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Self-reported and accelerometer physical activity levels and coronary artery calcification progression in older women: Results from the Healthy Women Study

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Abstract

Objective—Regardless of the well-supported biological link between PA and atherosclerosis, most previous studies report a null association between PA and CAC. To examine the relation between physical activity (PA) and coronary artery calcification (CAC) progression in 148 Healthy Women Study (HWS) participants over 28 years of observation.

Methods—The HWS was designed to examine cardiovascular risk factor changes from pre- to post-menopause. Based on CAC scores collected at two follow-up visits (EBT1 and EBT4) scheduled 12 years apart, participants were classified into one of three groups: 1) *no detectable* CAC (n=37; 0 CAC at both visits), 2) *incident* CAC (n=46; 0 CAC at the first- and >0 CAC at the last- visit), or 3) *prevalent* CAC (n=65; >0 CAC at both visits). PA data were collected regularly throughout the study using self-report questionnaires and accelerometers at EBT4.

Results—The percentage of HWS participants with *no detectable* CAC decreased from 56.1% at EBT1 to 25.0% at EBT4. Time spent per day in accumulated and bouts of moderate- to vigorous-intensity (MV)PA were each significantly higher in the *no detectable* CAC group when compared to the *prevalent* CAC group (both $p < .01$). After covariate adjustment, these differences remained statistically significant (both $p < .05$). Although self-reported summary estimates collected

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throughout the study were significantly associated with accelerometer data at EBT4, there were no significant differences in self-reported physical activity levels by CAC groups after covariate adjustment.

Conclusions—Study findings suggest that low levels of accelerometer-derived MVPA may be indicative of subclinical disease in older women.

Keywords

coronary heart disease; motor activity; ambulatory monitoring; coronary calcification; women

INTRODUCTION

Cardiovascular disease (CVD), which includes coronary heart disease (CHD), is the leading cause of death among U.S. women.¹ There is substantial scientific evidence to support the importance of physical activity (PA) to reduce lifetime risk of CHD.^{1,2} This reduction in risk may be due to the beneficial effect of PA on several related risk factors, including obesity, hypertension, elevated triglyceride levels, low concentrations of high density lipoprotein (HDL-c), high insulin resistance and glucose intolerance.³ It is also possible that the benefits of PA are independent of traditional risk factors and impact plaque morphology and risk of thrombosis⁴ or coronary blood flow and myocardial metabolism.⁵ Regardless of mechanism, inadequate PA levels are thought to be both a sign of existing disease⁶, as well as a predictor of future disease.^{2,7} Yet the specific mechanisms by which PA supports cardiovascular health in women remain unclear.⁸

Clarifying the biological link between PA and CHD is an important public health priority given that a large proportion of related deaths occur in women without clinical symptoms.⁹ The amount of calcification in the coronary arteries, as measured by electron beam tomography (EBT), provides a non-invasive measure of subclinical atherosclerosis and is strongly independently related to risk of clinical CHD. Coronary artery calcium (CAC) scores via EBT are associated with coronary atherosclerosis detected during pathology¹⁰ and angiographic studies.¹¹ CAC scores are also directly associated with many cardiovascular risk factors, especially apolipoprotein B, HDL-c, blood pressure, smoking, and diabetes.^{12–19} Given the beneficial effect of PA on CHD and related risk factors, it seems intuitive that PA would also be inversely related to CAC.

Although previous studies have explored the association between PA and CAC, most have reported null findings.^{4,19–23} Past studies have principally examined the cross-sectional relationship between PA and extent of CAC, which is not reflective of the atherosclerotic process that develops over several decades. Several studies have also used self-report methods to assess the PA exposure. Therefore, one possible explanation for previous null findings might relate to the limitations of self-report PA instruments to produce an estimate that is reflective of CAC. Recent results by Hamer and colleagues²³ also failed to show a significant relationship between accelerometer-derived PA estimates and extent of CAC. However, the associations between accelerometer estimates and CAC were not presented separately by sex.²³ PA levels²⁴ and CAC scores²⁵ tend to be higher in men than in women. Therefore, non-stratified analysis, regardless of statistical adjustment, could lead to inappropriate inferences. Therefore, the purpose of this study was to examine the association of self-report and accelerometer derived estimates of PA to CAC measured over 12 years in a cohort of women followed for up to 28 years. This design provides the unique opportunity to explore the relations of PA, assessed via self-report and accelerometer, with the progression of CAC in a well-characterized study of women and CVD.

METHODS

Study design overview

Detailed descriptions of the HWS have been previously published.^{26,27} Briefly, the HWS, a prospective cohort study, was designed to examine changes in biological and behavioral risk factors for CVD as women progressed through the menopausal transition. From 1983–84, women aged 42–50 years were recruited from driver's license lists within selected zip codes in Allegheny County, Pennsylvania. Eligible women were invited to a baseline visit. After the baseline assessment, women reported their menstrual status on monthly postcards. Menopause was defined as no menses for 12 consecutive months or initiation of hormone therapy. Post-menopausal women were then scheduled for a follow-up evaluation (1st year postmenopausal visit). Subsequent evaluations were repeated at 2, 5, and 8 years post-menopause. After the 8th postmenopausal visit, women were invited to have an EBT scan of their heart and aorta (1997–98). EBT scans were repeated in 2002–03 (EBT2), 2004–07 (EBT3), and 2010–11 (EBT4). All measures relevant to these analyses were completed at the EBT1 and EBT4 visits.

