ASSOCIATION OF PHYSICAL ACTIVITY WITH INSULIN RESISTANCE, SUBCLINICAL INFLAMMATION, COAGULATION, AND FIBRINOLYTIC BIOMARKERS AMONG POPULATION AT HIGH RISK FOR TYPE 2 DIABETES

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ABSTRACT

Objective: To investigate the association of physical activity with insulin resistance and biomarkers of inflammation, coagulation, and fibrinolysis in a population at high risk for type 2 diabetes.

Patients and Methods: A total of 778 subjects from the Risk factors in Impaired Glucose Tolerance for Atherosclerosis and Diabetes (RIAD) study aged 40-70 years were included in the present cross-sectional analysis.

Results: Participants classified as having low physical activity (PA) were more insulin resistant in comparison to participants with medium (P = 0.042) and high PA (P = 0.015). Individuals with high physical activity had a significantly lower leucocytes count than individuals with low PA (P = 0.027) and significantly lower hs-CRP and fibrinogen concentrations than individuals with medium (P = 0.011 and P = 0.021) and low physical activity (P = 0.04 and P = 0.007). Although a trend towards a decrease in plasminogen activator inhibitor-1 (PAI-1) and tissue plasminogen activator (tPA) levels with increasing physical activity was present, significant differences were observed only between subjects with high and medium physical activity (P = 0.045 and P = 0.033). In multivariate regression analyses physical activity was an independent determinant of insulin resistance, leucocytes count, hs-CRP, and fibrinogen concentrations.

Conclusions: Physical activity was independently associated with insulin resistance and biomarkers of inflammation, whereas only a tendency towards decreased concentrations of coagulation and fibrinolytic biomarkers with increasing physical activity was observed.

Key words: physical activity, insulin resistance, inflammation, coagulation, metabolic syndrome, type 2 diabetes mellitus

INTRODUCTION

Sedentary lifestyle is one of the major risk factors for the development of obesity, the metabolic syndrome (MetS), type 2 diabetes mellitus (T2DM), and cardiovascular disease (CVD). 1 Regular physical activity, on the other hand, has been associated with lower MetS2 and T2DM3 prevalence even among individuals genetically predisposed to these diseases4 and with decreased CVD morbidity and mortality in lean as well as in obese individuals5.

Physical activity has been suggested to decrease metabolic and CVD risk through its effect on insulin resistance, inflammation, and coagulation.3,6 Although the inverse relationship between physical activity and insulin resistance has been demonstrated in numerous studies, the optimal weekly volume of exercise that may yield beneficial changes on insulin sensitivity is still questionable.7,8

Reports concerning the association of physical activity with markers of inflammation, coagulation, and fibrinolysis are ambiguous. Some studies have found independent effect of physical activity on C-reactive protein (CRP)9-11, leucocytes count9,10, fibrinogen9-11, plasminogen activator inhibitor-1 (PAI-1)12, tissue plasminogen activator (tPA)9, and von Willebrand factor9, whereas others have not13,14. In addition, relatively little is known about the influence of the volume of physical activity of these biomarkers among high-risk individuals.
Furthermore, to our knowledge the relationship of physical activity with insulin sensitivity and biomarkers of inflammation, coagulation, and fibrinolysis has not been examined within the same population. Thus, the aim of the present study was to investigate the association of physical activity with insulin sensitivity, CRP, leucocytes count, fibrinogen, PAI-1, tPA, and von Willebrand factor in a population at high risk for the development of T2DM.

**PATIENTS AND METHODS**

**PARTICIPANTS AND DESIGN**

Subjects were consecutive participants in the Risk factors in Impaired Glucose Tolerance for Atherosclerosis and Diabetes (RIAD) study, details on which have been previously published. In brief, 1139 subjects, aged 40-70 years, who were at risk for T2DM and had a family history of diabetes, overweight or obesity and/or hyper/dyslipoproteinemia were included in the study and underwent baseline examination. Known diabetes, medication affecting glucose tolerance, liver and kidney diseases, thyroid gland functional disorders and acute infections were exclusion criteria. The study conforms to the principles outlined in the Declaration of Helsinki; all subjects gave written informed consent prior to participation.

