ORIGINAL ARTICLE

Resistance exercise does not affect the serum concentrations of cell adhesion molecules

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Background: Cell adhesion molecules are proteins expressed on the surface of a variety of cells and mediate the leucocyte response to inflammation. Some of these molecules are released to the plasma as soluble forms, whose presence indicates the degree of vascular endothelial activation or dysfunction. Increased concentrations of soluble adhesion molecules are thought to hamper the immune response and mediate the atherosclerotic inflammatory process. Studies on the effect of exercise on the concentrations of soluble adhesion molecules have almost exclusively used aerobic exercise.

Aim: To assess the effect of resistance exercise on the serum concentrations of five cell adhesion molecules during and immediately after 30 min of exercise in lean and obese participants.

Methods: Fourteen healthy young men (eight lean and six obese) performed 3 sets of 10 resistance exercises with 10–12 repetitions at 70–75% of one repetition maximum in a circuit training fashion. Venous blood samples were drawn at baseline and at the end of the first, second and third sets. The serum concentrations of vascular cell adhesion molecule-1, intercellular cell adhesion molecule-1, E-selectin, P-selectin and L-selectin were measured in a biochip array analyser.

Results: No significant changes were observed in the concentrations of these cell adhesion molecules during exercise, or between lean and obese participants.

Conclusion: Our data indicate that resistance exercise of moderate to high intensity does not affect the serum concentrations of cell adhesion molecules in healthy young lean or obese men, suggesting no considerable negative effect on immune function.

Cell adhesion molecules are glycoproteins expressed on the surface of a variety of cells (such as vascular endothelial cells, leucocytes and platelets) and mediate the leucocyte response to inflammation.[1] Four main groups of cell adhesion molecules are recognised: the integrin receptor family; the immunoglobulin superfamily, which includes intercellular cell adhesion molecules (ICAM) and vascular cell adhesion molecule-1 (VCAM-l); selectins, including E-selectin, L-selectin and P-selectin; and cadherins.[2]

Some of the cell adhesion molecules are released to the plasma as soluble forms, whose presence indicates the degree of vascular endothelial activation or dysfunction.[3 4] Increased concentrations of soluble adhesion molecules are thought to hamper the immune response by occupying the binding sites meant to be used by the corresponding cell-bound adhesion molecules; this may have a temporary negative influence on the ability of leucocytes to adhere to and transmigrate the endothelium.[5] Cell adhesion molecules have also been suggested to be mediators of the atherosclerotic inflammatory process.[6] Their plasma concentrations have been positively correlated with the risk for cardiovascular disease,[7] and are increased in patients with heart failure.[8]

Body weight and obesity have been found to affect the plasma concentrations of cell adhesion molecules, as soluble ICAM-1 and E-selectin were positively correlated with obesity, especially central obesity.[9] Weight reduction resulted in decreased serum concentrations of cell adhesion molecules, which may suggest a down regulation of endothelial activation.[9] Similarly, increased serum concentrations of VCAM-1, ICAM-1 and E-selectin were found in obese compared with lean children,[10] leading the authors to the conclusion that endothelial activation appears in obese children and that cell adhesion molecules are related to the earliest stages of atherosclerosis. By contrast, Matsumoto *et al*[11] found no differences in serum VCAM-1 and ICAM-1 between obese and lean patients with type 2 diabetes, although the obese patients had increased E-selectin concentrations.

Acute exercise, both endurance and resistance, induces a marked increase in the circulating leucocyte count. The cell surface expression of adhesion molecules makes an important contribution to such changes by altering patterns of leucocyte trafficking and redistribution.[12] Studies on the effect of endurance exercise on the plasma concentrations of cell adhesion molecules in healthy participants have produced controversial results, as some studies reported no changes with exercise,[6 13–16] whereas others found increased concentrations after exercise,[5 17 18] indicating a reduced capacity to combat infectious agents during the immediate post-exercise period.[5]

In contrast with this abundance of data on endurance exercise, we found only one study that measured soluble cell adhesion molecules after resistance exercise.[1] The authors found a reduction in P-selectin 24–144 h after exercise but no changes in E-selectin, VCAM-1 and ICAM-1 1.5–144 h after exercise. This dearth of data on the effect of resistance exercise on soluble cell adhesion molecules is rather unfortunate, given their important role in inflammatory processes and the fact that resistance exercise is prescribed more and more commonly as a therapeutic agent.[19–21] Thus, the aim of this study was to investigate the effect of resistance exercise on the serum concentrations of VCAM-1, ICAM-1, E-selectin, L-selectin and P-selectin during and immediately after exercise.