Setting and participants

Recruitment and data collection were conducted at the University of Pittsburgh. Women were initially interviewed by telephone to determine study eligibility. Eligibility criteria for study enrollment included: menstrual bleeding within the previous three months; no surgical induced menopause; diastolic blood pressure <100 mmHg; not currently using lipid-lowering, anti-hypertensive or psychotropic medications, insulin, thyroid hormone, or estrogens. Of the 2,405 women contacted by phone, 88.9% (n=2,138) consented to an eligibility interview and 42.1% (n=901) were deemed eligible at that time and during a subsequent home interview. Sixty percent of eligible women (n=541) enrolled into the study.²⁷ The average age at baseline examination was 47.6 ± 1.6 years. Each participant provided written informed consent and all protocols were approved by the institutional review board at the University of Pittsburgh.

Participant characteristics

Socio-demographic characteristics and health behavior data were collected repeatedly in the HWS using standardized questionnaires. Prescription medication use (i.e., hormone therapy, lipid-lowering, hypertensive, and diabetic medication) was also collected throughout the 28 years of participant follow-up.

Coronary artery calcification

EBT scans were performed using a GE-Imatron C-150 (Ultrafast CT®) scanner (Imatron, South San Francisco, California). For evaluation of the coronary arteries, 30 to 40 contiguous 3-mm thick transverse images were obtained from the level of the aortic root to the apex of the heart. Images are obtained during maximal breath holding using electrocardiogram triggering so that each 100-millisecond exposure is obtained at 80% of the R-R interval. CAC scores were calculated by the method of Agatston²⁸ using a densitometric program available on the Imatron C-150 workstation. Calcification was considered present in the coronaries when at least 3 contiguous pixels of 130 Hounsfield units were detected overlying the vessels of interest. HWS participants were classified into one of three groups based on CAC scores collected at the EBT1 and EBT4 visits. The *no detectable* CAC group was defined as 0 CAC score at both EBT1 and EBT4, the *incident* CAC group as a CAC score of 0 at EBT1 and >0 at EBT4, and the *prevalent* CAC group as CAC scores >0 at both the EBT1 and EBT4 visits.

Physical activity

Paffenbarger Physical Activity Questionnaire (PPAQ)—The PPAQ^{29,30} is a reliable and valid estimate of previous week PA. The PPAQ was interviewer administered by trained study staff at baseline, 1 and 5 years postmenopausal, and EBT1 (approximately 8 years postmenopausal) follow-up visits. PA levels were calculated as the sum of walking, stair-climbing, and sports and recreational activity participation. Walking one block was equivalent to 56 kilocalories per week ($\text{kcal}\cdot\text{wk}^{-1}$), and climbing up and down one flight of stairs was equivalent to 14 $\text{kcal}\cdot\text{wk}^{-1}$. Energy expended in sports and recreational activity was computed as the product of the duration and frequency of each reported activity (in hours per week [$\text{hr}\cdot\text{wk}^{-1}$]), weighted by an estimate of the metabolic equivalent (MET) of that activity³¹ and summed for all activities performed. Derived estimates were multiplied by the individual's body weight (kilograms) to estimate physical activity energy expenditure ($\text{kcal}\cdot\text{wk}^{-1}$).

Modifiable Activity Questionnaire (MAQ)—At EBT4, the PPAQ was replaced with the MAQ to better reflect the types of activities common among older women. The MAQ is an interviewer-administered questionnaire that assesses past-year leisure-time and occupational PA³². Due to the limited reported occupational activity in the HWS population³³, only the leisure-time estimate is reported. PA levels were calculated as the product of the duration and frequency of 39 common leisure activities ($\text{hr}\cdot\text{wk}^{-1}$), weighted by a standardized estimate of the MET of each activity³¹, and then summed for all activities performed. Leisure-time PA was expressed as $\text{MET}\cdot\text{hr}\cdot\text{wk}^{-1}$. The MAQ is a reliable and valid estimate of self-reported PA.³⁴

Accelerometer—At the EBT4 follow-up study, an accelerometer ancillary study was added to the study protocol. Accelerometer data were collected using the ActiGraph GT1M accelerometer (Pensacola, Florida). The ActiGraph GT1M accelerometer is a small ($3.8\text{cm} \times 3.7\text{cm} \times 1.8\text{cm}$), uni-axial piezoelectric activity monitor that measures acceleration in the vertical plane. Data output from the accelerometer are activity counts (ct), which quantify the amplitude and frequency of detected accelerations, and activity counts are summed over an investigator-specified time interval (i.e., epoch). For the current study, a 60-second epoch was reported. Technical specifications, as well as reliability and validity of the ActiGraph accelerometer^{35,36} have been described previously.

Participants wore the accelerometer on the dominant hip every day for seven consecutive days. Participants were asked to record the time at which they put on the monitors (or got up, if monitor was worn during sleep) in the morning and the time they took off the monitors (or went to bed, if monitor was worn during sleep) at night in a PA diary provided by study staff. We asked participants to wear the monitor for 24 hours each day to allow for future comparisons with objective sleep assessments. At the end of each week, the participant returned the accelerometer and PA diary to study staff.

Data from the accelerometer were downloaded and screened for wear-time using methods described by Troiano et al.³⁷ Briefly, device non-wear was defined as 60 consecutive minutes of 0 counts, with an allowance for 1–2 minutes of detected counts between 0–100. Wear time was determined by subtracting derived non-wear time from 24 hours.³⁷ Summary estimates were computed if daily accelerometer wear time was at least 10 hours. Total accelerometer counts per day (ct/d) were calculated using summed daily counts detected over wear periods. Time spent per day (min/d) in different intensity levels were estimated using threshold values proposed by Matthews et al.³⁵ Resulting activity count ranges for sedentary [0–99 counts per minute (ct/min)], light- (100–759 ct/min), moderate- (760–5724 ct/min), and vigorous- (5725 ct/min) intensity. Two summary estimates of time spent per

day in moderate- to vigorous- intensity PA (MVPA) were computed using thresholds of 760 ct/min. The first MVPA estimate included every minute above threshold; whereas, the second estimate only included accumulated time spent in *modified activity bouts* as defined by Troiano et al³⁷ [10 consecutive minutes above the 760 ct/min threshold with an allowance of 1–2 minutes below threshold]. Moderate- to vigorous- intensity activities are defined as those requiring ≥ 3 METS (e.g., brisk walking).^{38,39} Weekly summary estimates were computed by averaging daily estimates across total number of days worn for participants with ≥ 4 days with ≥ 10 hours per day of wear-time.