The RIAD participants underwent a standard examination according to a special protocol including: anthropometric measurements, physical examination, resting ECG; lifestyle questionnaire, own and familial medical history; blood sample analyses for determination of various cardiometabolic parameters. All participants were asked to refrain from heavy exercise or sedentary behaviour as well as from food excess or deprivation for three days prior to the test.

For the purpose of the present cross-sectional report from the 1139 subjects who participated in the baseline visit we excluded individuals with missing homeostasis model assessment of insulin resistance (HOMA-IR), leucocytes count, hs-CRP, fibrinogen, PAI-1, tPA, and von Willebrand factor data (n=361) and performed the analyses in the remaining 778 subjects.

**ANTHROPOMETRICAL MEASUREMENT AND BLOOD PRESSURE ASSESSMENT**

Weight and height were measured by standard techniques. The body mass index (BMI) was calculated as body weight (kg) divided by height squared (m²). The waist circumference was determined with a plastic tape at the midpoint between the lower rib margin and the iliac crest and the hip circumference at the level of the trochanter. Blood pressure was examined in a sitting position after at least a 5-minute rest. Two consecutive measurements were performed within 3 minutes and the second one was taken into consideration.

**PHYSICAL ACTIVITY LEVEL ASSESSMENT**

Physical activity was assessed using interviewer-administered questionnaire. Participants were asked to report the different kinds of activities they participated in, the average time spent on these activities per occasion and the total time per week spent on each activity during the past year. This information was used to calculate subjects’ weekly physical activity energy expenditure, expressed in metabolic equivalent-minutes per week (MET-min/week) using the compendium of physical activities. Based on the weekly volume of physical activity participants were classified into 3 physical activity categories in accordance with the U.S. Department for Health and Human Services “2008 Physical activity guidelines for Americans”: “low activity” < 500 MET-min/week, “medium activity” 500-1000 MET-min/week, and “high activity” > 1000 MET-min/week.

**LABORATORY EXAMINATION**

Venous blood was drawn between 7:00 am and 8:00 am after an overnight fast of at least 10 hours. EDTA plasma and serum were separated by centrifugation (4000 rpm for 8 minutes at 4 °C). Aliquots of plasma and serum were immediately frozen with liquid nitrogen and were stored at -80 °C until further analyses of insulin, CRP and other inflammatory and coagulation parameters. Plasma glucose, lipids, HbA1c, and leucocytes count were determined using fresh material.

Plasma glucose was measured by the hexokinase method (interassay coefficient of variation (CV)-1.5%). HbA1c was examined by high-performance liquid chromatography on a Diamat analyzer (Bio-Rad Laboratories, Munich, Germany). Plasma triglycerides and total cholesterol were measured enzymatically on a Ciba Corning Express Plus analyzer using commercially available kits (Boehringer Mannheim, Mannheim, Germany). High-density lipoprotein (HDL) cholesterol was determined after precipitation with dextran sulfate on a Ciba Corning Express Plus analyzer (Boehringer Mannheim). Low-density lipoprotein (LDL) cholesterol level was calculated using Friedewald equation. Serum free fatty acid concentrations were analyzed by enzyme colorimetric assay with a Boehringer
Mannheim test kit.

Fasting serum specific insulin was measured by enzyme immunoassays (Medgenix Diagnostics, Fleurus, Belgium; interassay CV: 7.6%) and showed no cross-reactivity to human proinsulin. Insulin resistance was evaluated by the homeostasis model assessment (HOMA-IR).

CRP was determined by a highly sensitive method, using an immunological agglutination test (Boehringer Mannheim). Fibrinogen was measured by the method of Clauss (Fibrinogen; Boehringer Mannheim; interassay CV: 2.9% to 5.5%). Leucocyte count was performed using standard technique.

The concentration of active plasminogen activator inhibitor 1 (PAI-1) antigen was determined using commercially available enzyme immunoassay (Immuno AG, Heidelberg, Germany). Tissue plasminogen activator (tPA) antigen was measured by enzyme immunoassay (Tint Elize; Biopool, Umea, Sweden) and von Willebrand factor antigen by electroimmunoassay (Immuno AG).

