Brief communication: Pedometer Step Counts and Oxidized Low-Density Lipoprotein Levels Among Asymptomatic Subjects

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Abstract. While daily step counts are considered to be a useful measure of cardiovascular health, the biochemical predictors of step counts have not been fully characterized. This study investigated the correlation between pedometer-determined daily step counts and cardiometabolic variables, including the serum level of malondialdehyde-modified low-density lipoprotein (MDA-LDL), among asymptomatic subjects (n = 50, mean age 63 years). Simple and stepwise multiple linear correlation tests revealed that there was a significant inverse correlation between the step counts and MDA-LDL levels (r = -0.41, P < 0.01; β = -0.38, P < 0.01). The data suggest that daily steps may be beneficially associated with atherosclerosis in correlation with reduced oxidized low-density lipoprotein, and in addition that the MDA-LDL level may be used as a measure reflective of the daily steps.

Key words: Atherosclerosis, MDA-LDL, oxidative stress marker, oxidized lipoprotein, physical activity

Introduction

The beneficial effects of physical activity, even at the mild-to-moderate level (i.e. walking), on cardiovascular health have been well documented [1-3]. Therefore, various objective measures of physical activity have long been explored as a means of evaluating said activity, since subjective measures have several limitations, e.g. reporting bias [4,5]. While daily steps have recently decreased over time, a problematic phenomenon in Japan [6], pedometers are growing in popularity and have received much attention as a useful tool for assessing physical activity. As a result, pedometers can play a significant role in the improvement of health conditions [1,2,4-10].

The identification of biochemical variables correlated with step counts is thus necessary to better our understanding of the pathophysiological mechanism(s) of the health effects of pedometer-based physical activity; however, few studies have focused on this topic. To our knowledge, only one prior study showed a direct correlation of step counts with the blood levels of glucose and lipids (triglycerides [TG] and high-density lipoprotein cholesterol [HDL-C]) [7]. Furthermore, one issue with the use of pedometers is whether subjects wear the device consistently [5]. The application of biochemical variables reflective of pedometer-based physical activity to evaluating the health effects of such a device may therefore improve the accuracy of such evaluation.

In addition to conventional cardiovascular risk variables, oxidized markers of low-density lipoprotein (LDL) have been studied in association with physical activity with much interest [11]. Oxidized LDL (oxLDL) is involved in atherosclerotic processes, and its levels are thought to be a relevant marker for cardiovascular disease (CVD) [12-14]. Several [10,15-17], but not all [18,19], studies have shown that physical activity is inversely associated with the blood oxLDL levels, although these studies have not directly examined their association by using step counts. Taking the background of the previous studies into consideration, the aim of the present study was to investigate the correlation between the step counts and the circulating level of malondialdehyde-modified LDL (MDA-LDL, a form of oxLDL markers) among asymptomatic subjects.
Subjects and Methods

A total of 50 subjects (mean age: 63 years) were studied. Eligible subjects were asymptomatic, in good health, and not taking any medication. The excluded subjects were current smokers, regular drinkers, and those with a history of CVD, endocrine disorders, or severe kidney or liver disease. The institutional ethics committee approved the study, and all subjects gave their informed consent.

All data were obtained from subjects in an overnight fasted state. The body mass index (BMI) was calculated as the weight divided by the height squared. The blood pressure (BP) was measured in the right arm using a mercuric sphygmomanometer with the subject in a seated position, and the mean BP (MBP) was calculated based on the equation: diastolic BP + (systolic BP − diastolic BP)/3. Fasting plasma glucose (FPG), serum LDL-cholesterol (LDL-C), TG and HDL-C levels were enzymatically measured. Serum high sensitivity C-reactive protein (hs-CRP) level was measured by an enzyme-linked immunosorbent assay (ELISA) system (Assaypro Co. Ltd., St. Charles, MO, USA). Serum malondialdehyde-low-density lipoprotein (MDA-LDL) level was also measured by an ELISA system (Sekisui Co. Ltd., Tokyo, Japan) [13,14].