Abbreviations: BMI, body mass index; ICAM, intercellular cell adhesion molecule; VCAM, vascular cell adhesion molecule

Table 1 Characteristics of participants (mean (SE))

	Lean (n = 8)	Obese (n = 6)
Age (years)	23.8 (1.1)	24.2 (1)
Body weight (kg)	80.2 (2.7)	112.1 (6)*
Height (m)	1.85 (0.03)	1.86 (0.03)
BMI (kg/m^2)	23.4 (0.5)	32.5 (1.2)*

BMI, body mass index.
*Significantly different from lean ($p<0.01$).

PARTICIPANTS AND METHODS

Participants

Fourteen healthy men, aged 21–31 years, who volunteered to participate in the study, were assigned to a lean group (n = 8, body mass index (BMI; weight (kg)/height^2 (m^2) $\leqslant$25 kg/m^2) and an obese group (n = 6, BMI >30 kg/m^2). Participants were performing resistance training recreationally. They did not have any acute or chronic illness, and were not taking any drugs or dietary supplements. After being informed orally and in writing of the design and probable risks of the research, they signed a consent form. The study was approved by the institutional ethics committee, and all the procedures were in accordance with the 1975 Declaration of Helsinki, as revised in 1996.

Participants visited the laboratory on two occasions. During the first visit, a health history questionnaire was filled out, body weight and height were measured, and maximal muscle strength (one repetition maximum) was determined in the exercises used in the subsequent exercise protocol, which was performed during the second visit.

Resistance exercise protocol

Participants participated in a supervised resistance exercise protocol, lasting approximately 30 min, in the morning after an overnight fast. They performed 3 sets of 10 resistance exercises with 10–12 repetitions at 70–75% of one repetition maximum in a circuit training fashion on 10 resistance exercise machines from Vita Fitness (Rome, Italy). The exercises, selected to stress the major muscle groups, were chest press, seated row, leg press, shoulder press, leg extension, leg curls, arm curls, triceps extension, abdominal curls and lower back extensions, in this order. Participants were instructed to perform each repetition in 3–4 s with a 30 s pause between exercises and 2 min rest between sets.

Blood sampling

Blood samples were obtained from an antecubital vein into an evacuated test tube at baseline and at the end of the first, second and third sets of exercise. A portion of the blood was mixed with anticoagulant (EDTA) for the measurement of haemoglobin and haematocrit to calculate the plasma volume changes, and for the measurement of the leucocyte count as an index of the inflammatory effect of exercise. After the clotting of the remaining blood, serum was prepared by centrifugation at 1500 *g* for 10 min and was stored at −80℃ for the determination of cell adhesion molecules.

Assays

VCAM-1, ICAM-1, E-selectin, L-selectin and P-selectin were quantified using the Evidence biochip array analyser from Randox (Crumlin, UK). The biochip used consisted of a 9×9 mm substrate, on which discrete test regions were constructed. The binding ligands (antibodies) are attached to predefined sites on the chemically modified surface of the biochip. After a simple ELISA procedure, each spot is imaged to capture chemiluminescent signals generated on the array. The light signal is captured by a charge-coupled device camera as part of an imaging station, and is converted by image-processing software to provide results compared with calibration curves for each location on the biochip.

All analyses were performed according to the manufacturer's protocols. The intra-assay imprecision (as coefficent of variation) was calculated from one run before analysing the samples. The inter-assay imprecision (as coefficent of variation) was calculated from the data for two controls, run over the 5 days of sample analysis. Intra-assay imprecision was 8.4–11%, and inter-assay imprecision was 8.9–13%.

Plasma volume relative to baseline was calculated according to Dill and Costill[22] after measuring haemoglobin and haematocrit in the Sysmex M 2000 whole-blood autoanalyser (TOA Sysmex, Kobe, Japan). The cell adhesion molecule concentrations were then corrected for plasma volume changes. Leucocyte count was measured in the same analyser.

Statistical analysis

Results are reported as mean (standard error (SE)). Characteristics of the participants were compared by independent Student's t test. Comparisons of the cell adhesion molecule concentrations and the leucocyte counts were carried out by two-way (group × time) analysis of variance with repeated measures on time. The level of statistical significance was set at $\alpha = 0.05$. Data were analysed using SPSS V.12.0.

RESULTS

Table 1 presents the characteristics of the two groups. As a result of the study design, the obese group had significantly higher body weight and BMI than the lean group.

Plasma volume relative to baseline was 0.99 (0.01) at the end of the first set, 0.97 (0.01) at the end of the second set and 0.96 (0.02) at the end of the third set (cumulative data for both groups). The leucocyte count increased significantly with time ($p<0.001$), the value at the end of exercise being higher than at baseline by 52% in the lean group (7.1 (0.5) to 10.7 (0.7) k/μl) and by 58% in the obese group (7.2 (0.3) to 11.3 (0.8) k/μl). There were no differences between groups with regard to the leucocyte count.

