

ORIGINAL PAPER  
ΕΡΕΥΝΗΤΙΚΗ ΕΡΓΑΣΙΑ

## A 12-week aerobic training program reduced serum C-reactive protein in women with metabolic syndrome

**OBJECTIVE** It is widely accepted that individuals with metabolic syndrome present a proinflammatory state that may finally result in an increased cardiovascular risk profile. This study was designed to determine the effect of regular exercise on serum C-reactive protein (CRP) in women with metabolic syndrome. **METHOD** Sixty adult women with metabolic syndrome according to the National Cholesterol Education Program Adult Treatment Panel III criteria volunteered for this study, of whom 45 were randomly included in the experimental intervention group. These women performed a 12-week aerobic training program, 3 days/week, consisting of warm-up (10 min), main part (20–35 min, increasing by 5 minutes each three weeks) at a work intensity of 60–75% of peak heart rate (increasing by 5% each three weeks) and cool-down (10 min). The control group of 15-age and BMI-matched women with metabolic syndrome did not perform any training program. Written informed consent was obtained from all participants and the protocol was approved by an institutional ethics committee. Levels of serum high-sensitivity CRP (hs-CRP) were assessed by immunonephelometric assay twice, 72 hours before starting the program (pre-intervention) and after its completion (post-intervention). Indices of body fat distribution were also calculated. **RESULTS** When compared to the baseline, hs-CRP levels decreased significantly following the exercise program ( $5.2 \pm 0.9$  vs  $3.7 \pm 0.7$  mg/L;  $P < 0.05$ ). A moderate association was found between hs-CRP and waist circumference. No changes were reported in the controls. **CONCLUSIONS** A 12-week aerobic training program reduced serum hs-CRP levels in women with metabolic syndrome.

Although serum lipid levels have traditionally been cited to explain the incidence of atherosclerosis, other risk factors, such as chronic inflammation are now recognized as important contributors. In this respect, it is widely accepted that individuals with metabolic syndrome present a proinflammatory state with high circulating cytokine levels that may finally result in an increased cardiovascular risk profile.<sup>1–3</sup>

In a population-based cohort of 1,035 middle-aged subjects Ukkola and Kesaniemi<sup>4</sup> reported a sex-specific interplay between metabolic and inflammatory markers in the pathogenesis of metabolic syndrome. Metabolic syndrome was associated independently with high leptin in men and with high sensitivity C-reactive protein (hs-CRP) in women. Further, in a sample representative of a Spanish Mediterranean community, patients with metabolic

syndrome showed significantly higher levels of CRP than their counterparts, even after adjustment for body mass index (BMI) and age.<sup>5</sup>

Fortunately there is evidence from randomized intervention studies that physical training is effective in improving not only the lipid profile<sup>6</sup> but also the proinflammatory status in adult women, as regular exercise reduced the biochemical markers of inflammation in participants. The main problem is that the programs reported had a duration of several months: 6 months,<sup>6–8</sup> or 4 months,<sup>9</sup> which may compromise the adherence of the participants to such intervention programs.<sup>10</sup>

For these reasons the present study was designed to determine the influence of a 12-week intervention program based on aerobic exercise in serum levels of hs-CRP in women with metabolic syndrome.

ARCHIVES OF HELLENIC MEDICINE 2008, 25(3):363–366  
ΑΡΧΕΙΑ ΕΛΛΗΝΙΚΗΣ ΙΑΤΡΙΚΗΣ 2008, 25(3):363–366

M. Rosety-Rodriguez,  
I. Rosety,  
M.A. Rosety,  
I.M. Macias,  
R.I. Cavaco,  
G. Fernieles,  
H. Belghiti,  
F. Gomez,  
F.J. Ordonez

Medicine Department, School of  
Medicine, University of Cadiz, Cadiz,  
Spain

Πρόγραμμα αερόβιας άσκησης  
12 εβδομάδων μείωσε τη  
C-αντιδρώσα πρωτεΐνη γυναικών  
με μεταβολικό σύνδρομο