The step counts were assessed using a pedometer (Omron Health Care Co. Ltd., Kyoto, Japan). Subjects wore the pedometer at the waist level during the day (except when sleeping and bathing) for seven consecutive days before blood was sampled, and the average of daily step counts was used in this study. The subjects were required to maintain their previous lifestyles while wearing the pedometer.

The data are expressed as the means ± standard deviations for parametric variables or medians plus the interquartile ranges for nonparametric variables. The correlations of the step counts with other variables were examined by Pearson’s correlation tests. Subsequently, a stepwise multiple linear regression analysis model, into which all of the measured variables (age, gender, BMI, MBP, LDL-C, TG, HDL-C, FPG, hs-CRP, and MDA-LDL) were entered, was utilized to detect the predictive variables for the step counts. The values of TG, hs-CRP, MDA-LDL and step counts were calculated after a log-transformation because of their skewed distributions. A P-value ≤ 0.05 was considered to be significant.

Results

The clinical characteristics of the studied subjects and correlations between the step counts and other variables are shown in Table 1. There was a significant inverse correlation between the step counts and subject age or MDA-LDL level. A subsequent stepwise multiple linear regression analysis identified age and the MDA-LDL level to be variables that were independently, significantly, and inversely associated with the step counts.

Discussion

The present study showed a significant inverse correlation between the levels of circulating MDA-LDL and step counts among asymptomatic subjects. The finding of an inverse correlation between the MDA-LDL level and step counts suggests that steps may be beneficially associated with atherosclerosis in correlation with MDA-LDL reduction. The subject age was also inversely correlated with the step counts in this study, and this is consistent with prior data showing a decreasing trend in the daily steps with age (in particular after the forties) [6].

Pedometers have recently been used in health promotion and related research [1,2], and the MDA-LDL level is considered to be a risk marker for CVD [13,14], so the present study is relatively small but nevertheless significant. The findings of the present study appear to support a recent study showing that accelerometer-determined physical activities are significantly and inversely related to the MDA-LDL level in older people, although the levels of clinical variables were not described and steps-specific analyses were not done in that study [10]. In addition, our present study results raise the possibility that the MDA-LDL level can be used as
Steps and oxidized LDL in asymptomatic subjects

Malondialdehyde is a major product of lipid peroxides, and therefore MDA-LDL is a representative form of oxLDL markers [13,14]. Once LDL is oxidized, then a variety of oxidized lipids and proteins in LDL particles are formed. OxLDL consists of heterogeneously modified LDL particles [20]. Accordingly, even though MDA-LDL is assayed for a part of oxLDL, the oxidation of the LDL particles may be seen in the whole particles [20].

While the detailed mechanism responsible for the correlation between the oxLDL and step counts remains unclear, there are several possible explanations. While the circulating MDA-LDL can stem from the vasculature, regular physical activity increases the vascular nitric oxide bioavailability, which induces the up-regulation of antioxidative molecules (i.e. superoxide dismutases) and the down-regulation of oxidative molecules (i.e. nicotinamide adenine dinucleotide phosphate-oxidase) in the vasculature [21]. Increased circulating levels of endogenous antioxidant enzyme activity (i.e., glutathione reductase) in physically active people (conversely, the oxidative milieu present in sedentary people) [22] may also be involved in the formation of oxLDL in the circulation and vasculature. Because LDL particles are more prone to oxidative processes due to their long retention in the circulation, a substantial removal of LDL particles via increased LDL receptors and/or their activity induced by physical activity, mainly in the liver, could contribute to a reduction of the oxLDL in the circulation [15]. Further biological evidence of this process will need to be obtained in future studies for confirmation.

