Effects of an Off-Site Walking Program on Fibrinogen and Exercise Energy Expenditure in Women

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Purpose Increased fibrinogen levels may trigger cardiac events in patients with atherosclerosis. Early control of fibrinogen levels before the progression of atherosclerosis that occurs with aging and menopause may benefit women, but the effects of exercise on fibrinogen levels as a preventive value have not been examined in early to middle adulthood women with lack of regular exercise. The present study aims to identify the effect of an off-site walking-based exercise program on fibrinogen levels in such women.

Methods A prospective, 12-week, randomized and controlled study was used. Fifty-two women aged 32 to 57 years who did not exercise regularly or exercised with a weak intensity level were randomly assigned to either an intervention group (IG, n = 26) or a control group (CG, n = 26) for a 12-week study. Exercise energy expenditure (EEE) was measured using a microelectronic device. Fibrinogen levels were assessed using the clotting time method before and after the exercise program.

Results The mean change from baseline EEE was 1.17 ± 0.98 kcal/kg/day in IG subjects (n = 24) and 0.46 ± 0.68 kcal/kg/day in CG subjects (n = 25), a 30% difference between groups (p = .01). The mean change in fibrinogen levels was −8.0 ± 34.5 mg/dl (3% decrease) in IG subjects (n = 24) and −3.6 ± 40.0 mg/dl (1% decrease) in CG subjects (n = 25). No significant difference in fibrinogen levels was seen between groups (F = 1.179, p = .279).

Conclusion EEE increased significantly, but fibrinogen levels did not decrease significantly. The effects of a 12-week off-site walking program on fibrinogen levels were inconclusive. As implications for nursing practice, our findings have suggested fibrinogen levels are not a novel cardiovascular risk factor any more, and provide important information on safe exercise to minimize adverse effects from fibrinogen arising from exercise intensity, especially in women with advanced atherosclerosis when nurses increase exercise intensity levels. Further studies with larger sample sizes in women to confirm the effect of exercise on reducing fibrinogen levels are necessary. [Asian Nursing Research 2008;2(1):35–45]

Key Words exercise energy expenditure, fibrinogen, walking, women

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INTRODUCTION

The life expectancy of women in Japan has been increasing. Because the incidence of cardiovascular disease increases with age, consequently there has been an increase in the number of women with cardiovascular disease in Japan (Nakamura, Sakata, Ojima, Tanihara, & Yanagawa, 1997). Exercise during early adulthood has been recommended (Caspersen, Pereira, & Curran, 2000) to help mediate atherosclerosis, which causes cardiovascular disease. In many Japanese women with a sedentary lifestyle, atherosclerosis has already progressed significantly before age 40 compared with women who take part in some type of physical activity (Miyazaki et al., 1998). However, only one-fifth of women around the age of 40 exercise regularly, although this number slightly increases to one-third of women older than 60 (data from Ministry of Health, Labor and Welfare, Japan, 2004).

Exercise is beneficial even if begun later in life (Rothenbacher, Koenig, & Brenner, 2006), but some studies warn that exercise causes adverse effects among subjects who already have atherosclerosis (Hilberg, Nowacki, Muller-Berghaus, & Gabriel, 2000; Montgomery et al., 1996; Tisi, Hulse, Chulakadabba, Gosling, & Shearman, 1997). In particular, strenuous exercise enhanced both coagulation and fibrinolytic potential (van den Burg, Hospers, Mosterd, Bouma, & Huisveld, 2000). These adverse effects occur because of increased fibrinogen levels triggered by catecholamine release as well as by local ischemic effects that occur during exercise, which may accelerate the preexisting prothrombotic potential of the atherosclerotic vessel wall (Mustonen, Lepantalo, & Lassila, 1998; van den Burg et al., 1995). With increased fibrinogen levels and preexisting advanced atherosclerosis, habitual behaviors such as sitting up and standing up abruptly may trigger a cardiac event, as platelet aggregation occurs as a result of compensatory homeostatic mechanisms responding to the initial decrease in central blood volume and stroke volume from the heart induced by such postures (Ahmadizad, El-Sayed, & Maclaren, 2006a; Muller, Tofler, & Stone, 1989). Fibrinogen levels have been recognized as a novel cardiac risk factor (Hughes, 2003), but the progression of atherosclerosis in women who do not exercise regularly may result in a critical condition that arises from changes in fibrinogen levels in conjunction with physical activity.