Cardiovascular risk factors

Height, body weight, waist circumference, and a fasting (12-hour) blood draw were repeatedly collected in the HWS throughout the 28 years of follow-up. Height and weight were measured with a stadiometer and calibrated balance beam scale, and BMI was computed as body mass (kg) / height (m)². Waist circumference (centimeters) was measured in the standing position at the navel (horizontal plane at the center of the navel) using a fiberglass retractable tape measure. Blood pressure was measured using the Multiple Risk Factor Intervention Trial (MRFIT) protocol.¹² Total cholesterol, high density lipoprotein cholesterol (HDL-c), triglycerides, and glucose were determined by conventional methods. Low density lipoprotein cholesterol (LDL-c) was estimated by the Friedewald equation, and insulin was measured via radioimmunoassay.

Statistical methods

Summary measures (mean and standard deviation) and frequency distribution (proportion and 95% confidence interval) were computed. The assumption of normality was tested using Shapiro-Wilk tests. The distributions of several PA estimates were positively skewed; therefore, a square root transformation was applied to reach normality. These variables were then back-transformed and presented as means and standard deviations. Pearson's correlations were used to examine associations between: (1) self-reported PA estimates collected over 28 years of follow-up with accelerometer data collected at EBT4 and (2) accelerometer data and CVD risk factors collected at EBT4. Then, analysis of variance (ANOVA) or chi-square tests were used to compare CVD risk factors, medication use, and PA levels collected at the EBT1 and EBT4 visits by CAC groups. Dunnett's post hoc tests were used to examine differences in continuous variables between the *no detectable* CAC group (referent group) and the *incident*- and *prevalent*- CAC groups. Generalized linear mixed models were used to compare PA levels between the *no detectable* CAC group (referent group) and the *incident*- and *prevalent*- CAC groups after adjustment for participant age (years) and BMI (kg/m²) at each relevant visit and reported lipid-lowering or anti-hypertensive medication use at the EBT1 and EBT4 visits. Statistical analyses were generated using SAS/STAT software, Version 9.2 of the SAS System for Windows (Cary, NC).

RESULTS

Of the 245 women who attended the EBT4 visit, 166 (67.8%) also completed the accelerometer ancillary study. Of those, 156 (94.0%) women had valid accelerometer data. HWS participants with accelerometer data were significantly less likely to report current cigarette smoking at EBT4 when compared to those who completed the EBT4 visit, but did not participate in the accelerometer ancillary study (0% vs. 2.8%; $p=.001$). Although no other statistically significant differences related to participant characteristics, CVD risk factors, or CAC score were noted, qualitative differences in CVD risk factors at EBT4 are reported to aid in the interpretation of results. Participants who completed the accelerometer ancillary study were slightly younger [73.3 ± 1.6 vs. 73.5 ± 1.7 years], had a slightly larger

BMI [27.3 ± 5.7 vs. 27.2 ± 5.0 kg/m²] and waist circumference [89.7 ± 13.1 vs. 89.4 ± 14.7 cm], lower systolic and diastolic blood pressure [123.5 ± 20.2 vs. 125.2 ± 17.7 and 65.4 ± 10.8 vs. 67.3 ± 9.8 mmHg, respectively], higher total cholesterol and LDL-c [218.5 ± 45.6 vs. 216.8 ± 36.6 and 126.8 ± 40.5 vs. 124.5 ± 32.3 mg/dL, respectively], similar HDL-c levels [67.8 ± 14.3 vs. 67.9 ± 18.2 mg/dL], and lower triglyceride and glucose levels [118.8 ± 50.2 vs. 122.4 ± 56.9 and 103.3 ± 14.0 vs. 105.2 ± 14.8 , respectively] when compared to those who did not participate. Of the 156 HWS participants with valid accelerometer data, 8 did not have CAC scores at EBT1, which resulted in a final analytical sample of 148 HWS participants.

Participant characteristics are shown in Table 1. The majority were white (92.6%), reflecting the racial composition of the HWS population at baseline. Given that the prevalence of medication use known to influence cardiovascular risk factor changed so drastically over the 12 year interval between visits, statistical differences between the visits were not computed. More specifically, the proportion of HWS participants reporting current lipid lowering- or anti-hypertensive- therapy was substantially higher at the EBT4 follow-up (6.1 to 46.0% and 10.1% to 48.7%, respectively). This change in medication use status likely contributed to the more favorable levels of many cardiovascular risk factors at EBT4 (i.e., diastolic BP, LDL-c, HDL-c, and triglycerides) when compared to the EBT1 follow-up visit. However, the proportion of *no detectable* CAC decreased from the first EBT visit across all successive follow-up visits (EBT1: 56.1%; EBT2: 45.0%; EBT3: 35.6%; and EBT4: 25.0%).

The association between self-reported PA collected over 28 years with accelerometer data collected at EBT4 is shown in Table 2. Total accelerometer counts were significantly correlated with self-reported PA estimates collected at 1 year post-menopausal, EBT1, and EBT4 visits ($r = 0.22$ to 0.39 ; all $p < .01$). Sedentary time (min/d) was significantly related to self-reported PA estimates collected at 5 years post-menopausal, EBT1, and EBT4 visits ($r = -0.20$ to -0.27 ; all $p < .05$). MVPA time, both accumulated ($r = 0.17$ to 0.38 ; all $p < .05$) and within activity bouts ($r = 0.21$ to 0.42 ; all $p < .05$), were significantly related to self-reported PA estimates collected at all visits, except at baseline.