We acknowledge that there are several limitations to this study. First, the sample size was relatively small. Second, the cross-sectional design of the study did not clearly elucidate the cause-and-effect relationship of the results. Third, the present study was limited to asymptomatic subjects. In general, the step counts are positively associated with the

Table 1. Clinical characteristics of the subjects and correlations of each variable with the step counts (median level: 6962 [interquartile range 5496-8552])

<table>
<thead>
<tr>
<th>Variables</th>
<th>Levels</th>
<th>r (P-value)</th>
<th>β (P-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>63 ± 6</td>
<td>-0.35 (0.01)*</td>
<td>-0.35 (&lt; 0.01)*</td>
</tr>
<tr>
<td>Gender (male/female, n)</td>
<td>15/35</td>
<td>0.05 (0.72)</td>
<td>Not extracted</td>
</tr>
<tr>
<td>Body mass index (kg/m2)</td>
<td>23.6 ± 2.9</td>
<td>-0.08 (0.59)</td>
<td>Not extracted</td>
</tr>
<tr>
<td>Mean blood pressure (mmHg)</td>
<td>98 ± 14</td>
<td>-0.06 (0.68)</td>
<td>Not extracted</td>
</tr>
<tr>
<td>LDL-cholesterol (mmol/L)</td>
<td>3.21 ± 0.64</td>
<td>-0.13 (0.37)</td>
<td>Not extracted</td>
</tr>
<tr>
<td>Triglycerides (mmol/L)</td>
<td>1.02 (0.68-1.27)</td>
<td>-0.03 (0.82)</td>
<td>Not extracted</td>
</tr>
<tr>
<td>HDL-cholesterol (mmol/L)</td>
<td>1.61 ± 0.30</td>
<td>0.19 (0.18)</td>
<td>Not extracted</td>
</tr>
<tr>
<td>Plasma glucose (mmol/L)</td>
<td>5.50 ± 0.71</td>
<td>-0.12 (0.40)</td>
<td>-0.15 (0.24)</td>
</tr>
<tr>
<td>High sensitivity CRP (mg/dL)</td>
<td>0.04 (0.02-0.06)</td>
<td>-0.14 (0.35)</td>
<td>Not extracted</td>
</tr>
<tr>
<td>MDA-LDL (U/L)</td>
<td>22.3 (16.9-38.8)</td>
<td>-0.41 (&lt; 0.01)*</td>
<td>-0.38 (&lt; 0.01)*</td>
</tr>
</tbody>
</table>

LDL: low-density lipoprotein, HDL: high-density lipoprotein, CRP: C-reactive protein, MDA-LDL: malondialdehyde-low-density lipoprotein. The levels of the respective variables are expressed as the means ± standard deviation for parametric variables or the medians (interquartile range) for nonparametric variables. The correlations are expressed as Pearson's correlation coefficients (r [P-value]) and stepwise multiple linear regression coefficients (β [P-value]) between the steps and other variable. The values for triglycerides, high sensitivity CRP, MDA-LDL and steps were log-transformed for these correlation analyses. Significance level: *P ≤ 0.05.
HDL-C levels and are inversely associated with the TG levels [3], but no apparent correlation was observed between the step counts and these lipid levels in this study. This can be, in part, due to the characteristics of the study subjects who were asymptomatic and showed relatively normal lipid levels (there is also a report showing that the association between physical activity and the TG or HDL-C levels could be attenuated in this case [23]). Fourth, no data regarding atherosclerosis (i.e., carotid artery intima-media thickness) were available. Therefore, more studies with larger populations, including diseased patients, with prospective/interventional designs and with atherosclerosis-related indices will be necessary to confirm our findings.

In summary, there was a significant inverse correlation between the circulating MDA-LDL levels and step counts among asymptomatic subjects. These data suggest that daily steps may be beneficially associated with atherosclerosis in correlation with ox-LDL reduction, and also that the MDA-LDL level may be used as a measure reflecting the daily steps. Further investigations should be undertaken to establish the observed relationship and clinical utility of MDA-LDL levels in association with steps-based strategies for CVD prevention.

References