A single bout of exercise in patients with coronary artery disease (Lee, Blann, Ingram, Jolly, & Lip, 2005) or conditioning exercises in elderly subjects (Schuit et al., 1997) have been shown to increase fibrinogen levels, and increased fibrinogen levels can trigger cardiac events (Germing et al., 2000). In contrast, fibrinogen levels were not shown to increase in young healthy subjects undergoing a conditioning 12-week exercise program (El-Sayed & Davies, 1995). Chronic physical fitness for 10 weeks has been shown to decrease fibrinogen levels in young healthy subjects (Montgomery et al., 1996). Furthermore, physically active people tend to have lower fibrinogen levels (Fransson, Alfredsson, de Faire, Knutsson, & Westerholm, 2003; Koenig & Ernst, 2000; Pitsavus, Panagiotakos, Chrysohoou, Kavouras, & Stefanadis, 2005).

These findings suggest fibrinogen levels are critical when exercise is initiated, and that an exercise program in early adulthood, continued into later years, may help control risks associated with increasing fibrinogen levels that occur after the menopause and with aging (Brunner et al., 1993; DeSouza, Jones, & Seals, 1998). In addition, these findings suggest that low to moderate intensity of exercise, for example, walking for a short-term, do not affect fibrinogen levels compared with a single bout of exercise or endurance training, which can affect fibrinogen levels. Thus, moderate exercise enhances blood fibrinogen activity without a concomitant activation of blood coagulation mechanisms (El-Sayed, Sale, Jones, & Chester, 2000). Brisk walking, which is moderate intensity exercise, increased exercise energy expenditure for a 12-week intervention in middle-aged women (Yanagibori, Kawakubo, Gunnni, Aoki, & Miyashita, 1993). However, most of the exercise in those studies was measured by self-reported questionnaires, which may result in less accurate data due to the subjective nature of data collection.
(Wilber, Chandler, & Miller, 2001). Objective data, such as exercise energy expenditure (EEE), are needed when the effects of exercise intervention are evaluated (Furukawa et al., 2003).

Several theories have been suggested to explain the role of exercise in reducing fibrinogen levels. One mechanism of decreased fibrinogen levels induced by exercise may be an increase in circulating plasma volume due to a plasma shift from the intravascular space to the extravascular space (Ahmadizad, El-Sayed, & Maclaren, 2006b; El-Sayed, Ali, & El-Sayed, 2005; El-Sayed, Jones, & Sale, 1999). Another explanation is that changes in adiposity are affected by metabolic variables (Bodary et al., 2003). For example, adiposity is associated with inflammation, which may stimulate fibrinogen formation; adiposity lost by EEE leads to a decrease in fibrinogen levels; in addition, cytokines, which induced an acute phase reaction that increases fibrinogen levels, may be reduced by exercise (Panagiotakos, Pitsavos, Chrysohoou, & Kavouras, 2005).

According to important recognition of the adverse effects of exercise intensity under progressed atherosclerosis with aging and menopause (Sakakibara, Fujii, & Naito, 2004; van den Burg et al., 2000), first the effects of weak to moderate intensity exercise on fibrinogen levels in healthy women must be confirmed prior to a study focused on female patients with high fibrinogen levels, because we have little evidence about how fibrinogen levels are changed by weak to moderate exercise in the Japanese female population. Subjects were excluded if they had been instructed not to exercise for medical reasons or pregnancy. In this report, which focuses on the effects of exercise on fibrinogen levels, 52 subjects aged 32–57 years were willing to participate in the study. Also, subjects with an abnormal atherosclerotic index (i.e., ratio of total cholesterol [TC] to high density lipoprotein cholesterol [HDL-C]) (Raider, Stampfer, & Rifai, 2001) were excluded to avoid the adverse effects arising from fibrinogen levels on atherosclerosis. However, there were no subjects excluded due to a high TC/HDL-C ratio in the study.