The relations between CVD risk factors and accelerometer- derived PA data are presented in Table 3. Total accelerometer counts were inversely related to BMI, waist circumference, systolic blood pressure, triglycerides, and insulin ($r = -0.17$ to -0.30 ; all $p < .05$) and directly related to HDL-c ($r = 0.21$; $p < .05$). Sedentary time was directly related to BMI, waist circumference, systolic blood pressure and insulin ($r = 0.17$ to 0.24 ; all $p < .05$). Accumulated time spent in MVPA was inversely related to BMI, waist circumference, systolic blood pressure, triglycerides, insulin, and glucose ($r = -0.16$ to 0.30 ; all $p < .05$) and directly related to HDL-c ($r = 0.19$; $p < .05$). Similar associations were shown between MVPA bouts and CVD risk factors; however, the relation with systolic blood pressure was not statistically significant. Time spent in light- intensity PA was not significantly related to any CVD risk factors.

Thirty-seven (25%) participants were classified in the *no detectable* CAC group, 46 (31.1%) in the *incident* CAC group, and the remaining 65 (43.9%) in the *prevalent* CAC group. CVD risk factors and medication use at the EBT1 and EBT4 visits are shown in Table 4, stratified by CAC groups. At EBT1, BMI, waist circumference, and glucose were significantly higher in the *prevalent* CAC group when compared to the *no detectable* CAC group. The proportion of lipid-lowering and hypertensive medication use also significantly varied by CAC group. At EBT4, BMI and glucose were significantly higher in the *prevalent* CAC group when compared to the *no detectable* CAC group. Total cholesterol, LDL-c, and HDL-c levels were significantly lower in the *prevalent* CAC group when compared to the *no detectable* CAC group. The lower total cholesterol and LDL-c found among the *prevalent*

CAC group is likely due to the increased proportion of current lipid-lowering therapy use shown in this group (63.1% vs. 27.0% and 37.0% in the *no detectable*- and *incident*- CAC group, respectively $p=.001$). Given this, the lower HDL-c levels in the *prevalent* CAC group are worth noting. Hypertensive or diabetes medication use did not significantly vary by CAC group. There were no significant differences in self-reported PA levels at baseline, 1 year-, 5 years-, and 8 years- post menopause by CAC group (data not shown). Further, PA levels at EBT1 were not significantly different between groups; however, self-reported PA at EBT4 was significantly higher in the *no detectable* versus *prevalent* CAC group. Total accelerometer counts and time spent in MVPA, including sustained bouts of MVPA, were significantly lower in the *prevalent* CAC group when compared to the *no detectable* CAC group. PA levels were not significantly different between the *incident*- and *no detectable*-CAC group.

The multivariate adjusted PA levels by CAC group are shown in Table 5. There were no statistically significant differences in self-reported PA estimates, collected at any time-point, between CAC groups. The difference in accumulated time spent in MVPA was significantly lower in the *prevalent* CAC group when compared to the *no detectable* CAC group ($p<.05$). Furthermore, time in sustained bouts of MVPA was significantly lower in the *prevalent* CAC group versus the *no detectable* CAC group ($p<.04$).

DISCUSSION

The current investigation adds to the limited number of studies that have examined the relationship between PA and CAC. This study adds to previous work through serial CAC measures that characterize CAC progression (i.e., *no detectable*-, *incident*-, and *prevalent*-CAC). Results of our study showed that accelerometer-derived estimates of time spent in MVPA was lowest among women in the *prevalent* CAC group and highest in the *no detectable* CAC group. These results lend additional support that healthier individuals tend to participate in higher intensity physical activity. Interestingly, in the current study light intensity physical activity was not significantly associated with any CVD risk factors. Further, time spent being sedentary or in light intensity PA was not significantly different among the CAC groups. Together these findings suggest that the ability to perform lower intensity activities may not be limited by underlying disease.

One proposed mechanism to support the protective role of PA on atherosclerosis is through modification of related risk factors.^{3,4} The atherosclerotic process is initiated when the intimal layer of the arteries is damaged.⁴⁰ This damage is brought on by factors, including elevated cholesterol and triglyceride levels and resultant abnormal lipoprotein concentrations, hypertension, and cigarette smoking. PA helps prevent or manage elevated triglyceride levels and hypertension, and with concomitant weight loss, improves LDL-c concentrations.³ However, the magnitude of this effect is influenced by individual-level differences as well as characteristics of PA (i.e., activity type, intensity, frequency, and duration).³ Over time, lipid accumulation and connective tissue matrix production by smooth cells increases the volume of one or more key atherosclerotic plaques, which can become calcified with time. These plaques can encroach on the lumen and disrupt blood flow. If the plaque becomes unstable and ruptures, the resultant thrombus can occlude the lumen of the same or distal vessels.⁴⁰ Given the dramatic differences in medication use between CAC groups, it is difficult to discern whether the observed association between higher intensity PA and CAC was mediated through improvements to cardiovascular risk factors. However, significant associations were found between accelerometer estimates of higher intensity PA and obesity, HDL-c, triglycerides, glucose and insulin, which lend support to this proposed mechanism.

In a 2008 case-control study by Möhlenkamp and colleagues⁴¹, 108 male marathon runners aged 50–72 years were matched to age- and Framingham Risk Score (FRS)- controls selected from the Heinz Nixdorf Recall Study.⁴² While marathon runners (cases) had significantly higher PA levels when compared to both control groups, correlations with CAC were not statistically significant among marathon runners or age-matched controls. Further, CAC distribution (CAC score ≥ 100) was similar between marathon runners and age-matched controls (36.1% vs. 36.6%, respectively). However, the proportion of CAC ≥ 100 was significantly higher in marathon runners when compared to FRS-matched controls (36.1% vs. 21.8%, respectively). Authors suggest that the divergence between FRS and extent of CAC among cases might reflect the initiation of marathon training during middle-age, which is not necessarily indicative of lifelong PA levels. Also, while PA results in positive CVD risk factor changes, it may not result in the regression of atherosclerotic plaque once present. Therefore, physical activity might confer benefit by slowing or controlling the atherosclerotic process, rather than reversing the process. Unfortunately, clarifying the specific mechanisms by which PA prevents or modifies coronary atherosclerosis is challenging given that change values from serial measures of the extent of calcification are often not clinically meaningful. Additional work related to the estimating changes in the atherosclerotic process using CAC scores is needed.

