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Feature Article

Effects of endurance exercise training on risk components for metabolic syndrome, interleukin-6, and the exercise capacity of postmenopausal women

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A B S T R A C T

We conducted this study to investigate how an exercise program affects the risk components of metabolic syndrome (MS), serum interleukin (IL)-6 levels, and exercise capacity in postmenopausal women. A randomized clinical trial design was used. Women in an exercise group participated in a treadmill-exercise program for 12 weeks, whereas women in a control group maintained their customary lifestyle. Data on variables were collected at baseline and after 12 weeks of the study, which was completed by 46 women (mean age, 56.0 ± 7.0 y). Our results indicate endurance exercise exerted significant beneficial effects on waist circumference, serum high-density lipoprotein cholesterol (HDL-C) and IL-6 levels, and exercise capacity (all $P < 0.05$). The beneficial effects on IL-6 and exercise capacity were correlated with improvements in HDL-C levels ($r = -0.33$, $P = 0.03$ and $r = 0.31$, $P = 0.04$, respectively). Our results suggest that health-care providers can incorporate an exercise program in treatments to improve the health of postmenopausal women.

Introduction

Metabolic syndrome (MS) and elevated levels of inflammatory markers are predictors of future cardiovascular events that are more prevalent in postmenopausal women than in women who have not yet reached menopause.[1–3] According to the National Cholesterol Education Program Adult Treatment Panel (NCEP/ATP III)[4] and the International Diabetes Federation (IDF),[5] MS features a constellation of risk components that include abdominal obesity, hypertension, dyslipidemia (elevated levels of triglyceride (TG) and diminished high density lipoprotein cholesterol (HDL-C)), and insulin resistance. In the development of MS, a role of a proinflammatory state has been proposed in addition to those of the components of NCEP/ATP III.[6,7] MS is associated with increased carotid intima-media thickness values and the prevalence of plaque, with elevated numbers of metabolic abnormalities occurring even in asymptomatic postmenopausal women.[8]

The MS prevalence in postmenopausal women approaches 50% in American people,[9] 35% in Chinese people aged 50–59 years,[10] and 31.2% in Korean people.[11] The high incidence of MS after menopause is induced by numerous factors including a sedentary lifestyle, diminished exercise capacity, weight gain, and central obesity, and is facilitated by low levels of estrogens, dyslipidemia, low glucose tolerance, elevated blood pressure, and an increase in the proinflammatory state.[12,13]

Abnormalities of MS components are related to the accumulation of adipose tissues, which is associated with a proinflammatory state.[6] Adipose tissue is an active secretory organ that produces a variety of molecules known as adipocytokines that include interleukin (IL)-6, which mediates numerous metabolic changes in people: IL-6 is associated with the production of acute-phase

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reactants in hepatocytes and endothelial cells, and IL-6 influences energy metabolism, vascular function, and inflammatory responses.[14] Kim and colleagues suggested that in healthy nonobese women, IL-6 is a more reliable marker of chronic low-grade inflammation than are hs-C-reactive protein (CRP), tumor necrosis factor (TNF)-α, and IL-1β.[15] After menopause, an increase in the level of IL-6 is a key factor associated with disorders such as MS,[16] cancer,[17] and cardiovascular disease (CVD).[18] Previously, serum IL-6 levels were reported to be negatively associated with physical activity in elderly people who exhibited low HDL-C concentrations,[19] and also with exercise capacity measured using a 6-min walking test in elderly women.[20]

Increasing evidence suggests that boosting physical activity can improve a person's exercise capacity,[21] lipid profile,[22] risk components of MS, and inflammation,[23] and thereby lower the risk of chronic diseases. Previous exercise studies conducted on postmenopausal women have mostly focused on women who were obese,[24,25] overweight,[26,27] had elevated blood pressure,[21] or had Type 2 diabetes.[28] Various exercise programs were used in these studies, including resistance exercise,[22] partially supervised aerobic exercise (3-d supervised and 2-d home-based aerobic exercise),[29] and a combined intervention of diet and aerobic exercise.[27,30] The duration of the exercise intervention also varied among 12 weeks,[22] 16 weeks,[25] 6 months,[31] and 1 year.[29] The exercise intensity ranged from 50% of the heart-rate reserve (HRR)[21] to 60% of the HRR[32] and 70%–80% the HRR.[29] The results of these exercise studies cannot be generalized to develop a comprehensive exercise recommendation suitable for most postmenopausal women.