Figure 1 shows the serum concentrations of VCAM-1, ICAM-1, E-selectin, L-selectin and P-selectin in the lean and obese participants during the 30-min resistance exercise protocol. There were no significant main effects of group or time and no significant interaction of the two factors in any of the cell adhesion molecules. Numerically, differences between groups were negligible, with the exception of VCAM-1, which was higher by 22% in the obese group than in the lean group at baseline (491 (50) *v* 401 (16) ng/ml, respectively). This difference tended to decrease with exercise. Finally, there were small changes with time, ranging from a 4% decrease of VCAM-1 in the obese group to an 8% increase of P-selectin in the lean group.

DISCUSSION

The aim of this study was to examine the effect of resistance exercise on the serum concentrations of cell adhesion molecules in lean and obese young healthy men. The exercise protocol used was strenuous enough to cause a significant rise in the leucocyte count, similar to the transient leucocytosis reported after resistance exercise,[23] but also after endurance exercise.[12] A limitation of our study was the small sample size, which was attributable to the difficulty in finding obese participants with some experience in resistance exercise training to be able to carry out the strenuous exercise protocol used.

Our data show that three sets of resistance exercise of moderate to high intensity did not affect the serum concentrations of VCAM-1, ICAM-1, E-selectin, L-selectin and P-selectin,

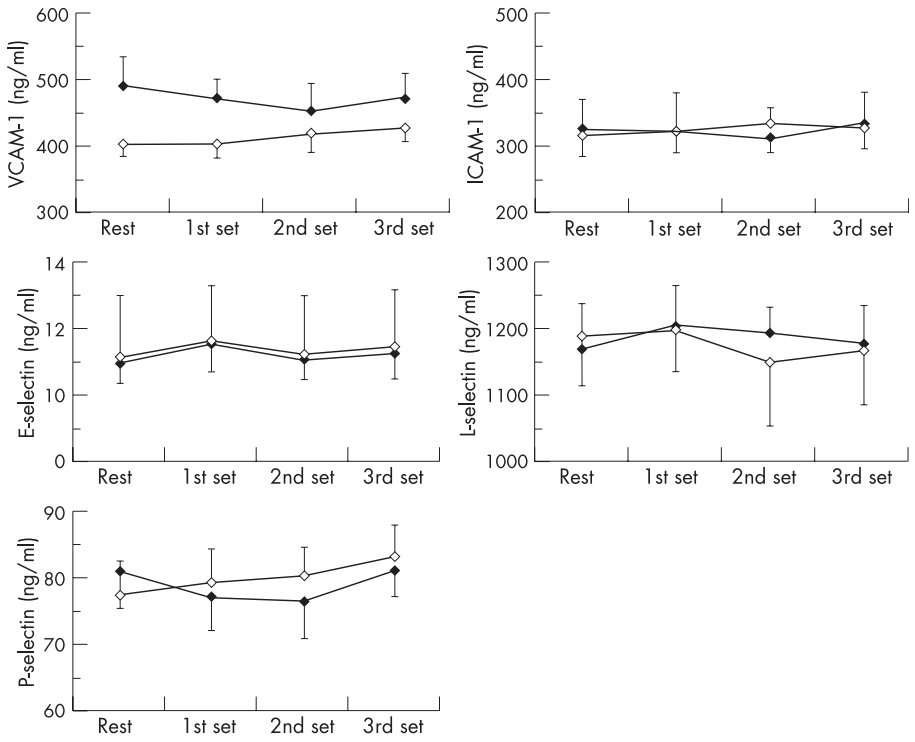

Figure 1 Serum concentrations of vascular cell adhesion molecule (VCAM-1), intercellular cell adhesion molecule (ICAM-1), E-selectin, L-selectin and P-selectin at rest and at the end of the first, second and third sets of resistance exercise. Open diamonds correspond to the lean group and full diamonds to the obese group. Error bars represent standard error.

and that there was no effect of obesity on the response of these soluble cell adhesion molecules to the exercise protocol. To our knowledge, this is the first study investigating the concentrations of soluble cell adhesion molecules during and immediately after strenuous resistance exercise. The only other study that investigated the effect of resistance exercise on soluble cell adhesion molecules[1] measured their concentrations 1.5–144 h after exercise, and found a reduction in P-selectin 24–144 h after exercise but no changes in E-selectin, VCAM-1 and ICAM-1. As Rehman *et al*[17] reported a significantly increased serum concentration of ICAM-1 immediately after endurance exercise and a return to baseline after 1 h, we wondered whether resistance exercise had a similar short-lived effect on the serum concentrations of cell adhesion molecules.

