Objective—Physical activity is related to lower risk of cardiovascular disease, but data relating to coronary lesions have been conflicting. These inconsistencies may in part be due to unreliable assessment of physical activity and limitations imposed by self-reported data. The purpose of this study was to determine the relationship between objectively measured physical activity and coronary artery calcium (CAC).

Methods and Results—Participants were 443 healthy men and women (mean age = 66 ± 6 years), without history or objective signs of coronary heart disease, drawn from the Whitehall II epidemiological cohort. Physical activity was objectively measured using accelerometers worn during waking hours for 7 consecutive days (average daily wear time = 889 ± 68 minutes/day). CAC was measured in each participant using electron beam computed tomography and was quantified according to the Agatston scoring system. On average, 54.4% of the sample recorded at least 30 minutes/day of moderate to vigorous physical activity (MVPA). There was no association between MVPA and presence of detectable CAC. For the participants with detectable CAC (n = 283) a weak inverse relationship between MVPA (minutes/day) and log Agatston score was observed (B = −0.008, 95% CI: −0.16 to 0.00, P = 0.05), although the association was no longer present after adjustments for age, sex, and conventional risk factors. No associations were seen for light activity or sedentary time.

Conclusion—Our results confirm no association between objectively assessed physical activity and CAC. Because CAC measures cannot identify more vulnerable lesions, additional studies are required to examine whether physical activity can promote plaque stability. (Arterioscler Thromb Vasc Biol. 2012;32:500-505.)

Key Words: calcification ■ coronary artery disease ■ epidemiology ■ exercise ■ prevention

Physical activity is important for maintaining cardiovascular health in older age,1–3 although the mechanisms remain poorly understood. Evidence from training studies and epidemiological cohorts has demonstrated that various mechanisms could play a role in the cardioprotective effects of exercise, including improvement in cardiac performance, aerobic capacity, endothelial function, and inflammatory and metabolic factors.4–10 However, the association of physical activity with coronary lesions and atherosclerotic processes remains unclear. Various studies have examined associations between physical activity and markers of subclinical atherosclerosis, although the data are equivocal.11–19 These inconsistencies may in part be due to differences in the assessment of physical activity and limitations imposed by self-reported data. In the only study to date to have used an objective assessment of physical activity, there was an inverse association between vigorous activity and 3-year progression in common carotid artery intima media thickness.19

Few studies have specifically examined physical activity and coronary artery calcium (CAC), which is thought to be a more direct marker of coronary atherosclerosis than measures of carotid artery intima media thickness.20,21 In the Multi-Ethnic Study of Atherosclerosis, self-reported brisk walking pace was associated with lower CAC in men but not in women, although null associations were observed for overall physical activity level and CAC in both sexes.14 Because there are currently no available data on objectively measured physical activity and CAC, this formed the rationale for the present study.

Methods

Participants

A sample of participants was drawn from the Whitehall II epidemiological cohort22 for a substudy in 2009/2010. The criteria for entry into the study included no history or objective signs of coronary heart disease, no previous diagnosis or treatment for hypertension, inflammatory diseases, or allergies. This information was confirmed by a telephone interview and verified from clinical data collected from the previous 7 phases of the main Whitehall II study. Volunteers were of white European origin, aged 56 to 79 years. Selection was stratified by grade of employment (current or most recent) to include higher
Physical Activity Assessment

Participants were asked to wear an accelerometer (Actigraph GT3X) mounted at the hip, which records movement on the vertical and horizontal axis, during waking hours for 7 consecutive days. The accelerometer provides a measure of the frequency, intensity, and duration of physical activity and allows classification of activity levels as sedentary, light, moderate, and vigorous. The raw accelerometer data were processed using specialist software (MAHUffe, Cambridge [http://www.mrc-epid.cam.ac.uk/Research/Programmes/Programme_5/InDepth/Programme%205_Downloads.html]) to produce a series of standardized outcome variables. All participants included in the present analysis recorded a minimum of 10 hours per day wear time for 6 to 7 days. The first and last day of data were excluded from the analysis and nonwear time was defined as intervals of at least 60 consecutive minutes of 0 count/minute (cpm).