Statistical analyses

Data are presented as n, mean ± SEM, or percentage (%) as respectively indicated. The distribution of variables was assessed by the Kolmogorov-Smirnov test for homogeneity of variances. The distribution of high sensitive CRP levels was highly skewed, therefore, logarithmic transformation was performed. One-way ANOVA and chi-square tests were used to compare participants’ characteristics in categories of physical activity. Difference in HOMA-IR, serum free fatty acid concentrations, and inflammatory, coagulation, and fibrinolytic biomarkers between categories of physical activity were compared using analysis of covariance (ANCOVA) with age, sex, and BMI as covariates. Correlation analyses were performed using Spearman’s correlation coefficient. Multiple linear regression analyses were conducted to check whether physical activity determines insulin sensitivity or any of the examined inflammatory, coagulation, and fibrinolytic biomarkers independently of potential confounding factors. Differences were considered significant at P < 0.05. All statistical analyses were executed using SPSS for Windows, version 17.0 (SPSS Inc., Chicago, IL).

RESULTS

The characteristics of study participants in categories of physical activity are presented in Table 1. Of all examined individuals 13%, 53%, and 34% were classified as having low (< 500 MET-min/week), medium (500-1000 MET-min/week), and high (> 1000 MET-min/week) physical activity level, respectively. Subjects in the three categories of physical activity were of middle age and had body mass index (BMI) in the overweight range. The individuals with low activity had a significantly higher BMI and waist circumference when

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Low activity (n = 99)</th>
<th>Medium activity (n = 417)</th>
<th>High activity (n = 262)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>53 ± 0.8</td>
<td>54.4 ± 0.4</td>
<td>54.3 ± 0.5</td>
</tr>
<tr>
<td>Sex (men/women)</td>
<td>45/54</td>
<td>204/213</td>
<td>133/129</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>28.3 ± 0.6</td>
<td>27.3 ± 0.2 *</td>
<td>26.6 ± 0.2 *</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>95.9 ± 1.4</td>
<td>94.2 ± 0.7 *</td>
<td>91.6 ± 0.7 *</td>
</tr>
<tr>
<td>Hip circumference (cm)</td>
<td>106.1 ± 12.4</td>
<td>104.8 ± 10.9</td>
<td>102.4 ± 9.7 †</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>138.4 ± 0.9</td>
<td>135.5 ± 0.9</td>
<td>134.5 ± 1.2</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>85.7 ± 1.1</td>
<td>84.7 ± 0.5</td>
<td>83.3 ± 0.6 *</td>
</tr>
<tr>
<td>Fasting plasma glucose (mmol/l)</td>
<td>6.1 ± 0.1</td>
<td>6.0 ± 0.1</td>
<td>6.1 ± 0.1</td>
</tr>
<tr>
<td>Total cholesterol (mmol/l)</td>
<td>5.9 ± 0.1</td>
<td>5.9 ± 0.1</td>
<td>5.7 ± 0.1 †</td>
</tr>
<tr>
<td>LDL cholesterol (mmol/l)</td>
<td>3.6 ± 0.1</td>
<td>3.6 ± 0.1</td>
<td>3.5 ± 0.1</td>
</tr>
<tr>
<td>HDL cholesterol (mmol/l)</td>
<td>1.5 ± 0.1</td>
<td>1.4 ± 0.02</td>
<td>1.4 ± 0.03</td>
</tr>
<tr>
<td>Triglycerides (mmol/l)</td>
<td>1.9 ± 0.2</td>
<td>2.0 ± 0.1</td>
<td>1.8 ± 0.1</td>
</tr>
<tr>
<td>Fasting serum insulin (pmol/l)</td>
<td>104.4 ± 10.5</td>
<td>84.9 ± 2.7</td>
<td>77.5 ± 2.8</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>5.8 ± 0.1</td>
<td>5.7 ± 0.03</td>
<td>5.7 ± 0.1</td>
</tr>
<tr>
<td>Family history of diabetes (%)</td>
<td>62.6</td>
<td>59</td>
<td>55</td>
</tr>
<tr>
<td>Smoking history (%)</td>
<td>13.1</td>
<td>13.9</td>
<td>16.4</td>
</tr>
</tbody>
</table>

Data are n, %, or mean ± SEM. * P < 0.05 vs. low activity; † P < 0.05 vs. medium activity.
compared with individuals with medium and high activity. Hip circumference was also significantly higher in participants with low and medium physical activity in comparison with participants with high physical activity. In the high physical activity category diastolic blood pressure and total cholesterol level were significantly lower than in the low and in the medium activity category, respectively. No differences in fasting plasma glucose concentration or any of the other examined parameters between categories of physical activity were observed, although a tendency towards a decrease in fasting serum insulin concentrations and systolic blood pressure was seen with increasing physical activity.