Of the limited previous investigations examining the association between PA and CAC, only two have reported a statistically significant association between PA and CAC^{43,44}, while the remaining investigations found no significant relationship.^{4,19–23,41} These previous studies of PA and CAC as a surrogate marker for atherosclerosis are often plagued by three basic problems. First, most studies used self-report methods to ascertain the PA exposure. However, self-report estimates can be influenced by recall issues or incomplete assessment of PA across multiple domains and intensity levels.^{45,46} Second, the development of atherosclerosis and/or calcification reflects a long incubation period.⁴⁰ Therefore, measurement of current PA versus current CAC does not take into account the evolution of the atherosclerotic process and assumes that PA levels are stable over the life course. In the current study, estimates reflecting past PA levels were obtained via self-report methods which weaken our ability to examine the predictive role of PA on atherosclerotic progression. Third, examining associations between PA and CAC in men and women combined, regardless of whether sex was included as a covariate in the model, may be inappropriate. In the Hamer et al.²³ study, average accelerometer counts per minute and the proportion of participants accumulating at least 30 minutes of MVPA per day was significantly higher in men when compared to women. Furthermore, although not reported in the Hamer et al. study²³, CAC scores tend to be much higher in men when compared to women.²⁵ Gender differences in both PA levels and extent of CAC do not support presentation of related associations with men and women combined.

There are limitations to consider when interpreting the results of the current investigation. First, women included in the current investigation were specifically recruited for being in good health (i.e., no existing chronic disease at baseline) and most were white. Therefore, HWS participants may not be representative of the general population. Second, CAC measures do not provide information about changes to atherosclerotic plaque that eventually progress to clinical disease.¹² This, coupled with the fact that accelerometer data were collected at the EBT4 visit, limit our ability to establish causality between PA and CAC, including the ways in which PA may modify risk for future cardiac events. It is possible that women with *detectable* CAC at EBT1 might have reduced their PA by EBT4, which is supported by the PA levels of the *incident* CAC group. It is also possible that the higher MVPA levels shown in the *no detectable* CAC group are indicative of life-long participation in PA, which would make them less vulnerable to calcification of plaques. Measures of inflammation, which some studies suggest could be indicative of greater atherosclerotic

burden or a high-risk atherosclerotic phenotype⁴⁷, were not available at the most recent HWS follow-up visits. Third, due to limited sample size, we were unable to further categorize the *incident* CAC group to determine whether PA levels differed between those that developed CAC at EBT2, EBT3, or EBT4. This smaller sample size may have also influenced the ability to detect statistically significant associations between self-reported PA and categories of CAC progression. The current study consisted of a secondary data analysis to explore a research question not considered in the original design of HWS. Finally, waist-worn, uni-axial accelerometers provide an accurate measure of predominantly ambulatory activities and; therefore, do not capture all activities that may contribute to improved health.³⁷ Walking is one of the most common activities reported by older women⁴⁸; therefore, we feel confident that the accelerometer detected the majority of PA among this group of older women.

CONCLUSION

The current study adds to previous research by exploring the longitudinal relationship between PA and atherosclerotic progression over 28 years of follow-up in a well-characterized population-based cohort of women. Further, we were able to report both self-report and device-based estimates of physical activity in relation to level of CAC progression. In both the unadjusted and adjusted analyses, accelerometer-derived MVPA levels were higher in the *no detectable* versus *prevalent*-CAC group. These findings suggest that low levels of higher intensity PA, as measured by an accelerometer, may be indicative of underlying, subclinical disease. Additional work, using larger population-based studies with longer follow-up, is needed to clarify whether PA is predictive of atherosclerotic progression or regression.

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REFERENCES

1. Roger VL, Go AS, Lloyd-Jones DM, et al. Heart Disease and Stroke Statistics--2011 Update: A Report From the American Heart Association. *Circulation*. 2011 Feb 1; 123(4):e18–e209. [PubMed: 21160056]
2. U. S. Department of Health and Human Services. [Accessed October 10, 2008] 2008 Physical Activity Guidelines for Americans. www.health.gov/paguidelines.
3. Thompson PD, Buchner D, Pina IL, et al. Exercise and Physical Activity in the Prevention and Treatment of Atherosclerotic Cardiovascular Disease. *Arterioscler Thromb Vasc Biol*. 2003; 23:1319–1321. [PubMed: 12909570]
4. Taylor AJWT, Bell D, Carrow J, Bindeman J, Scherr D, Feuerstein I, Wong H, Bhattarai S, Vaitkus M, O'Malley PG. Physical Activity and the Presence and Extent of Calcified Coronary Atherosclerosis. *Medicine and Science in Sports and Exercise*. 2002; 34(2):228–233. [PubMed: 11828230]
5. Hambrecht R, Wolf A, Gielen S, et al. Effect of exercise on coronary endothelial function in patients with coronary artery disease. *N Engl J Med*. 2000 Feb 17; 342(7):454–460. [PubMed: 10675425]
6. Fried LP, Kronmal RA, Newman AB, et al. Risk factors for 5-year mortality in older adults: the Cardiovascular Health Study. *Jama*. 1998 Feb 25; 279(8):585–592. [PubMed: 9486752]
7. Nelson ME, Rejeski WJ, Blair SN, et al. Physical activity and public health in older adults: recommendation from the American College of Sports Medicine and the American Heart Association. *Med Sci Sports Exerc*. 2007 Aug; 39(8):1435–1445. [PubMed: 17762378]