We used cutoff points previously used in an older sample of adults23 to calculate daily times in each activity intensity band: sedentary (<1.5 metabolic equivalent [MET]); 0 to 199 cpm; light (1.5–3 MET) 200 to 1998 cpm; moderate to vigorous physical activity (MVPA) (>3 MET); ≥1999 cpm. Sensitivity analyses were also performed using a more conservative cutoff of 0 cpm to differentiate sedentary time from activity.24 All physical activity variables were converted to time (in minutes) per valid day.

To obtain self-reported physical activity data, we retrospectively linked our data with several previous phases (phase 5 in 1997 and phase 7 in 2004) of the main Whitehall II study. The questionnaire administered in these phases consisted of 20 items on frequency and duration of participation in walking, cycling, sports, gardening, housework, and home maintenance.25 Frequency and duration of each activity were combined to compute hours per week of physical activity. A compendium of activity energy costs was then used to derive a MET score for each of the 20 physical activities assessed. We calculated average MVPA MET-hours/week across phases 5 and 7.

Coronary Artery Calcification

The assessment of CAC was performed using electron beam computed tomography (Imatron C-150, GE Healthcare, San Francisco, CA) as previously described.26 In brief, 40 contiguous 3-mm slices were obtained during a single breath-hold starting at the carina and proceeding to the level of the diaphragm. Scan time was 100 milliseconds/slice, synchronized to 40% of the R-R interval. Agatston and volumetric calcium scores were calculated to quantitate the extent of CAC by a single experienced investigator blinded to the physical activity and clinical data on an Aquarius workstation. CAC (Agatston score) was measured 3 times (using an automated UA-779 digital monitor) with participants in a seated position, and a mean value was taken from the second and third readings.

Statistical Analysis

Based on the present physical activity guidelines,27 we created 3 categories from the MVPA variable (<10, 10–<30, and ≥30 minutes/day). To examine differences in baseline characteristics between MVPA groups, we used χ² tests and 1-way analysis of variance to examine categorical and continuous variables, respectively. Test for trend was analyzed by using the /contrast subcommand in a general linear model design. In addition, we used Pearson correlation, partially adjusted for age, sex, and wear time, to examine associations between Actigraph counts/minute and risk factors. Multivariate logistic regression analyses were used to examine the association between physical activity and the presence of detectable CAC (Agatston score >0). We calculated odds ratios (OR) and 95% confidence intervals (CI) for the risk of CAC according to MVPA categories, adjusting for age, sex, Actigraph wear time, employment grade (as a marker of social position), use of statins, smoking (never/former/current smoker), resting systolic blood pressure, HDL cholesterol, triglycerides, HbA1c, and BMI. In addition, we used linear regression to examine the association between physical activity and CAC as a continuous measure, in which Agatston score was log transformed (using log [Agatston+1]). In these analyses, the data are presented both as unstandardized coefficients (B) and standardized coefficients (β) with 95% CI. The standardized coefficient reflects the association in relation to a 1-standard deviation increase in the physical activity variable. Statistical significance was denoted at P<0.05. All analyses were conducted using SPSS version 15.

Results

From the initial sample of 510 participants, 64 did not provide Actigraph data, and 3 had missing data on other variables. Thus, the final analytic sample comprised 443 participants (mean age=66±6 years; range, 57–79 years). Participants excluded from the analysis tended to be younger (64 versus 66 years, P=0.007) than those included, although there was no difference in CAC (log Agatston scores, 3.00±2.39 versus 2.60±2.47, P=0.21).

The sample as a whole was relatively active, and 59.8% of men and 49.3% of women recorded at least 30 minutes/day of MVPA, although men were significantly more active than women (338.0±145.0 versus 303.8±130.2 cpm, P=0.009). In partial correlations controlling for age, sex, and wear time, average daily counts/minute was inversely related to BMI (Pearson r=-0.23, P<0.001), triglycerides (r=-0.15, P=0.001), and HbA1c (r=-0.10, P=0.04) and positively related to HDL cholesterol (r=0.25, P<0.001). Sedentary time was related to BMI (r=0.10, P=0.03) and inversely with HDL cholesterol (r=-0.16, P=0.001), although these associations did not remain significant after adjustment for MVPA. Participants who recorded at least 30 minutes/day of MVPA were younger, were from higher work grades, and had lower BMI and lower levels of HbA1c (Table 1). There was no difference in total registered Actigraph wear time between MVPA groups.