When HOMA-IR was compared between groups of physical activity significantly higher values were observed in low vs. moderately active (4.2 ± 0.45 vs. 3.4 ± 0.13, P = 0.01) and vs. highly active individuals (4.2 ± 0.45 vs. 3.1 ± 0.13, P = 0.001). This was also confirmed after adjustment for age, sex and BMI (Fig. 1a). A similar trend was observed for serum free fatty acid concentration (Fig. 1b), results being statistically significant after age, sex and BMI adjustment between the low and the high activity category (0.50 ± 0.02 vs. 0.45 ± 0.001 mmol/l, P = 0.047).

With respect to biomarkers of inflammation physically active participants had significantly lower leucocytes count in comparison with sedentary participants (5.8 ± 0.1 vs. 6.6 ± 0.3 GPt/l, P = 0.01) (Fig. 2a). Subjects classified as active also had significantly lower high sensitive CRP (hs-CRP) concentration than moderately active and sedentary subjects (1.3 ± 0.03 vs. 1.41 ± 0.03 mg/l, P = 0.006 and 1.3 ± 0.03 vs. 1.46 ± 0.07 mg/l, P = 0.02, respectively) (Fig. 2b). Similarly, active individuals exhibited lower fibrinogen concentration than moderately active and sedentary individuals (2.8 ± 0.02 vs. 3 ± 0.03 g/l, P = 0.002 and 2.8 ± 0.02 vs. 3.1 ± 0.1, P = 0.004, respectively) (Fig. 2c). Results were also confirmed after age, sex, and BMI adjustment.

PAI-1 active complex antigen and tPA antigen concentrations were significantly lower among participants in the high activity category compared with those in the medium activity category (43.1 ± 2.7 vs. 49.9 ± 2.1 ng/ml, P = 0.045, and 9.6 ± 0.2 vs. 10.2 ± 0.2, P = 0.033, respectively) (Figs 3a, 3b). No significant differences between categories of physical activity were observed with respect to von Willebrand factor antigen concentration (Fig. 3c).

In univariate analyses significant inverse correlation was observed between physical activity level and HOMA-IR, leucocytes count, hs-CRP, and fibrinogen (r² = -0.074, P = 0.04; r² = -0.080, P = 0.035; r² = -0.116, P = 0.002; and r² = -0.172, P < 0.001, respectively). These associations were only slightly attenuated, but remained significant, when a partial correlation was performed with age, gender, BMI, and smoking history as controlling variables. No association was found between the level of physical activity and any of the examined coagulation and fibrinolytic biomarkers (data not shown).

In multivariate linear regression analyses low physical activity was found to be a significant predictor of HOMA-IR, leucocytes count, hs-CRP, and fibrinogen concentrations independent of age, sex, BMI, family history of obesity and type 2 diabetes, and smoking history (Table 2).

**DISCUSSION**

In the present cross-sectional analysis of individuals at high risk for T2DM a significant inverse relationship between physical activity and insulin resistance, and biomarkers of inflammation independent of confounding factors was observed. In addition, total weekly physical activity in the range 500-1000 MET-
**Table 2.** Multiple regression analyses of various cardiometabolic risk factors and physical activity as determinants of insulin resistance, inflammatory, coagulation, and fibrinolytic biomarkers