8. Oguma Y, Shinoda-Tagawa T. Physical activity decreases cardiovascular disease risk in women: review and meta-analysis. *Am J Prev Med.* 2004 Jun; 26(5):407–418. [PubMed: 15165657]
9. Mosca L, Banka CL, Benjamin EJ, et al. Evidence-based guidelines for cardiovascular disease prevention in women: 2007 update. *Circulation.* 2007 Mar 20; 115(11):1481–1501. [PubMed: 17309915]
10. Sangiorgi G, Rumberger JA, Severson A, et al. Arterial calcification and not lumen stenosis is highly correlated with atherosclerotic plaque burden in humans: a histologic study of 723 coronary artery segments using nondecalcifying methodology. *J Am Coll Cardiol.* 1998 Jan; 31(1):126–133. [PubMed: 9426030]
11. Nallamothu BK, Saint S, Bielak LF, et al. Electron-beam computed tomography in the diagnosis of coronary artery disease: a meta-analysis. *Arch Intern Med.* 2001 Mar 26; 161(6):833–838. [PubMed: 11268225]
12. Kuller LHM, Sutton-Tyrrell K, Edmundowicz D, Bunker CH. Coronary and Aortic Calcification Among Women 8 Years After Menopause and Their Premenopausal Risk Factors: The Healthy Women Study. *Arterioscler Thromb Vasc Biol.* 1999; 19:2189–2198. [PubMed: 10479662]
13. Wong ND, Kouwabunpat D, Vo AN, et al. Coronary calcium and atherosclerosis by ultrafast computed tomography in asymptomatic men and women: relation to age and risk factors. *Am Heart J.* 1994 Feb; 127(2):422–430. [PubMed: 8296711]
14. Taylor AJ, Wong H, Barko W, Brazaitis M, O'Malley PG. Do Conventional Risk Factors Predict Subclinical Coronary Artery Disease? Results From the Prospective Army Coronary Artery Calcium Project. *American Heart Journal.* 2001; 141:463–468. [PubMed: 11231446]
15. Hecht HS, Superko HR, Smith LK, McColgan BP. Relation of coronary artery calcium identified by electron beam tomography to serum lipoprotein levels and implications for treatment. *Am J Cardiol.* 2001 Feb 15; 87(4):406–412. [PubMed: 11179523]
16. Pohle K, Maffert R, Ropers D, et al. Progression of aortic valve calcification: association with coronary atherosclerosis and cardiovascular risk factors. *Circulation.* 2001 Oct 16; 104(16):1927–1932. [PubMed: 11602496]
17. Meigs JB, Larson MG, D'Agostino RB, et al. Coronary artery calcification in type 2 diabetes and insulin resistance: the framingham offspring study. *Diabetes Care.* 2002 Aug; 25(8):1313–1319. [PubMed: 12145227]
18. Newman AB, Naydeck BL, Whittle J, Sutton-Tyrrell K, Edmundowicz D, Kuller LH. Racial differences in coronary artery calcification in older adults. *Arterioscler Thromb Vasc Biol.* 2002 Mar 1; 22(3):424–430. [PubMed: 11884285]
19. Folsom AR, Evans GW, Carr JJ, Stillman AE. Association of traditional and nontraditional cardiovascular risk factors with coronary artery calcification. *Angiology.* 2004 Nov-Dec;55(6): 613–623. [PubMed: 15547647]
20. Bertoni AG, Whitt-Glover MC, Chung H, et al. The association between physical activity and subclinical atherosclerosis: the Multi-Ethnic Study of Atherosclerosis. *Am J Epidemiol.* 2009 Feb 15; 169(4):444–454. [PubMed: 19075250]
21. Bild DE, Folsom AR, Lowe LP, et al. Prevalence and correlates of coronary calcification in black and white young adults: the Coronary Artery Risk Development in Young Adults (CARDIA) Study. *Arterioscler Thromb Vasc Biol.* 2001 May; 21(5):852–857. [PubMed: 11348886]
22. Nishino MM, Naya-Vigne J, Russell J, Kane JP, Redberg RF. Lack of Association of Lipoprotein(a) Levels with Coronary Calcium Deposits in Asymptomatic Postmenopausal Women. *Journal of the American College of Cardiology.* 2000; 35(2):314–320. [PubMed: 10676675]
23. Hamer M, Venuraju SM, Lahiri A, Rossi A, Steptoe A. Objectively assessed physical activity, sedentary time, and coronary artery calcification in healthy older adults. *Arterioscler Thromb Vasc Biol.* 2012 Feb; 32(2):500–505. [PubMed: 22075247]
24. Ainsworth BE, Bassett DR Jr, Strath SJ, et al. Comparison of three methods for measuring the time spent in physical activity. *Med Sci Sports Exerc.* 2000 Sep; 32(9 Suppl):S457–S464. [PubMed: 10993415]