Περίληψη στο τέλος του άρθρου

### Key words

Exercise  
hs-CRP  
Metabolic syndrome

Submitted 14.1.2008

Accepted 18.1.2008

## MATERIAL AND METHOD

Sixty adult women with metabolic syndrome according to the criteria reported by the National Cholesterol Education Program Adult Treatment Panel III volunteered for this study. Forty-five were randomly included in an intervention group to perform a 12-week aerobic training program, 3 days/week, consisting of warm-up (10 min), main part (20–35 min, increasing by 5 minutes each three weeks), at a work intensity of 60–75% of peak heart rate (increasing by 5% each three weeks) and cool-down (10 min). Participants in the program underwent a complete physical examination at the start of the program. None of the subjects was under any drug therapy (mainly drugs known to effect insulin resistance or lipids including hormone replacement therapy or oral contraceptives) and none had a prior history of disease or injury that would contraindicate daily exercise. The control group included 15 age-, sex- and BMI-matched women with metabolic syndrome that did not perform any training program during the course of the study.

Written informed consent was obtained from all participants and the protocol was approved by an institutional ethics committee.

Blood samples were drawn after a 12-h overnight fast twice: 3 days before starting the program (pre-intervention) and 3 days after its completion (post-intervention). Serum hs-CRP levels were assessed by immunonephelometric assay (N Latex CRP mono, Dade Behring, Germany). Indices of body fat distribution, including waist circumference and waist to hip ratio, were also calculated.

Statistical analysis was performed using the statistical package for social sciences (SPSS 11.0 for Mac). Results were expressed as mean±SD. Pre-intervention and post-intervention values were compared using matched paired t-tests. Pearson's "r" coefficient was used to determine potential correlations between assessed parameters. A value of  $P < 0.05$  was considered statistically significant.

## RESULTS

When compared to baseline, the mean hs-CRP level was significantly lower ( $5.2 \pm 0.9$  vs  $3.7 \pm 0.7$  mg/L;  $P < 0.05$ ) after the exercise program. Similarly, both waist circumference ( $96.2 \pm 2.1$  vs  $94.6 \pm 1.8$ ;  $P < 0.05$ ) and waist-to-hip ratio ( $0.88 \pm 0.06$  vs  $0.85 \pm 0.06$ ;  $P < 0.05$ ) were also decreased to a statistically significant degree. A moderate association was found between hs-CRP and both waist circumference

( $r = 0.49$ ;  $P < 0.001$ ) and waist-to-hip ratio ( $r = 0.42$ ;  $P < 0.05$ ). In contrast, no changes were reported in the hs-CRP levels of the control subjects over the course of the study period.

## DISCUSSION

This study was designed to investigate the effects of a short-term intervention program based on aerobic exercise in adult women with metabolic syndrome. The findings suggested that a 12-week training program may reduce proinflammatory biomarkers such as hs-CRP in participants.

Several authors, including Kadoglou et al<sup>8</sup> and Thompson et al,<sup>9</sup> have recently reported that regular exercise improved proinflammatory status in adult women, reducing significantly plasmatic cytokines and acute phase reactants. The most striking feature of the present study was that the exercise program lasted only 12 weeks.

Laboratory analyses to detect acute phase reactants in general and hs-CRP in particular are expensive, complex and invasive.<sup>17</sup> Consequently this study was also designed to identify potential bioindicators of serum CRP. The results suggested that both waist circumference and waist-to-hip ratio may be considered cheap, easy and non-invasive bioindicators of hs-CRP levels in women with metabolic syndrome before and after training.

Similarly, Santos et al<sup>12</sup> reported that central obesity in general, and waist circumference in particular, were among the most important determinants of the low-grade chronic inflammation present in metabolic syndrome, based on a representative sample of 1,022 urban adults. Similar results were reported by Lim et al<sup>13</sup> in a community-based cohort of 9,773 Koreans aged 40–59 years. These findings may be explained at least in part by the role of abdominal adipose tissue as an important source of proinflammatory cytokines, which may finally increase the production of acute phase reactants such as CRPs.<sup>1,12,14</sup>

From the findings of this study it may be concluded a 12-week aerobic training program reduced serum hs-CRP levels in women with metabolic syndrome. Further studies on this topic are required to confirm this effect.