<table>
<thead>
<tr>
<th></th>
<th>HOMA-IR</th>
<th>Leucocytes count</th>
<th>hs-CRP</th>
<th>Fibrinogen</th>
<th>PAI-1</th>
<th>tPA</th>
<th>vWF</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>β coefficient</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>(P value)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>0.075 (0.022)</td>
<td>0.055 (NS)</td>
<td>0.011 (NS)</td>
<td>0.171 (&lt; 0.001)</td>
<td>0.061 (NS)</td>
<td>0.211 (&lt; 0.001)</td>
<td>0.161 (&lt; 0.001)</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td>-0.170 (&lt; 0.001)</td>
<td>-0.076 (NS)</td>
<td>0.115 (0.002)</td>
<td>0.111 (0.011)</td>
<td>-0.178 (&lt; 0.001)</td>
<td>-0.257 (&lt; 0.001)</td>
<td>0.065 (NS)</td>
</tr>
<tr>
<td><strong>BMI</strong></td>
<td>0.423 (&lt; 0.001)</td>
<td>0.153 (&lt; 0.001)</td>
<td>0.226 (&lt; 0.001)</td>
<td>0.246 (&lt; 0.001)</td>
<td>-0.367 (&lt; 0.001)</td>
<td>-0.278 (&lt; 0.001)</td>
<td>0.123 (0.001)</td>
</tr>
<tr>
<td><strong>Family history obesity</strong></td>
<td>0.029 (NS)</td>
<td>0.025 (NS)</td>
<td>0.097 (0.011)</td>
<td>0.063(NS)</td>
<td>-0.094 (0.013)</td>
<td>-0.015 (NS)</td>
<td>0.066 (NS)</td>
</tr>
<tr>
<td><strong>Family history T2DM</strong></td>
<td>0.018 (NS)</td>
<td>-0.016 (NS)</td>
<td>-0.044 (NS)</td>
<td>0.01 (NS)</td>
<td>0.003 (NS)</td>
<td>-0.036 (NS)</td>
<td>0.031 (NS)</td>
</tr>
<tr>
<td><strong>Physical activity level</strong></td>
<td>-0.072 (0.029)</td>
<td>-0.084 (0.03)</td>
<td>-0.082 (0.028)</td>
<td>-0.121 (0.004)</td>
<td>-0.057 (NS)</td>
<td>-0.048 (NS)</td>
<td>0.019 (NS)</td>
</tr>
</tbody>
</table>

* Models were additionally adjusted for smoking history; Data on hs-CRP are logarithmically transformed.

**Figure 2.** a) leucocytes count, b) hs-CRP concentrations, and c) fibrinogen concentrations in groups of physical activity. White, grey and black bars: individuals with low, medium and high physical activity, respectively. Mean ± SEM; * P < 0.05 vs. individuals with low activity; † P < 0.05 vs. individuals with medium activity.

**Figure 3.** a) plasminogen activator inhibitor-1 (PAI-1), b) tissue plasminogen activator (tPA), and c) von Willebrand factor concentrations in groups of physical activity. White, grey and black bars: individuals with low, medium and high physical activity, respectively. Mean ± SEM; † P < 0.05 vs. individuals with medium activity.
minutes was found to have considerable beneficial effect on insulin sensitivity, whereas higher volume of activity (> 1000 MET-min/week) was associated with lowering of subclinical inflammation in this population. With respect to coagulation and fibrinolytic biomarkers a tendency towards a decrease in their concentrations with increasing physical activity was present. These findings confirm and further extend previous reports providing evidence that physical activity improves insulin sensitivity and subclinical inflammation, coagulation, and fibrinolysis and may thus decrease metabolic and CVD risk.

In the present study a significant inverse association between physical activity level and HOMA-IR was observed, which is in line with previous reports highlighting the beneficial effect of physical activity on insulin sensitivity in various populations. Physical activity has been found to improve insulin sensitivity through changes in body fat mass as well as through fat mass loss-independent mechanisms such as: increased GLUT4 translocation and subsequent glucose utilization in skeletal muscle; improved capacity of skeletal muscle to oxidise fat; increased intramyocellular lipid turnover and decreased quantity of lipid metabolites. Accordingly the relationship between physical activity and insulin resistance observed in the present study was slightly attenuated, but remained significant after adjustment for BMI. Thus, our findings support the results of previous studies demonstrating BMI- and weight loss-independent effect of physical activity on insulin sensitivity.

We also found a significant negative association of physical activity with leucocytes count, hs-CRP, and fibrinogen concentrations. This is consistent with previous reports. In this context physical activity was inversely associated with leucocytes count, hs-CRP, and fibrinogen in elderly, healthy middle-aged individuals and in individuals from the general population. Similarly, higher levels of physical activity were found to be related to lower CRP concentrations in patients with CVD. Recently, it was also reported that objectively measured physical activity using accelerometers is associated with CRP in US adults. On the contrary, however, other studies have observed no relationship between physical activity and markers of inflammation and data remain equivocal.

