (cm)  | 117.0 ± 10.0 | 107.0 ± 10.0 | 0.08 |
| BMI (Kg/m <sup>2</sup> )                        | 34.0 ± 6.0   | 28.0 ± 6.0   | 0.03 |
| Body fat (%)                                    | 39.0 ± 5.0   | 37.0 ± 3.0   | 0.41 |
| Triglycerides (mg/dL)                           | 133.0 ± 47.0 | 142.0 ± 49.0 | 0.74 |
| Blood glucose (mg/dL)                           | 95.0 ± 11.0  | 99.0 ± 12.0  | 0.58 |
| Cholesterol (mg/dL)                             | 201.0 ± 45.0 | 206.0 ± 54.0 | 0.84 |
| LDL (mg/dL)                                     | 123.0 ± 35.0 | 133.0 ± 45.0 | 0.68 |
| HDL (mg/dL)                                     | 50.0 ± 6.0   | 44.0 ± 6.0   | 0.08 |
| Peak VO <sub>2</sub> (L/min)                    | 1.4 ± 0.3    | 1.3 ± 0.2    | 0.56 |
| Peak VO <sub>2</sub> (mL.kg.min <sup>-1</sup> ) | 17.5 ± 3.0   | 19.2 ± 6.0   | 0.50 |

\*Values expressed as mean±standard deviation  
CT – continuous training group; IT – interval training group; BMI – body mass index; LDL – low density lipoprotein; HDL – high density lipoprotein; Peak VO<sub>2</sub> – higher oxygen uptake

**Table 2**  
C-reactive protein response in both training groups

| Groups    | CRP (mg/L)<br>Pre-intervention | RP (mg/L)<br>Post-intervention | Δ (absolute)   | Δ (%)            |
|-----------|--------------------------------|--------------------------------|----------------|------------------|
| CT (n=8)  | 2.2 (0.6-4.1)                  | 2.1 (0.8-5.5)                  | 0.0 (-0.7-1.0) | 0.0 (-36.0-75.0) |
| IT (n=11) | 3.9 (0.7-8.6)                  | 3.2 (1.2-5.7)                  | 0.0 (-2.6-1.5) | 0.0 (-30.0-46.0) |

Values expressed as median (interquartile interval).  
CT – continuous training group; IT – interval training group; CRP – C-reactive protein; Intra-group comparison (p=0.75 and p=0.90, respectively CT and IT). Inter-group (Δ) PCR comparison, p=0.49.

**Table 3**  
Correlation between CRP and anthropometric and cardiorespiratory fitness variables in the study population (n=19)

| Variables                                       | Spearman correlation (rho) | p-value |
|---|----------------------------|---------|
| BMI (kg/m <sup>2</sup> )                        | 0.35                       | 0.13    |
| Weight (kg)                                     | 0.26                       | 0.27    |
| Body fat (%)                                    | 0.28                       | 0.23    |
| Waist circumference (cm)                        | 0.27                       | 0.26    |
| Hip (cm)  | 0.36                       | 0.13    |
| Peak VO <sub>2</sub> (ml.kg.min <sup>-1</sup> ) | 0.05                       | 0.82    |

BMI – body mass index; peak VO<sub>2</sub> – higher oxygen uptake

However, decreases in submitted obesity markers were not enough to influence the correlation between these variables with the PCR deltas in the IT group ( $\Delta$  BMI and  $\Delta$ CRP,  $\rho=-0.25$ ,  $p=0.47$ , and  $\Delta$ WC and  $\Delta$ CRP,  $\rho=-0.09$ ,  $p=0.78$ ) and in CT ( $\Delta$ BMI and  $\Delta$ CRP,  $\rho=0.44$ ,  $p=0.26$ ;  $\Delta$ CC and  $\Delta$ CRP,  $\rho=0.15$ ,  $p=0.73$ ).

## Discussion

This randomized controlled intervention has shown that continuous and interval training methods did not caused a significant change in CRP levels of women with central obesity. Regardless of the training method, there was no reduction in the number of women with CRP levels above the median at baseline.

When analyzed, the association between the inflammatory marker and the anthropometric variables has shown no significant correlation between CRP and BMI. Although there has been significant reduction in BMI and WC in the IT group, the correlation between delta PCR, BMI and WC has shown to have no statistical significance. However, it is important to consider that it usually takes a large number of participants to reach the ideal correlation analysis.

