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The influence of regular walking at different times of day on blood lipids and inflammatory markers in sedentary patients with coronary artery disease

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ABSTRACT

Objective. To examine the influence of walking at different times of day on lipids and inflammatory markers in sedentary patients with coronary artery disease (CAD).

Methods. A total of 330 patients recruited from Nanjing between September 2011 and November 2012 were randomly assigned to a control group (n = 110), morning (n = 110) or evening walking group (n = 110). Both the walking groups were asked to walk 30 min/day or more on at least 5 days/week either in the morning or evening for 12 weeks. Lipids and inflammatory markers were measured before and after exercise intervention.

Results. Compared with baseline, total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C) were improved in all groups. Significances were shown in the changes of fibrinogen, high sensitivity C-reactive protein (hsCRP), white blood cell (WBC) count, TC, triglycerides, LDL-C, lipoprotein(a) between groups. The evening walking group had a larger decrease in fibrinogen (0.16 ± 0.19 g/L, $P < 0.001$), hsCRP (1.16 ± 1.07 mg/L, $P < 0.001$), WBC count (0.76 ± 1.53 · 10^9/L, $P = 0.004$) and LDL-C (0.34 ± 0.31 mmol/L, $P < 0.001$) than the other two groups.

Conclusions. Our walking program successfully resulted in a favorable change in lipids and inflammatory markers. Patients in the evening walking group gained more benefits than those walking in the morning walking group.
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Introduction

Atherosclerosis is the key pathophysiologic process of coronary artery disease (CAD). Dyslipidemia and inflammation play important roles in the development of atherosclerosis and are strongly associated with an increased risk of CAD (Pai et al., 2004; Yusuf et al., 2004). As the widespread inflammatory markers, high sensitivity C-reactive protein (hsCRP) (Ridker et al., 2000) and fibrinogen (Maresca et al., 1999) are believed to be important predictors of ischemic events and cardiovascular mortality.

It has been well known that moderate and regular levels of physical activity have a favorable effect on many of the established risk factors related to CAD (Thompson et al., 2003). Accumulating evidences have demonstrated that regular exercise can decrease hsCRP (Milani et al., 2004) and fibrinogen levels (Wosornu et al., 1992) and make a favorable change in lipids and lipoprotein (Martins et al., 2010). By comparison of the type of physical activity, the authors suggested that both aerobic training and resistance training attained improvements in lipoprotein levels for elderly women in 10 weeks (Fahlman et al., 2002). As for the intensity and duration, results proved that the highest amount of weekly exercise provided broad beneficial effects on lipoproteins, which was not related to the intensity of exercise (Kraus et al., 2002).

Interestingly, a large number of epidemiologic evidences have shown a pronounced circadian variation in the occurrence of cardiovascular events, with a peak incidence between 6 and 12 AM, and a low frequency during the night (Muller, 1999). Just like the above descriptive characteristic, the peak of fibrinogen (Bremner et al., 2000) and hsCRP (Koc et al., 2010) generally occurs in the morning. Moreover, certain functional variables also exhibit a remarkable diurnal rhythmicity, such as blood pressure, platelet activation, sympathetic nervous activity, fibrinolytic activity, catecholamine and cortisol levels (Andreotti et al., 1988; Kanaley et al., 2001; Marfella et al., 2003; Winther et al.,

Abbreviations: CAD, coronary artery disease; WBC, white blood cell; TC, total cholesterol; TG, triglycerides; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; Lp(a), lipoprotein(a); hsCRP, high sensitivity C-reactive protein.

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1992). It is implied that these variables have been responsible for cardiovascular events. Obviously, the prescription of exercise is beneficial to the long-term management of cardiac patients (Thompson, 2001). Given that exercise in the morning has a greater potential for inducing sudden cardiac death and myocardial ischemia (Krantz et al., 1996), it may be sensible for patients with CAD not to take exercise at this time. Our previous study indicated that the protective effect of exercise in the evening was greater than the morning (Zhao et al., 2013). However, which times of day to exercise could achieve the greatest improvements in lipids and inflammatory markers remains unclear.

The purpose of the present study was to investigate the responses of lipid profiles and inflammatory markers to walking at different times of day in sedentary patients with CAD.

Methods

Subjects

From September 2011 to November 2012, 330 patients with CAD between the ages of 40 and 78 years were recruited from the inpatient cardiology department of the First Affiliated Hospital of Nanjing Medical University. Inclusion criteria were as follows: Firstly, the patients were younger than 80 years and had been diagnosed with CAD by coronary angiography (at least 1 main coronary artery having >50% luminal diameter stenosis); Secondly, they were able to walk but had a sedentary lifestyle which was defined as no regular physical activity in excess of 30 min/day, for more than 3 days/week over the last 3 months. Patients were excluded if they had valvular heart disease, atrial fibrillation, cardiomyopathy, myocarditis, uncontrolled chronic diseases and congestive heart failure or ejection fraction <50% by echocardiogram.