IL-6 is a key factor associated with MS in postmenopausal women.[15] However, previous studies have reported that as a result of exercise training, IL-6 levels are decreased[9,33] or left unchanged.[29] This discrepancy in the results likely arises from an insufficient reduction in adiposity after exercise training[29] or from the use of distinct exercise modes.[33] The amount of exercise necessary to reduce IL-6 levels in postmenopausal women has not been described, and few studies have investigated the overall effects of exercise training on the risk components of MS, IL-6 levels, and exercise capacity in postmenopausal women. In view of these considerations, we designed this trial to (1) explore the overall effects of a supervised endurance-exercise training program on the risk components of MS, serum IL-6 levels, and exercise capacity of postmenopausal women; and (2) test the hypothesis that the beneficial effects of exercise on MS components are related to a decline in serum IL-6 levels and an enhanced exercise capacity.

Methods

Study design and participants

This study was conducted at a university-based medical center in Taiwan between April 2011 and February 2012. A randomized clinical trial design was used, and the participants in this study were postmenopausal women who visited the hospital's metabolic and cardiovascular outpatient department seeking a health checkup. Eligible participants were contacted by our research staff members and then recruited in our study. Postmenopause was defined as the absence of menstruation for at least 12 months under natural menopause conditions in the absence of medication or surgery.[34] Inclusion criteria of this study were the following: (1) postmenopausal women aged 45–70 years; (2) a sedentary lifestyle (not exercising $>$ 30 min on $>$3 d/wk) for the past 6 months; and (3) not taking any medication including lipid-lowering agents, nonsteroidal antiinflammatory drugs, antihypertension drugs, and hormone-replacement therapy. Exclusion criteria included (1) the presence of chronic heart failure; (2) a positive history or clinical signs of ischemic heart disease; (3) diabetes mellitus (fasting glycemia $>$ 126 mg/dL); (4) systolic blood pressure (SBP) $>$ 160 mm Hg or diastolic blood pressure (DBP) $>$ 100 mm Hg; and (5) orthopedic limitations.

The study protocol was approved by the ethics committee of the medical center where the study was conducted. Written informed consent was obtained from each participant before the study. Eligible participants were randomly assigned to either an exercise group or a control group. Women in the exercise group completed a supervised 12-week treadmill-exercise program. Women in the control group were asked to maintain their customary lifestyle. At the end of the study, we provided the control-group participants with instructions and educational materials related to exercise. All participants reported to the laboratory in the morning after fasting overnight and having abstained from caffeine, tea, and alcohol for at least 12 h before the tests. Blood sampling, physiological assessments of study variables, and symptom-limited exercise tests were performed at baseline and after 12-week study. Study variables were measured by one of the members of our research staff, who was unaware of the group allocation of the participants. All data were stored securely and only members of the research team had access to the data.

Risk components of MS and the MS score

In our study, MS was defined by the presence of central obesity (waist circumference $>$ 80 cm in Asian women) plus any 2 of the following 4 metabolic risk components identified by the IDF[5]: (1) SBP $\geq$ 130 mm Hg or DBP $\geq$ 85 mm Hg; (2) HDL-C $<$ 50 mg/dL; (3) a fasting-glucose level of 100–125 mg/dL; and (4) TG $\geq$ 150 mg/dL.

To measure the overall effects of exercise training, the MS score and the risk components of MS were examined in our study. The MS score is a clinically useful index of MS severity that is correlated with atherosclerotic risk factors and the severity of CVD.[35] The value of the MS score was calculated as the sum of each participant's risk components of MS (waist circumference, serum TG, inverted HDL-C, SBP, DBP, and fasting glucose).[36] The MS score ranged from 0 (no risk components of MS) to 5 (presence of all 5 risk components of MS).

Anthropometric assessment and blood pressure

The waist circumference of each participant was determined on the study day by following the guidelines of the American College of Sports Medicine (ACSM).[37] The waist circumference of each participant was assessed twice, using a Gulick measuring tape (Creative Health Products, Plymouth, MI, USA); at the end of exhalation, the circumference was measured to the nearest 0.1 cm in a horizontal plane around the abdomen at the level of the iliac crest. Blood pressure was measured using a calibrated automated oscillometric blood-pressure monitor (Datascope, Mahwah, NJ, USA). After a rest period of 10 min, participants were fitted with an appropriately sized cuff when they were seated and blood pressure was assessed 3 times at 2-min intervals.[37] All study variables were measured again after the 12-week study.

Blood sampling

Blood samples were collected at 08:00–10:00 AM after an overnight fast. Blood samples were drawn from an antecubital vein by using standard venipuncture methods; the participants were seated during the sampling. Blood concentrations of TG, HDL-C, and fasting glucose were determined in the hospital laboratory by using standard equipment and assays. Blood serum collected for analyzing IL-6 levels were stored frozen in aliquots at -70 °C. The