CRP has established itself as an extremely important biomarker of cardiovascular events, primarily associated with acute coronary syndromes<sup>24</sup>. Other studies have

demonstrated that CRP levels are associated with carotid artery intima thickness<sup>21</sup>, and with the clinical instability and vulnerability of the carotid plaque<sup>25</sup>. However, CRP is not only an inflammatory marker. It also participates in the atherogenic process, modulates endothelial function, induces the expression of endothelial adhesion molecules ICAM-1 and VCAM-1, and increases the uptake of LDL-c by endothelial cells<sup>26</sup>.

Therefore, a reduction in central obesity would justify a possible decrease in CRP levels, as the abdominal fat has an influence on the levels of pro-inflammatory cytokines that stimulate the production of CRP in the liver<sup>27</sup>.

Although the practice of moderate-intensity aerobic exercise is widely recommended<sup>12,13</sup>, its impact on the reduction in obesity<sup>28</sup> and inflammatory condition<sup>29</sup> appears to be modest and still not consensual. Similarly, studies on the role of the interval exercise show conflicting results. In 2010, a meta-analysis<sup>30</sup> of behavioral counseling (physical activity and diet) and prevention of CVD was published. This study demonstrated that only intensive counseling was able to promote significant reductions in BMI, blood pressure and LDL cholesterol. However, no reduction in cardiovascular events was demonstrated.

Accordingly, the Look AHEAD study<sup>31</sup> showed that diet and exercise can promote a significant weight loss in diabetic patients, but did not alter the risk of death,

myocardial infarction and stroke. However, this study deals with a specific type of exercise, not allowing for generalizations to all other methods and forms of exercises.

The hypothesis of benefit of high intensity training can be justified by the increased mobilization of lactic anaerobic metabolism during intense stimuli and increased oxidative metabolism during periods of active recovery. This type of training can cause increased cardio-respiratory fitness, mitochondrial mass, oxidative enzymes and oxygen uptake in the post-exercise period<sup>19,32</sup>. Moreira et al.<sup>33</sup> have shown that this type of training can reduce the total body mass, waist circumference, body fat percentage and other anthropometric variables.

Other studies support these data and suggest that the weight loss can influence CRP levels<sup>34,35</sup>. Yatsuya et al.<sup>36</sup> observed that by the eighteenth month (while participants were instructed to lose weight), there was a decrease in CRP associated with decreased BMI; however, from the moment in which participants failed to obtain guidance on weight loss (between the eighteenth and thirty month) CRP levels and BMI increased again.

Reduction in weight is suggested to be able to decrease the activation of macrophages in adipose tissue and the production of pro-inflammatory cytokines (such as TNF-alpha and IL-6). Therefore, there would be reduced hepatic production of CRP, thereby decreasing one of the cardiovascular risk factors<sup>37,38</sup>.

So far, there have been found no studies with similar intervention, assessing the inflammatory response of women with abdominal obesity. However, some studies evaluate aerobic exercise in relation to sedentary lifestyle or aerobic exercise, compared to resistance exercise.

Stensvold et al.<sup>21</sup> compared physical aerobic training and high-intensity strength training in relation to the inflammatory response in women with metabolic syndrome. This study has shown no significant difference in CRP after the training period. Similar data were presented by Arsenault et al.<sup>39</sup>, who observed no

significant changes in CRP, IL-6, TNF-alpha and adiponectin. However, they showed changes in weight, waist circumference and maximal oxygen uptake.

On the other hand, the exercise effect, combined with diet or not, can promote changes in levels of inflammatory markers in women with overweight and obesity in the long run. Imayama et al.<sup>38</sup> have shown that moderate-to-high intensity exercise was able to reduce inflammatory markers (CRP and IL-6).

In this study, although the IT group has had a significant decrease in BMI and WC, this was not sufficient to demonstrate the association of deltas BMI, WC and decreased CRP. However, this reduction in BMI is not clinically relevant. This suggests that exercising during 10 weeks, regardless of the type, did not significantly affect systemic inflammation.

Non-significant results may have occurred due to either a low volume of weekly exercise or uncontrolled diet. However, a previously published study demonstrated that even weekly low-volume exercises were able to reduce anthropometric measures and improve ventilatory threshold<sup>40</sup>.

## Conclusion

In women with central obesity, continuous or interval training was not able to modify CRP levels after 10 weeks of intervention, despite the reduction in BMI and waist circumference after the interval training.

### Potential Conflicts of Interest

No relevant conflicts of interest.

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### Academic Association

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