**METHODS**

**Subjects**

This study is part of a previous study that reported exercise effects on serum lipid levels and glucose metabolism (Furukawa et al., 2003). Female nurse managers aged 30–59 years were recruited from a general hospital in Japan. Participants had to be working full-time, tenured in a management position for more than 2 years, and with a lack of regular exercise (3–4 times per week for more than 1 year). We used these inclusion criteria because daily physical activity, especially in women with a lack of regular exercise, is determined by types of occupation (Piazza, Conrad, & Wilbur, 2001). Based on the study of Piazza et al., we assume that physical adaptation to a lifestyle may occur after more than 2 years, and that walking-based physical activity undertaken by nurse managers is less than that undertaken by staff nurses. Subjects were excluded if they had been instructed not to exercise for medical reasons or pregnancy. In this report, which focuses on the effects of exercise on fibrinogen levels, 52 subjects aged 32–57 years were willing to participate in the study. Also, for safe practice, subjects with an abnormal atherosclerotic index (i.e., ratio of total cholesterol [TC] to high density lipoprotein cholesterol [HDL-C]) (Raider, Stampfer, & Rifai, 2001) were excluded to avoid the adverse effects arising from fibrinogen levels on atherosclerosis. However, there were no subjects excluded due to a high TC/HDL-C ratio in the study.
Study design
The study was conducted from November 1998 to January 1999. Subjects were recruited from the nursing department of a general hospital in Japan. A researcher approached this hospital because of its large size as a general hospital. The first approach for recruitment was done at a meeting to explain our study. Then cards were distributed to ask nurses about their intention regarding participation in the study; these cards were collected by mail. Based on the response of the cards, details of the study were provided. Those who agreed to participate were randomly allocated into two groups using the envelope method: inside each envelope was the number of a unit. When an envelope was selected, the nurse manager on that unit was assigned to either the intervention group (IG) or the control group (CG). The first envelope to be picked was allocated to the IG; the second was allocated to the CG, alternating between groups. The IG \((n=26; \text{age, } 40.8 \pm 5.1 \text{ years})\) was given instructions to follow a special exercise program and subsequently followed up weekly over 12 weeks. The CG \((n=26; \text{age, } 42.1 \pm 6.9 \text{ years})\) was instructed to continue with normal daily activities: exercise was allowed if it was part of the normal routine. The study was approved by the Institutional Review Board of the hospital where the data were collected and by the Review Board of the University of Tokyo, where the primary investigator was enrolled. Written informed consent was obtained from all subjects.

Off-site walking program designed for the study
The exercise intervention was designed to increase the level of exercise. The program has been described previously (Furukawa et al., 2003). The walking program for IG subjects was individualized, and subjects were actively involved in planning the time and place of any walking exercise during the 12-week period. A target level of EEE brought on by walking-based activities was specified as 5 kcal/1 kg body mass/day. The walking program consisted of combined brisk walking, which was defined as a combination of intense and intermittent brisk walking. Intense walking involved at least 20–30 minutes of brisk walking, two or three times per week. Intermittent walking involved an accumulation of brisk walks taken at any time during daily activities, either at home or at work. IG subjects were encouraged to use combined brisk walking. Subjects were instructed on the method of walking orally as well as via a brochure. The method of walking in the IG was evaluated by a walking specialist in a small group at week 2. Then, subjects in the IG continued their own plan while they kept an exercise journal regarding any feelings or concerns. The daily walking-based physical activity, appearing as EEE on the screen of the measurement tool, was observed by the IG. However, subjects in the CG were told not to look at the inside of the measurement tool so that they would not see their EEE.