Coronary calcium scores ranged from 0 to 3510 (median=10.8, SD=364.7), and 283 participants (63.9%) had detectable CAC. In multivariate models, the risk factors most strongly associated with odds of any detectable CAC were age (OR per year=1.09, 95% CI, 1.05–1.15), male gender (OR=3.37, 2.04–5.59), use of statins (OR=4.43, 2.23–8.67), and previous/current smoker (OR=1.70, 1.06–2.71). There was no association between physical activity counts/minute, MVPA,
or sedentary time and risk of detectable CAC (Table 2). After adjustment for age and sex, participants with zero detectable CAC recorded 36.0 ± 2.0 minutes/day MVPA; those with CAC 0 and 0–100 recorded 38.5 ± 1.9 minutes/day; those with CAC 100 to 400 recorded 35.4 ± 3.0 minutes/day; and those with CAC >400 recorded 35.4 ± 3.8 minutes/day (P trend = 0.72).

We also observed no associations between any of the physical activity variables and log-transformed Agatston score in continuous analyses (results not shown). When we performed sensitivity analysis only in participants with detectable CAC, there was an inverse association between MVPA and log-transformed Agatston score (Table 3). However, the association did not persist after adjustment for age (age-adjusted B in participants recording >30 minutes/day MVPA = −0.15, 95% CI, −0.60 to

### Table 1. Characteristics of the Study Population in Relation to Objectively Assessed MVPA (n=443)

<table>
<thead>
<tr>
<th>Variable</th>
<th>MVPA &lt;10 min/d (n=51)</th>
<th>MVPA 10 to &lt;30 min/d (n=151)</th>
<th>MVPA ≥30 min/d (n=241)</th>
<th>P Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>68.7±6.1</td>
<td>66.8±5.6</td>
<td>64.9±5.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Men, %</td>
<td>19 (37.3)</td>
<td>70 (46.4)</td>
<td>134 (55.6)</td>
<td>0.03</td>
</tr>
<tr>
<td>Highest work grade, %</td>
<td>14 (27.5)</td>
<td>53 (35.1)</td>
<td>102 (42.3)</td>
<td>0.01</td>
</tr>
<tr>
<td>Current smokers, %</td>
<td>5 (9.8)</td>
<td>8 (5.3)</td>
<td>11 (4.6)</td>
<td>0.41</td>
</tr>
<tr>
<td>Resting systolic BP, mm Hg</td>
<td>136.7±18.8</td>
<td>134.2±18.0</td>
<td>133.3±16.0</td>
<td>0.45</td>
</tr>
<tr>
<td>HDL cholesterol, mmol/L</td>
<td>1.69±0.41</td>
<td>1.67±0.48</td>
<td>1.76±0.50</td>
<td>0.17</td>
</tr>
<tr>
<td>LDL cholesterol, mmol/L</td>
<td>3.32±0.96</td>
<td>3.14±0.91</td>
<td>3.28±1.03</td>
<td>0.33</td>
</tr>
<tr>
<td>Triglycerides, mmol/L</td>
<td>1.43±0.77</td>
<td>1.44±0.75</td>
<td>1.33±0.65</td>
<td>0.25</td>
</tr>
<tr>
<td>HbA1c, %</td>
<td>5.85±0.85</td>
<td>5.75±0.67</td>
<td>5.64±0.30</td>
<td>0.02</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>27.7±5.4</td>
<td>26.4±4.1</td>
<td>25.3±3.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Statins use, %</td>
<td>8 (15.7)</td>
<td>41 (27.2)</td>
<td>47 (19.5)</td>
<td>0.11</td>
</tr>
<tr>
<td>Log Agatston score</td>
<td>2.63±2.74</td>
<td>2.89±2.47</td>
<td>2.41±2.39</td>
<td>0.17</td>
</tr>
<tr>
<td>Total activity, min/d</td>
<td>175.3±80.5</td>
<td>229.1±59.9</td>
<td>271.4±66.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Light activity, min/d</td>
<td>170.4±78.6</td>
<td>209.9±58.7</td>
<td>216.8±64.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MVPA, min/d</td>
<td>4.5±3.4</td>
<td>19.2±5.6</td>
<td>54.6±21.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sedentary time, min/d</td>
<td>700.4±143.5</td>
<td>654.6±67.4</td>
<td>623.5±72.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Registered wear time, min/d</td>
<td>875.7±100.6</td>
<td>883.7±55.6</td>
<td>894.8±60.9</td>
<td>0.10</td>
</tr>
</tbody>
</table>