The absence of changes in the concentrations of the circulating cell adhesion molecules with resistance exercise in this study is in agreement with findings derived after endurance exercise in other studies. Jilma *et al*[13] found no significant changes in the concentrations of VCAM-1, ICAM-1 and E-selectin after 1 h of exercise at 60% of the maximal work intensity. Likewise, Ciuffetti *et al*[14] found no significant changes in soluble VCAM-1, ICAM-1 and E-selectin in healthy subjects after walking, although VCAM-1 and ICAM-1 increased in patients with deep venous insufficiency. This was also the case in the study of Brevetti *et al*,[15] in which the plasma concentrations of VCAM-1, ICAM-1, E-selectin and P-selectin were not altered until 30 min after maximal exercise in healthy subjects, but VCAM-1 and ICAM-1 increased in claudicants. Similarly, Mizia-Stec *et al*[6] found no changes in the serum concentrations of VCAM-1, ICAM-1, E-selectin and P-selectin after treadmill electrocardiogram stress testing in healthy volunteers, but found considerable increases in VCAM-1 and E-selectin in patients with stable coronary artery disease. Finally, Wang *et al*[16] found no significant changes in VCAM-1, ICAM-1, E-selectin and L-selectin immediately after exercise of light (40% maximal oxygen consumption (VO_2 max), moderate (60% VO_2max) or high intensity (80% VO_2max).

By contrast, there are reports of increased concentrations of circulating cell adhesion molecules after endurance exercise in healthy adults. Rehman *et al*[17] found markedly increased ICAM-1 but not E-selectin after maximal treadmill exercise. Akimoto *et al*[18] found increased ICAM-1 after marathon running, and attributed it to muscle damage. Nielsen and Lyberg[5] reported increased plasma concentrations of VCAM-1, ICAM-1, E-selectin, P-selectin and L-selectin after marathon and half-marathon running. A common characteristic of these studies is the high exercise volume. Thus, it might be interesting to study the response of soluble cell adhesion molecules to resistance exercise of higher volume than the volumes achieved in the study of Smith *et al*[1] and this study.

The absence of significant differences between the obese and lean groups at baseline agrees with the finding of no differences in serum VCAM-1 and ICAM-1 between obese and lean patients with type 2 diabetes,[11] although the obese group had higher E-selectin. The data of this study do not support an effect of obesity on the resting concentrations of soluble cell adhesion molecules or on the response of these substances to resistance exercise.

On the basis of the claim that high concentrations of circulating cell adhesion molecules may hamper the immune response,[5] the lack of significant changes in soluble adhesion molecules during and after resistance exercise in this study suggests no considerable adverse effect on immune function. This adds to the safety and appropriateness of resistance exercise for maintaining and improving human health.

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What is already known on this topic

- Cell adhesion molecules are glycoproteins expressed on the surface of a variety of cells and mediating the leucocyte response to inflammation.
- Increased plasma concentrations of cell adhesion molecules are thought to hamper the immune response and have been suggested to be mediators of the atherosclerotic inflammatory process.
- Obesity increases the plasma concentrations of cell adhesion molecules.
- Studies on the effect of endurance exercise on soluble cell adhesion molecules have produced controversial results (no change or increase with exercise).
- One study measured soluble cell adhesion molecules 1.5–144 h after resistance exercise and found a reduction in P-selectin 24–144 h after exercise but no changes in E-selectin, vascular cell adhesion molecule-1 and intercellular cell adhesion molecule-1.

What this study adds

- This is the first study to investigate the concentrations of soluble cell adhesion molecules during and immediately after strenuous resistance exercise.
- Our data show that three sets of resistance exercise of moderate to high intensity did not affect the serum concentrations of vascular cell adhesion molecule-1, intercellular cell adhesion molecule-1, E-selectin, L-selectin and P-selectin and that there was no effect of obesity on the response of these soluble cell adhesion molecules to exercise.
- These findings suggest no considerable negative effect of resistance exercise on immune function.

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COMMENTARY

Adhesion molecules constitute factors responsible for intercellular adhesion, especially on endothelial surfaces. In inflammation—for example in atherosclerosis—increased activation of adhesion molecules has been observed. The paper shows the influence of resistance exercise on the serum levels of adhesion molecules. The form of exercise analysed and the group examined (healthy participants or participants with simple obesity only) are new aspects of the study. It should be emphasised that the paper is one of the few reports suggesting that resistance exercise has no major adverse effect on immune activation—this is an important finding, especially from the practical point of view.

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