25. Hoff JA, Chomka EV, Krainik AJ, Daviglius M, Rich S, Kondos GT. Age and gender distributions of coronary artery calcium detected by electron beam tomography in 35,246 adults. *Am J Cardiol.* 2001 Jun 15; 87(12):1335–1339. [PubMed: 11397349]
26. Matthews KA, Meilahn E, Kuller LH, Kelsey SF, Caggiula AW, Wing RR. Menopause and risk factors for coronary heart disease. *N Engl J Med.* 1989 Sep 7; 321(10):641–646. [PubMed: 2488072]
27. Matthews KA, Kelsey SF, Meilahn EN, Kuller LH, Wing RR. Educational attainment and behavioral and biologic risk factors for coronary heart disease in middle-aged women. *Am J Epidemiol.* 1989 Jun; 129(6):1132–1144. [PubMed: 2729252]
28. Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte M Jr, Detrano R. Quantification of coronary artery calcium using ultrafast computed tomography. *J Am Coll Cardiol.* 1990 Mar 15; 15(4):827–832. [PubMed: 2407762]
29. Ainsworth BE, Leon AS, Richardson MT, Jacobs DR, Paffenbarger RS Jr. Accuracy of the College Alumni Physical Activity Questionnaire. *J Clin Epidemiol.* 1993 Dec; 46(12):1403–1411. [PubMed: 8263567]
30. Washburn RA, Smith KW, Goldfield SR, McKinlay JB. Reliability and physiologic correlates of the Harvard Alumni Activity Survey in a general population. *J Clin Epidemiol.* 1991; 44(12): 1319–1326. [PubMed: 1753263]
31. Ainsworth BE, Haskell WL, Whitt MC, et al. Compendium of physical activities: an update of activity codes and MET intensities. *Med Sci Sports Exerc.* 2000 Sep; 32(9 Suppl):S498–S504. [PubMed: 10993420]
32. Pereira MA, FitzerGerald SJ, Gregg EW, et al. A collection of Physical Activity Questionnaires for health-related research. *Med Sci Sports Exerc.* 1997 Jun; 29(6 Suppl):S1–S205. [PubMed: 9243481]
33. Pettee KK, Kriska AM, Conroy MB, et al. Discontinuing hormone replacement therapy: attenuating the effect on CVD risk with lifestyle changes. *Am J Prev Med.* 2007 Jun; 32(6):483–489. [PubMed: 17533063]
34. Kriska AM, Knowler WC, LaPorte RE, et al. Development of questionnaire to examine relationship of physical activity and diabetes in Pima Indians. *Diabetes Care.* 1990 Apr; 13(4): 401–411. [PubMed: 2318100]
35. Matthews CE. Calibration of accelerometer output for adults. *Med Sci Sports Exerc.* 2005; 37 Supplement(11):S512–S522. [PubMed: 16294114]
36. Nichols JF, Morgan CG, Chabot LE, Sallis JF, Calfas KJ. Assessment of physical activity with the Computer Science and Applications, Inc., accelerometer: laboratory versus field validation. *Res Q Exerc Sport.* 2000 Mar; 71(1):36–43. [PubMed: 10763519]
37. Troiano RP, Berrigan D, Dodd KW, Masse LC, Tilert T, McDowell M. Physical activity in the United States measured by accelerometer. *Med Sci Sports Exerc.* 2008 Jan; 40(1):181–188. [PubMed: 18091006]
38. [Accessed March 19, 2011] Physical Activity Guidelines Advisory Committee Report. 2008. <http://www.health.gov/paguidelines/Report/pdf/CommitteeReport.pdf>.
39. Ainsworth BE, Haskell WL, Herrmann SD, et al. 2011 Compendium of Physical Activities: A Second Update of Codes and MET Values. *Med Sci Sports Exerc.* 2011 Aug; 43(8):1575–1581. [PubMed: 21681120]
40. Davies MJ, Woolf N. Atherosclerosis: what is it and why does it occur? *Br Heart J.* 1993 Jan; 69(1 Suppl):S3–S11. [PubMed: 8427761]
41. Mohlenkamp S, Lehmann N, Breuckmann F, et al. Running: the risk of coronary events : Prevalence and prognostic relevance of coronary atherosclerosis in marathon runners. *Eur Heart J.* 2008 Aug; 29(15):1903–1910. [PubMed: 18426850]
42. Erbel R, Mohlenkamp S, Lehmann N, et al. Sex related cardiovascular risk stratification based on quantification of atherosclerosis and inflammation. *Atherosclerosis.* 2008 Apr; 197(2):662–672. [PubMed: 17386928]
43. Storti KL, Pettee Gabriel KK, Underwood DA, Kuller LH, Kriska AM. Physical activity and coronary artery calcification in two cohorts of women representing early and late postmenopause. *Menopause.* 2010 Nov-Dec; 17(6):1146–1151. [PubMed: 20651620]

44. Desai MY, Nasir K, Rumberger JA, et al. Relation of degree of physical activity to coronary artery calcium score in asymptomatic individuals with multiple metabolic risk factors. *Am J Cardiol.* 2004 Sep 15; 94(6):729–732. [PubMed: 15374775]
45. Kriska AM, Caspersen CJ. Introduction to a Collection of Physical Activity Questionnaires. *Med Sci Sports Exerc.* 1997; 29(6):S5–S9.
46. Westerterp KR. Assessment of physical activity: a critical appraisal. *Eur J Appl Physiol.* 2009 Apr; 105(6):823–828. [PubMed: 19205725]
47. Khera A, de Lemos JA, Peshock RM, et al. Relationship between C-reactive protein and subclinical atherosclerosis: the Dallas Heart Study. *Circulation.* 2006 Jan 3; 113(1):38–43. [PubMed: 16380546]
48. Brownson RC, Eyler AA, King AC, Brown DR, Shyu YL, Sallis JF. Patterns and correlates of physical activity among US women 40 years and older. *Am J Public Health.* 2000 Feb; 90(2):264–270. [PubMed: 10667189]

Table 1

Participant characteristics of the analytic sample at the first (EBT1) and last (EBT4) Healthy Women Study (HWS) visits (n=148).