Outcome variable and measurement: EEE
A small microelectronic device with an accelerometer and expanded memory was used in all subjects to measure EEE. The function and structure of the device (Lifecorder®, Suzuken Co., Nagoya, Japan) are described elsewhere (Furukawa et al., 2003). The device is a small light microcomputer designed to estimate the EEE of daily activity through use of a step-counter pedometer; EEE is based on walking speed. The device is programmed with the subject’s age, height, weight, and sex to provide an adjusted basal metabolism for computing total energy, exercise energy, number of steps taken, and pattern of walking. All data were transferred to a computer for analysis. The accuracy of the device as a measurement tool for EEE has been confirmed previously (Suzuki, Kawasaki, & Shimizu, 1997). The device was worn during daily activity, and taken off while subjects slept. All subjects were asked to wear the device for more than 12 hours per day and for more than 90% of the 12-week exercise period; these time periods were regarded as necessary to provide a valid measurement for each individual (Rogers et al., 1987).

Before the exercise program was started, the Lifecorder® was used in all subjects to provide a baseline value of ordinary daily EEE from walking for a week. On the first day of the first week of the intervention, body weight and height were measured.
in all subjects. Subjects in the IG then underwent training for the off-site individual-based walking program. Subjects in the CG were told to continue their daily activities as usual. On the first day of the 13th week, the Lifecorder® was removed from all subjects, and measurements were discontinued.

Outcome variable and measurement: fibrinogen
To measure fibrinogen levels, blood samples were taken from subjects in both groups via the median cubital or lower cephalic vein of the left hand after 12 hours of fasting. Samples were taken on the first day of the first week of the intervention and again on the last day of the study. Serum was separated by slow centrifugation and frozen within 1 hour of collection by a certified medical technologist. The blood samples were analyzed within 32 hours by a laboratory (SRL Co. Ltd., Tokyo, Japan) with external validation from the New York State Department of Health Proficiency Testing and the College of American Pathologists Survey. The thrombin clotting time method was used for fibrinogen analysis.

Measurement of demographic and other health information
A self-assessment questionnaire was used to gather demographic and other health variable information. Survey questions included age, years of employment, marital status, menopausal status (menopause was defined as more than 12 months without a menstrual period), smoking, drinking, and habitual waking behavior (i.e., sudden upright posture or slow body movement). Body mass index (BMI) was calculated as body mass in kilograms divided by height in square meters.

Statistical analyses
To obtain a power of 80% with a medium effect size by using an $\alpha$ of .05 (Cohen, 1988), 74 subjects were needed for this study. However, we were only able to recruit 52 subjects. This may affect the high possibility of a Type II error. For testing of mean changes of energy expenditure between groups, the unpaired Student’s $t$ test was used. Because of the small sample size, baseline characteristics that could affect fibrinogen levels were adjusted by using a co-variance analysis if they were significantly different between the two groups. Then, for actual fibrinogen levels, the unpaired Student’s $t$ test was used to test the significance of mean changes in fibrinogen levels between groups. Furthermore, the statistical analysis of fibrinogen data was carried out using repeated measurements analysis of variance (ANOVA) to compare fibrinogen levels of IG and CG subjects before and after the intervention. A $p$ value less than .05 was considered statistically significant. The Statistical Analysis System version 6.12 (SAS Institute Japan Ltd., Tokyo, Japan) was used for analysis. Data from withdrawn subjects were excluded from the analysis.

RESULTS
Two subjects from the IG group were withdrawn due to health problems unrelated to exercise and one subject from the CG group was withdrawn due to pregnancy. Thus, 49 subjects completed the study (24 IG subjects, 92%; 25 CG subjects, 96%).