Values are means±SD. MVPA indicates moderate to vigorous physical activity; BP, blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

### Table 2. Association Between MVPA, Accelerometry Counts-Min, Sedentary Time, and Presence of Coronary Artery Calcium

<table>
<thead>
<tr>
<th>MVPA</th>
<th>Cases/n</th>
<th>Age- and Sex-Adjusted, Odds Ratio (95% CI)</th>
<th>Model 1, Odds Ratio (95% CI)</th>
<th>Model 2, Odds Ratio (95% CI)</th>
<th>P Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;10 min/d</td>
<td>30/51</td>
<td>1.00 (reference)</td>
<td>1.00</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>10 to &lt;30 min/d</td>
<td>104/151</td>
<td>1.66 (0.82–3.38)</td>
<td>1.53 (0.73–3.23)</td>
<td>1.47 (0.69–3.12)</td>
<td>0.24</td>
</tr>
<tr>
<td>≥30 min/d</td>
<td>108/241</td>
<td>1.20 (0.61–2.36)</td>
<td>1.17 (0.57–2.39)</td>
<td>1.09 (0.52–2.29)</td>
<td></td>
</tr>
<tr>
<td>P trend</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.42</td>
</tr>
<tr>
<td>Counts per min tertile</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.47</td>
</tr>
<tr>
<td>&lt;252</td>
<td>91/149</td>
<td>1.00 (reference)</td>
<td>1.00</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>252–357</td>
<td>98/148</td>
<td>1.25 (0.75–2.08)</td>
<td>1.16 (0.67–1.99)</td>
<td>1.14 (0.66–1.99)</td>
<td></td>
</tr>
<tr>
<td>&gt;357</td>
<td>95/148</td>
<td>1.22 (0.73–2.03)</td>
<td>1.17 (0.68–2.02)</td>
<td>1.19 (0.68–2.10)</td>
<td></td>
</tr>
<tr>
<td>P trend</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.65</td>
</tr>
<tr>
<td>Sedentary tertile</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.81</td>
</tr>
<tr>
<td>&lt;609 min/d</td>
<td>91/148</td>
<td>1.00 (reference)</td>
<td>1.00</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>609–671 min/d</td>
<td>98/150</td>
<td>1.24 (0.75–2.05)</td>
<td>1.25 (0.74–2.13)</td>
<td>1.18 (0.69–2.03)</td>
<td></td>
</tr>
<tr>
<td>&gt;671 min/d</td>
<td>93/147</td>
<td>0.92 (0.56–1.52)</td>
<td>0.96 (0.57–1.63)</td>
<td>0.93 (0.54–1.59)</td>
<td></td>
</tr>
<tr>
<td>P trend</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.50</td>
</tr>
</tbody>
</table>

Model 1: adjusted for wear time, age, sex, employment grade, use of statins, smoking; Model 2: adjusted for wear time, age, sex, employment grade, use of statins, smoking, systolic blood pressure, high-density lipoprotein cholesterol, triglycerides, HbA1c, and body mass index. MVPA indicates moderate to vigorous physical activity.
of Accelerometry Data on Log Agatston Score in Participants With Detectable Coronary Artery Calcium (n=283)

<table>
<thead>
<tr>
<th>Counts/min</th>
<th>Sedentary, min/d</th>
<th>Light Activity, min/d</th>
<th>Moderate to Vigorous Activity, min/d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unadjusted</td>
<td>(β)=−0.001 (−0.003, 0.000)*</td>
<td>(β)=0.001 (−0.002, 0.003)</td>
<td>(β)=0.001 (−0.003, 0.004)</td>
</tr>
<tr>
<td>Model 1</td>
<td>(β)=−0.099 (−0.216, 0.018)</td>
<td>(β)=0.039 (−0.078, 0.157)</td>
<td>(β)=0.019 (−0.099, 0.137)</td>
</tr>
<tr>
<td>Model 2</td>
<td>(β)=−0.038 (−0.158, 0.082)</td>
<td>(β)=0.003 (−0.111, 0.118)</td>
<td>(β)=0.054 (−0.060, 0.168)</td>
</tr>
</tbody>
</table>

Data are presented as unstandardized coefficients (β) with 95% CI and standardized coefficients (β) with 95% CI. Model 1: adjusted for wear time, age, and sex; Model 2: fully adjusted for wear time, age, sex, employment grade, use of statins, smoking, systolic blood pressure, high-density lipoprotein cholesterol, triglycerides, HbA1c, and body mass index.