## ΠΕΡΙΛΗΨΗ

**Πρόγραμμα αερόβιας άσκησης 12 εβδομάδων μείωσε τη C-αντιδρώσα πρωτεΐνη γυναικών με μεταβολικό σύνδρομο**

M. ROSETY-RODRIGUEZ, I. ROSETY, M.A. ROSETY, I.M. MACIAS, R.I. CAVACO, G. FERNIELES, H. BELGHITI, F. GOMEZ, F.J. ORDONEZ

Medicine Department, School of Medicine, University of Cadiz, Cadiz, Spain

Αρχεία Ελληνικής Ιατρικής 2008, 25(3):363–366

**ΣΚΟΠΟΣ** Είναι γνωστό ότι τα άτομα με μεταβολικό σύνδρομο εμφανίζουν μια προφλεγμονώδη κατάσταση, που μπορεί τελικά να οδηγήσει σε αυξημένο καρδιαγγειακό κίνδυνο. Ο σχεδιασμός της μελέτης έγινε για τον καθορισμό της επίδρασης της άσκησης στη C-αντιδρώσα πρωτεΐνη σε γυναίκες με μεταβολικό σύνδρομο. **ΥΛΙΚΟ-ΜΕΘΟΔΟΣ** Έλαβαν μέρος 60 ενήλικες γυναίκες με μεταβολικό σύνδρομο σύμφωνα με τα διεθνή παραδεκτά κριτήρια. Σαράντα πέντε γυναίκες αποτέλεσαν τυχαία την πειραματική ομάδα για να συμμετάσχει σε ένα πρόγραμμα αερόβιας άσκησης, διάρκειας 12 εβδομάδων, 3 ημέρες/εβδομάδα, που περιλάμβανε από προθέρμανση (10 min), κύριο μέρος (20–35 min, με αύξηση 5 min κάθε 3 εβδομάδες), σε επίπεδο εργασίας 60–75% της ανώτερης καρδιακής συχνότητας (αύξηση 5% κάθε 3 εβδομάδες) και χαλάρωση (10 min). Η ομάδα ελέγχου περιλάμβανε 15 γυναίκες, τυχαίοποιημένες όσον αφορά στην ηλικία και το δείκτη μάζας σώματος (BMI), που δεν έλαβαν μέρος σε κάποιο πρόγραμμα. Όλες οι συμμετέχουσες έδωσαν γραπτή συγκατάθεση και το πρωτόκολλο έγινε αποδεκτό από την Επιτροπή Δεοντολογίας του Κέντρου. Οι τιμές της υψηλής ευαισθησίας C-αντιδρώσας πρωτεΐνης (hs-CRP) ελήφθησαν με διπλή μέτρηση, με ανοσοανεφελομετρική μέθοδο, 72 ώρες πριν από την έναρξη του προγράμματος και μετά τη λήξη αυτού. Επίσης, έγινε προσδιορισμός του δείκτη κατανομής του σωματικού λίπους. **ΑΠΟΤΕΛΕΣΜΑΤΑ** Σε σύγκριση με τις βασικές τιμές, τα επίπεδα της hs-CRP βρέθηκαν σημαντικά μειωμένα μετά από την άσκηση ( $5,2 \pm 0,9$  έναντι  $3,7 \pm 0,7$  mg/L,  $P < 0,05$ ). Επιπλέον, βρέθηκε μια μέτρια συσχέτιση μεταξύ της hs-CRP και της περιμέτρου της μέσης. Αντίθετα, δεν παρατηρήθηκαν μεταβολές στην ομάδα ελέγχου. **ΣΥΜΠΕΡΑΣΜΑΤΑ** Ένα πρόγραμμα αερόβιας άσκησης 12 εβδομάδων μειώνει τα επίπεδα της hs-CRP του ορού σε γυναίκες με μεταβολικό σύνδρομο.