Results showed that 92% (22 of 24) of the IG and 100% (25 of 25) of the CG subjects met the study requirements in terms of wearing the device for the appropriate time period. Because the low number of subjects included in the study meant the study was not appropriately powered to show statistical differences between groups, all subjects who met the study requirements were used for analysis.

Baseline characteristics are shown in Table 1. The only significant difference between groups was in BMI (IG subjects had a significantly higher BMI than CG subjects; $p = .02$). The mean change in EEE/kcal/1 kg body mass/day was $1.17 \pm 0.98$ kcal/kg/day in IG subjects ($n = 24$) and $0.46 \pm 0.68$ kcal/kg/day in CG subjects ($n = 25$), a 30% difference between groups ($p = .01$). Changes in fibrinogen levels were adjusted for the statistically significant difference in BMI between groups and values were confirmed ($F = 1.4, p = .24$). This statistical insignificance indicated there was no influence of BMI on fibrinogen. Thus, for actual values, mean changes in fibrinogen levels were tested. Results showed
## Table 1

**Baseline Characteristics**

<table>
<thead>
<tr>
<th></th>
<th>Intervention group (n = 24)</th>
<th>Control group (n = 25)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>40.8 ± 5.1</td>
<td>42.1 ± 6.9</td>
<td>.43a</td>
</tr>
<tr>
<td>Years employed</td>
<td>19.3 ± 4.9</td>
<td>20.1 ± 7.0</td>
<td>.64a</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>24.5 ± 4.9</td>
<td>21.8 ± 2.3</td>
<td>.02a</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>156.3 ± 6.7</td>
<td>155.9 ± 4.9</td>
<td>.81a</td>
</tr>
<tr>
<td>Body mass (kg)</td>
<td>59.7 ± 11.0</td>
<td>53.0 ± 6.7</td>
<td>.01a</td>
</tr>
<tr>
<td>Self-reported medical history</td>
<td></td>
<td></td>
<td>.25b</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1 (4)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>1 (4)</td>
<td>4 (16)</td>
<td></td>
</tr>
<tr>
<td>Anemia</td>
<td>1 (4)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>5 (21)</td>
<td>4 (16)</td>
<td></td>
</tr>
<tr>
<td>Hormone user</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>NSb</td>
</tr>
<tr>
<td>Marriage status</td>
<td></td>
<td></td>
<td>.16b</td>
</tr>
<tr>
<td>Married</td>
<td>18 (75)</td>
<td>14 (56)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>6 (25)</td>
<td>11 (44)</td>
<td></td>
</tr>
<tr>
<td>Menopausal status</td>
<td></td>
<td></td>
<td>.61b</td>
</tr>
<tr>
<td>Premenopausal</td>
<td>23 (96)</td>
<td>23 (92)</td>
<td></td>
</tr>
<tr>
<td>Perimenopausal</td>
<td>0 (0)</td>
<td>1 (4)</td>
<td></td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>1 (4)</td>
<td>1 (4)</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td>.32b</td>
</tr>
<tr>
<td>Smoker</td>
<td>7 (29)</td>
<td>3 (12)</td>
<td></td>
</tr>
<tr>
<td>Ex-smoker</td>
<td>2 (8)</td>
<td>3 (12)</td>
<td></td>
</tr>
<tr>
<td>Never smoked</td>
<td>15 (63)</td>
<td>19 (76)</td>
<td></td>
</tr>
<tr>
<td>Behavior at awakening</td>
<td></td>
<td></td>
<td>.48b</td>
</tr>
<tr>
<td>Sudden upright posture</td>
<td>12 (50)</td>
<td>10 (40)</td>
<td></td>
</tr>
<tr>
<td>Slow body movement</td>
<td>12 (50)</td>
<td>15 (60)</td>
<td></td>
</tr>
<tr>
<td>Regular exercise</td>
<td></td>
<td></td>
<td>.47b</td>
</tr>
<tr>
<td>2–3 times/week</td>
<td>1 (4)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Once a week</td>
<td>2 (8)</td>
<td>1 (4)</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>21 (88)</td>
<td>24 (96)</td>
<td></td>
</tr>
<tr>
<td>Reason for no exercise</td>
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<td></td>
<td>.56b</td>
</tr>
<tr>
<td>Lack of time</td>
<td>20 (83)</td>
<td>21 (84)</td>
<td></td>
</tr>
<tr>
<td>No facilities</td>
<td>4 (17)</td>
<td>3 (12)</td>
<td></td>
</tr>
<tr>
<td>No company</td>
<td>0 (0)</td>
<td>1 (4)</td>
<td></td>
</tr>
</tbody>
</table>