*P<0.05.

have also reported no association between self-reported physical activity and CAC. In addition, a study in marathon runners and age-matched controls showed that there was no association between self-reported METs and CAC. In the only study to date to have used an objective assessment of physical activity, an inverse association between vigorous activity and 3-year progression in common carotid artery intima media thickness was found. In addition, this study demonstrated an association between sedentary time and subclinical atherosclerosis.

The largely null findings on physical activity and CAC suggest that the cardioprotective effects of exercise might act through alternative mechanisms, such as inflammatory and procoagulant processes. Indeed, recent epidemiological evidence suggests that inflammatory and hemostatic risk markers made the largest contribution to the inverse association between physical activity and cardiovascular events. Cardiorespiratory fitness might also act as an independent risk factor, and recent data suggest that exercise capacity, chronotropic response, and abnormal heart recovery during exercise stress testing were associated with CAC burden in the Heinz Nixdorf Recall study. Also, we previously demonstrated an association between walking speed (a proxy marker of fitness) and CAC in the present study sample. Nevertheless, data in apolipoprotein E−/− mice have demonstrated that 6 months of exercise training promotes more stable plaque phenotype, as shown by decreased macrophage and increased smooth muscle cell content compared with untrained mice. Thus, the association between physical activity and plaque stability might be more crucial than overall atherosclerotic burden.

An emerging body of evidence has shown that excessive sedentary behavior (sitting) may be linked to increased risk for obesity, dyslipidemia, and impaired glucose metabolism, independently of MVPA. In addition, several prospective studies have shown associations between excessive sitting and risk of incident cardiovascular disease. However, these studies have been largely based on measures of self-reported television time as a proxy marker of sedentary behavior. In the present study, sedentary time was related to BMI and inversely with HDL cholesterol, although there were no associations with any other risk factors or CAC. In addition, these associations did not remain significant after controlling for MVPA. Several previous studies using
accelerometry-based measures have observed detrimental, linear associations of sedentary time with waist circumference and other metabolic risk factors.\textsuperscript{33,35} Although not all studies have confirmed these findings.\textsuperscript{36,37} Using a different objective technique to assess sedentary behavior that involved individually calibrated minute-by-minute heart rate monitoring, Helmerhorst et al\textsuperscript{38} demonstrated an association between time spent sedentary and higher levels of fasting insulin over 5.6 years of follow-up. The discrepancy in these findings raises the possibility that television viewing does not simply represent a broader pattern of sedentary behavior but instead is a distinct behavior that carries its own risks. It is possible that self-reported television time is able to better capture prolonged periods of sitting than the present methods of objective assessment. Indeed, the accelerometry device used in the present study could not distinguish between sitting and standing.

**Limitations**

Because accelerometry measures were only collected over 1 week, this may not truly reflect habitual physical activity levels. Nevertheless, other data in British adults have demonstrated strong test-retest reliability for MVPA ($r=0.89$ for men, $r=0.76$ in women), measured using accelerometers for 2 nonconsecutive weeks over a 1-month period.\textsuperscript{39} Given that the associations found with objective physical activity data are consistent with those for self-reported physical activity averaged across 2 separate assessments, this suggests that the null associations observed are not accounted for by measurement error. The participants included in the present analysis were generally healthier than the overall Whitehall II sample and demonstrated higher activity levels compared with similar aged British cohorts.\textsuperscript{23} Therefore, our results might not be representative of the wider community. The strengths of this study include the unique measurement of objectively assessed physical activity and CAC in a relatively large and well-characterized sample.

In summary, our results demonstrate no association between objectively assessed physical activity and CAC, which is largely consistent with existing evidence. Because CAC measures cannot reliably identify more vulnerable lesions, additional studies are required to examine whether physical activity can promote plaque stability.

**Acknowledgments**

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None.

**References**


Objectively Assessed Physical Activity, Sedentary Time, and Coronary Artery Calcification in Healthy Older Adults
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