It is now well established that adipose tissue is metabolically active organ that may induce inflammation through increased cytokine production. Therefore, physical activity is suggested to diminish inflammation mainly by reducing body weight. In the present study the association between physical activity and inflammatory markers remained significant after adjustment for BMI. This corroborates previous findings that the effect of physical activity on inflammation may be partially, but not entirely, mediated through changes in body weight.

In the present study, although a tendency towards a decrease in PAI-1 and tPA concentrations with increasing physical activity was observed, it was not statistically significant. In addition, no relationship between von Willebrand factor concentrations and level of physical activity was found. This is in accordance with the results of some investigators, but is not in line with those of others. Thus, among patients with stable coronary heart disease and healthy individuals leisure time physical activity was not associated with PAI-1 and von Willebrand factor concentrations. On the contrary, physical activity was independently associated with PAI-1 and tPA and von Willebrand factor in individuals from the general population. The discrepancies in literature may to a certain extent be explained by differences in study populations and methods of physical activity assessment. To date the association between physical activity and biomarkers of coagulation and fibrinolysis has not been observed using objective measures of physical activity.

Public health organizations recommend engagement in weekly physical activity in the range 500-1000 MET-minutes for substantial health benefits. However, the effect of physical activity on metabolic and cardiovascular disease risk factors seems to be dose-dependent and the optimal weekly volume of exercise that may yield beneficial changes in insulin resistance and systemic inflammation is still questionable.

With this respect we found that participants engaged in weekly physical activity in the range 500-1000 MET-minutes are significantly less insulin resistant in comparison to those engaged < 500 MET-minutes of physical activity per week. Weekly volume of exercise above 1000 MET-minutes was associated with even better insulin sensitivity, although the difference did not reach statistical significance. These findings are in accordance with the results of previous observations suggesting that physical activity may improve insulin sensitivity in a dose-dependent manner and that total duration of activity is a more important determinant of insulin sensitivity than activity intensity.

Mayer-Davis et al. in the Insulin Resistance Atherosclerosis Study (IRAS) reported that increased participation in vigorous as well as...
total and non-vigorous physical activity is associated with significantly higher insulin sensitivity in the general population. Their findings were later confirmed by Kavouras et al.\textsuperscript{25} and Esteghamati et al.\textsuperscript{24}. Recently, in the European Relationship between Insulin Sensitivity and Cardiovascular risk (RISC) study Balkau et al.\textsuperscript{7} demonstrated that objectively measured total physical activity is a major determinant of insulin sensitivity among healthy individuals. Ekelund et al.\textsuperscript{8} also reported that objective measured time spent in moderate-to-vigorous physical activity may predict insulin sensitivity independently of confounding factors among subjects at high risk for T2DM.

Similarly to insulin resistance physical activity has been shown to decrease systemic inflammation in a dose-dependent manner among individuals from the general population\textsuperscript{9-11}, healthy individuals\textsuperscript{22,23}, and patients with CVD\textsuperscript{9,10,14}. In the present analysis a tendency towards a decrease in the levels of inflammatory biomarkers with increasing physical activity was also observed. However, individuals with total weekly physical activity above 1000 MET-minutes exhibited significantly lower concentrations compared to both individuals with low (< 500 MET-min/week) and medium (500-1000 MET-min/week) physical activity, whereas the difference between those with low and medium activity was not significant. Hence, our results confirm the previously observed dose-response relationship between physical activity and inflammatory biomarkers, but also indicate that engagement in more than 1000 MET-min/week of physical activity may be necessary in order subclinical inflammation to be decreased among individuals at high risk for T2DM.

The results of the present analysis should be considered with respect to the cross-sectional design of the study that restricts any inference about the direction of causality. However, it adds to the existing body of scientific evidence concerning the relationship between physical activity, insulin resistance, inflammation, coagulation, and fibrinolysis among individuals predisposed to develop diabetes.

In summary, among individuals at high risk for T2DM physical activity was found to be independently inversely associated with insulin resistance and biomarkers of inflammation, whereas only a tendency towards decreased concentrations of coagulation and fibrinolytic biomarkers was observed with increasing physical activity. In addition, our results suggest that total weekly physical activity in the range of 500-1000 MET-minutes may already exert beneficial effect on insulin resistance, whereas engagement in more than 1000 MET-min/week may be necessary to diminish subclinical inflammation in this population.

REFERENCES