**Note.** Values are mean ± SD or n (%).

*aUnpaired Student’s t test (intervention group, n = 24; control group, n = 25); bχ² test (intervention group, n = 24; control group, n = 25 in all variables).*
–8.0 ± 34.5 mg/dl (3% decrease) in IG subjects and –3.6 ± 40.0 mg/dl (1% decrease) in CG subjects \((p = .68)\) (Table 2). Using repeated ANOVA, no significant difference in fibrinogen levels was found between groups \((F = 1.197, p = .279)\).

### DISCUSSION

Our study was conducted to identify the effects of an off-site walking program on fibrinogen levels and EEE in healthy early to middle aged adult working women. EEE in IG subjects increased significantly (a null hypothesis was rejected), but fibrinogen levels in CG subjects did not decrease significantly (a null hypothesis was not rejected). Yanagibori et al. (1993) reported that exercise energy expenditure increased by using individual-based exercise in the home in addition to exercise taken at on-sites group exercise. The walking program of our study increased EEE, but it could not reach the target level. This might occur because our study did not include group exercise. To reach the target level, group exercise will be useful, but it is not applicable for working women due to time constraints. However, EEE increased by off-site walking up to 5 kcal/1 kg of body mass/day might be expected to decrease fibrinogen levels by more than that found in the IG subjects this time.

Even though there were larger changes in fibrinogen levels in the IG subjects than CG subjects, the differences were not significant. There are several possible explanations for these findings. First, EEE increased by 14% \((3.42 ± 0.87 \text{ to } 3.88 ± 0.81 \text{ kcal/kg/day})\) in CG subjects. We did not expect any increase in EEE in CG subjects, but such an increase may have caused fibrinogen levels to become lower in this group. Consequently, the difference in fibrinogen levels between groups was smaller than expected. It can be assumed that wearing the measurement device itself contributes to an increase of EEE by providing an incentive to exercise. In addition, because the measurement device allowed subjects to view actual EEE, it might affect subjects in the CG even though they were told not to look at EEE findings in the device. Thus, biases arising from the measurement device may have affected the results of fibrinogen levels in our study. From a beneficial point of view on wearing the measurement device, it is expected to have an effect on not only exercise behavior but also eating or smoking habits. On the other hand, in general, we should be concerned that some people may not be willing to wear measurement devices.

Second, because the off-site individualized walking program was an individual-based activity in which subjects were actively involved in planning the time and place of exercise and practice by themselves, the daily amount of exercise during the 12-week study varied among IG subjects. Thus, fibrinogen levels might not be simultaneously altered by the walking program in all subjects at the end of the 12-week study. A previous study showed that a 12-week
Conditioning program (exercise bicycle, 3 times a week for 30 minutes) led to a 6% decrease in fibrinogen levels (El-Sayed & Davies, 1995). In contrast, the 3% decrease in fibrinogen levels in IG subjects in our study may be a result of exercise type, which was an individually based off-site walking program. It may be necessary to discuss time points to collect blood samples for evaluation of the exercise effects on fibrinogen after the intervention is ended. We measured fibrinogen levels soon after intervention on the first day of week 13. The time points of blood sampling for adequate evaluation remain to be examined.