Study design

This study employed a randomized controlled design to investigate the effects of walking at different times of day on the lipid profiles and inflammatory markers in patients with CAD. Informed consent was obtained from each participant after explaining the study protocols. Clinical data including CAD family history, current medications, cigarette smoking, drinking and a history of hypertension, diabetes and dyslipidemia were collected by trained physicians in hospital. Patients were randomly assigned to one of the three groups: control group ($n = 110$), morning walking group ($n = 110$) or evening walking group ($n = 110$). The control group was requested to maintain their usual level of physical activity, while the other two groups received a 12-week structured walking intervention. Atorvastatin was given at the dose of 20 mg per day for all participants during the intervention period. Additionally, all the participants were given an advice on quitting smoking and were provided with similar diets by a nutritionist, as to caloric intake and nutrients.

Measurements

Blood lipids and inflammatory markers were measured before and after intervention. Venous blood was collected from the antecubital fossa with patients in the sitting position in the early morning following an overnight fast. The plasma was separated by centrifugation to be used for lipids and inflammatory marker analysis. Total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and glucose were determined by enzymatic assay (Olympus AU5400, Japan). Low-density lipoprotein cholesterol (LDL-C) values were calculated using the Friedewald equation. Lipoprotein(a) [Lp(a)] level was measured by turbidimetric immunoassay system (BML, Tokyo, Japan). WBC count and platelet count were determined by an automated hematology analyzer (Technicon H4 automated system, USA). Fibrinogen was measured photometrically by a modified Clauss method and hsCRP concentrations were assessed by latex-enhanced immunoturbidometry on a BN II analyzer (Dade Behring, USA).

Participants were seated and rested for at least 10 min prior to measures being taken. Resting blood pressure was measured using an automated sphygmomanometer and the average value of three times was taken as the final data. Height was measured to the nearest 0.1 cm with patients in bare feet and weight was measured to the nearest 0.2 kg with patients in light clothing and without shoes. Body mass index (BMI) was calculated as weight (kg) divided by the square of height (m^2).

Intervention

Participants in both walking groups were requested to walk at the speed of 2.5 miles/h for 30 min/day or more on at least 5 days/week for a period of 12 weeks. The intensity of walking was moderate, which was equivalent to 3–6 metabolic equivalents (METs) as recommended (Haskell et al., 2007). The protocol of exercise was identical except that one group was asked for walking in the morning and the other group was asked for walking in the evening. The amount of walking undertaken was evaluated by self-report. Participants were told to record the situation of walking including duration, distance and frequency daily in a log book. Each participant was telephoned at least once a week to ensure the adherence to the exercise program. Patients were called back every month to hand in the log book and to understand the information about medication use. In the intervention groups, subjects whose compliance rate with their respectively walking program was less than 85% were excluded in the analysis. Furthermore, at the beginning and end of the 12-week program, patients in intervention groups were supervised by researchers to walk for continuous three days and the duration and distance of walking were recorded.

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Statistical analysis

The Kolmogorov–Smirnov test was used to check the normal distribution of all continuous variables. Fibrinogen, TC, TG, HDL-C, LDL-C and Lp(a) were not normally distributed, and they were log-transformed to establish normality before statistical analyses. The values of normal distribution were expressed as mean ± SD, and non-normal distribution data were presented as median (interquartile range). The normally distributed continuous variables with equal variances were examined by one-way analysis of variance and the Bonferroni test was used for multiple comparisons between groups. The significance of differences in proportions was tested with chi-square analyses. Baseline and follow-up values within each group were compared using the paired *t* test. General linear models were used to adjust the differences in baseline values for dependent variables. Two-way ANOVA was used for the determination of the changes of lipids and inflammatory markers in three groups. The significance level was defined as $P < 0.05$. All analyses were carried out using SPSS version 13.

Results

Subjects

A total of 330 participants were divided into three groups with 110 participants in each group. In the control group, 13 patients dropped out of the study (12% dropout rate). The dropout rate of the intervention groups was 19%, which included 11 patients in all who did not complete at least 85% of the walking program. Of the remaining 275 patients, there were 97 patients in the control group, 89 in the morning walking group and 89 in the evening walking group. The reasons for withdrawal were as follows: out of touch, moving out of the town, schedule conflict and personal circumstances. There was no significant difference in baseline between the subjects who dropped out of the study and those who remained. Baseline characteristics of the 275 patients are shown in Table 1. The groups were well matched and no significant differences were found in baseline for all variables.

Duration, distance and frequency of walking

The duration, distance, frequency and total time of walking were presented in Table 2. The walking speed was used to assess the intensity which was moderate in our study (3–6 METs, equal to 4–6.8 km/h) (Ainsworth et al., 2000). At baseline, the intensity and amount of walking were low and not at a level to gain health benefits. After 12 weeks of intervention, both walking groups significantly increased their duration, distance, speed and total time of walking. As we saw, there were no differences between the groups in each variable of walking at either preintervention or postintervention.