**Λέξεις ευρητηρίου:** Άσκηση, hs-CRP, Μεταβολικό σύνδρομο

## References

1. CAPUZZI DM, FREEMAN JS. C-reactive protein and cardiovascular risk in the metabolic syndrome and type 2 diabetes: Controversy and challenge. *Clin Diab* 2007, 25:16–22
2. FLOREZ H, CASTILLO-FLOREZ S, MENDEZ A, CASANOVA-ROMERO P, LARREAL-URDANETA C, LEE D ET AL. C-reactive protein is elevated in obese patients with the metabolic syndrome. *Diabetes Res Clin Pract* 2006, 71:92–100
3. RIDKER PM, HENNEKENS CH, BURING JE, RIFAI N. C-reactive protein and other markers of inflammation in the prediction of cardiovascular disease in women. *N Engl J Med* 2000, 342:836–843
4. UKKOLA O, KESÄNIEMI YA. Leptin and high-sensitivity C-reactive protein and their interaction in the metabolic syndrome in middle-aged subjects. *Metabolism* 2007, 56:1221–1227
5. GARCÍA-LORDA P, BULLÓ M, BALANZÀ R, SALAS-SALVADÓ J. C-reactive protein, adiposity and cardiovascular risk factors in a Mediterranean population. *Int J Obes* 2006, 30:468–474
6. KARAKIRIOU S, VOLAKLIS K, KARAKIRIOU M, TOKMAKIDIS S. The effect of a specific exercise program on the lipid profile and fitness of postmenopausal women. *Arch Hellen Med* 2005, 22:485–492
7. AUBERTIN-LEHEUDRE M, LORD C, KHALIL A, DIONNE IJ. Effect of 6 months of exercise and isoflavone supplementation on clinical cardiovascular risk factors in obese postmenopausal women: A randomized, double-blind study. *Menopause* 2007, 14:624–629
8. KADOGLOU NP, ILIADIS F, ANGELOPOULOU N, PERREA D, AMPATZIDIS G, LIAPIS CD ET AL. The anti-inflammatory effects of exercise training in patients with type 2 diabetes mellitus. *Eur J Cardiovasc Prev Rehabil* 2007, 14:837–843
9. THOMPSON AM, MIKUS CR, RODARTE RQ, DISTEFANO B, PRIEST EL, SINCLAIR E ET AL. Inflammation and exercise (INFLAME): Study rationale, design, and methods. *Contemp Clin Trials* 2007 Oct 11 [Epub ahead of print]
10. PETERSEN AM, PEDERSEN BK. The role of IL-6 in mediating the anti-inflammatory effects of exercise. *J Physiol Pharmacol* 2006, 57:43–51
11. ARMANI A, BECKER RC. The biology, utilization, and attenuation of C-reactive protein in cardiovascular disease. Part II. *Am Heart J* 2005, 149:977–983
12. SANTOS AC, LOPES C, GUIMARÃES JT, BARROS H. Central obesity as a major determinant of increased high-sensitivity C-reactive protein levels in the metabolic syndrome. *Arterioscler Thromb Vasc Biol* 2007, 27:1000–1005

- tive protein in metabolic syndrome. *Int J Obes* 2005, 29:1452–1456
13. LIM S, LEE HK, KIMM KC, PARK C, SHIN C, CHO NH. C-reactive protein level as an independent risk factor of metabolic syndrome in the Korean population. CRP as risk factor of metabolic syndrome. *Diabetes Res Clin Pract* 2005, 70:126–133
  14. FOROUHI NG, SALTAR N, McKEIGUE PM. Relation of C-reactive protein to body fat distribution and features of the metabolic syndrome in Europeans and south Asians. *Int J Obes* 2001, 25:1327–1331

*Corresponding author:*

F.J. Ordonez, Human Anatomy Department, School of Medicine, Pza, Fragela s/n 11003 Cadiz, Spain  
e-mail: franciscojavier.ordonez@uca.es