Third, our small sample size may have affected our ability to detect significant differences in fibrinogen levels (Type II error). We needed 74 subjects, but could only recruit 52. Thus, the study was not powered to reach statistical significance. Fourth, it has been reported that a high baseline value or abnormal serum lipids values tend to shift to the mean by exercise intervention and to show a large, significant change (Lokey & Tran, 1989). Lokey and Tran did not report on fibrinogen, but this tendency of abnormal values to normalize may apply to fibrinogen levels, based on the effects of exercise on those variables. We assumed such a tendency to the mean value did not occur because most of the baseline data in our study appeared within the range of normal values, and consequently significant changes in fibrinogen were not found. For example, one of the influential factors on fibrinogen levels in relation to physical activity is high BMI which increases fibrinogen levels (Mora, Lee, Buring, & Ridker, 2006). However, because the range of BMI in our study was within the upper level of normal values, fibrinogen levels were unlikely to be influenced by BMI. Similarly, the lack of changes in fibrinogen levels in our study might be explained by fact that fibrinogen levels were within normal values to begin with.

Because atherosclerotic changes in women are already present at early adulthood (Miyazaki et al., 1998), a small change in fibrinogen levels might be beneficial if it functions as a protective factor against atherosclerosis, which progresses with age (DeSouza, Jones, & Seals, 1998). Even though there were insignificant findings regarding fibrinogen levels, the small decrease of fibrinogen in IG subjects may indicate a preventive effect, taking into account our small sample size. Such a potential preventive effect in early adulthood may be beneficial based on current findings that indicate an increased fibrinogen level is a risk factor for cardiovascular disease in Japanese women (Sakakibara et al., 2004), and also that young persons with a high probability of having advanced atherosclerotic lesions were associated with earlier atherosclerotic lesions (McMahan et al., 2006). In addition, because coronary events increase linearly with fibrinogen levels (Mora, Cook, Buring, Ridker, & Lee, 2007; Rothwell et al., 2004), it is critical to control fibrinogen levels within normal values because fibrinogen levels increase with aging and the menopause (Sakakibara et al.; van den Burg et al., 2000). If a walking program is used for long life exercise, a decrease in fibrinogen might be expected because physically active people maintain its levels at a lower value (Pitsavus et al., 2005). However, future studies are needed to confirm this hypothesis for developing effective and safe exercise intervention as the study encourages implementation of increasing energy expenditure in the premenopausal period of life (Kocic, Spirovski, Cric, & Velija-Asimi, 2007).

Some limitations to our study should be noted. The small sample size did not allow us to detect significant differences between groups, and EEE was only measured during walking-based physical activity, that is, it was not measured during any other type of activity. Another study limitation is that other factors (except BMI and TC/HDL-C ratio) that may influence fibrinogen levels, such as white blood cells, C-reactive protein, and other inflammatory indicators, were not studied. Further studies should include those factors because coronary heart disease is an inflammatory process, and physical activity has been shown to reduce coronary heart disease risk by modifying levels of inflammatory and coagulation factors (Abramson & Vaccarino, 2002; Panagiotakos et al., 2005).

Although some limitations to this study exist, we were able to study the effects of exercise on fibrinogen levels objectively using a control group. Other studies have measured exercise through a
self-reported questionnaire (Koffman et al., 1999; Piazza et al., 2001), which is less objective than the measurement device we used. Also, our study might bring a contribution to understanding women’s cardiovascular health because female subjects in cardiovascular-related studies were less often compared with studies on male subjects.

In conclusion, the effects of the off-site walking program on fibrinogen levels in women were inconclusive even though the program increased EEE. As implications for nursing practice, our findings have implied that fibrinogen levels are not a novel cardiovascular risk factor anymore, and provide important information on safe exercise to minimize adverse effects from fibrinogen arising from exercise intensity, especially in women with advanced atherosclerosis, when nurses decide to increase exercise levels. Further studies with larger sample sizes in women to confirm the effect of exercise on reducing fibrinogen levels are necessary.

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