	EBT1 Follow-Up Visit	EBT4 Follow-Up Visit
Age ^a , years	61.9 ± 1.7	73.2 ± 1.7
Body mass index ^a , kg/m ²	27.2 ± 5.2	27.3 ± 5.1
Waist circumference ^a , cm	83.1 ± 12.9	89.7 ± 13.2
Cardiovascular Risk Factors		
Systolic blood pressure ^a , mmHg	121.7 ± 18.3	123.8 ± 20.4
Diastolic blood pressure ^a , mmHg	71.3 ± 8.9	65.4 ± 10.9
Total cholesterol ^a , mg/dL	215.2 ± 34.8	218.4 ± 45.9
Low density lipoprotein ^a , mg/dL	129.0 ± 34.2	126.7 ± 40.6
High density lipoprotein ^a , mg/dL	61.6 ± 17.1	67.7 ± 14.4
Triglycerides ^a , mg/dL	126.0 ± 74.6	119.3 ± 50.4
Glucose ^a , mg/dL	91.0 ± 14.1	103.4 ± 14.2
Insulin ^a , mU/dL	---	13.1 ± 5.1
Current cigarette smoker ^b	8.2 (3.7, 12.6)	0.0 (0.0, 0.0)
No detectable coronary artery calcification ^b	56.1 (48.1, 64.1)	25.0 (18.0, 32.0)
Medication Use		
Current hormone therapy use ^b	55.8 (47.4, 63.8)	4.7 (1.3, 8.2)
Hormone therapy use duration, years ^c	4.5 (2.0, 7.0)	22.4 (3.2, 24.8)
Current lipid lowering medication use ^b	6.1 (2.2, 9.9)	46.0 (37.9, 54.0)
Current hypertension medication use ^b	10.1 (5.2, 15.0)	48.7 (40.6, 56.7)
Current diabetes medication use ^b	---	6.1 (2.2, 9.9)
Physical activity (PA)*		
Self-reported leisure time PA ^c , kcal-wk ⁻¹	1848.7 ± 309.8	---
Self-reported leisure time PA ^c , MET-hr-wk ⁻¹	---	18.0 ± 4.3
Accelerometer- derived estimates		
Wear time ^a , min/d	---	1042.2 ± 114.5
Total accelerometer counts ^c , cts/d	---	172873.0 ± 7834.0
Sedentary ^a , min/d	---	745.3 ± 108.7
Light intensity PA ^c , min/d	---	227.7 ± 2.9
Moderate- to Vigorous- intensity PA ^c , min/d	---	61.8 ± 4.8
Moderate- to Vigorous- Intensity PA bouts ^c , min/d	---	14.3 ± 6.6

* Self-reported leisure time physical activity was assessed using the Paffenbarger Physical Activity Questionnaire at the EBT1 visit and the Modifiable Activity Questionnaire at EBT4.

Presented as: ^amean $\pm$ standard deviation; ^b percent (95% confidence interval); ^cmedian (interquartile range)

^cA square-root transformation was applied; data are back-transformed and presented as mean $\pm$ standard deviation

Table 2

Pearson correlation coefficients between self-reported physical activity estimates collected over 28 years of follow-up and accelerometer-derived physical activity at EBT4 follow-up visit in the Healthy Women Study (n=148).

	Self-reported Physical Activity				
	Baseline ^a n=148	1 year post-menopausal visit ^a n=139	5 years post-menopausal visit ^a n=138	EBT1 ^a n=147	EBT4 ^a n=146
	kcal·wk ⁻¹				MET·hr·wk ⁻¹
Total accelerometer counts ^a , cts/d	0.13	0.22 ^{**}	0.17 [‡]	0.24 ^{**}	0.39 ^{***}
Sedentary, min/d	-0.14 [‡]	-0.10	-0.27 ^{**}	-0.20 [*]	-0.24 ^{**}
Light intensity ^a , min/d	0.03	0.01	-0.11	0.02	0.07
Moderate- to Vigorous- intensity ^a , min/d	0.12	0.22 [*]	0.17 [*]	0.24 ^{**}	0.38 ^{***}
Moderate- to Vigorous- intensity bouts ^a , min/d	0.08	0.22 ^{**}	0.21 [*]	0.22 ^{**}	0.42 ^{***}

Self-reported leisure time physical activity was assessed using the Paffenbarger Physical Activity Questionnaire at baseline, 1 year post-menopausal visit, 5 years post-menopausal visit, 8 years post-menopausal visit, and EBT1 visit. At the EBT4 visit, self-reported leisure time physical activity was assessed using the Modifiable Activity Questionnaire

^a A square-root transformation was applied

 $t_{p<.10;}$

*
 $p < .05$;

p<.01;

 $p < .001$

Table 3

Pearson correlation coefficients between traditional cardiovascular risk factors and accelerometer- derived physical activity (PA) estimates collected at EBT4 visit in the Healthy Women Study (n=148).

	Total accelerometer counts ^a , cts/d	Sedentary ^a , min/d	Light intensity ^a , min/d	Moderate- to Vigorous- Intensity PA ^a , min/d	Moderate- to Vigorous- Intensity PA ^a bouts, min/d
Age, years	-0.16 [‡]	-0.06	-0.05	-0.16 [*]	-0.09
Body mass index, kg/m ²	-0.25 ^{***}	0.18 [*]	-0.002	-0.26 ^{**}	-0.34 ^{***}
Waist circumference, cm	-0.31 ^{***}	0.21 ^{**}	0.03	-0.30 ^{***}	-0.37 ^{***}
Systolic blood pressure ^a , mmHg	-0.17 [*]	0.17 [*]	-0.12	-0.19 [*]	-0.11
Diastolic blood pressure ^a , mmHg	-0.02	0.11	-0.07	-0.01	0.04
Total cholesterol ^a , mg/dL	0.07	0.02	0.01	0.10	0.08
Low density lipoprotein ^a , mg/dL	0.05	0.05	0.02	0.08	0.06
High density lipoprotein ^a , mg/dL	0.21 [*]	-0.15 [‡]	-0.002	0.19 [*]	0.23 ^{**}
Triglycerides ^a , mg/dL	-0.21 [*]	0.13	-0.07	-0.17 [*]	-0.23 ^{***}
Glucose ^a , mg/dL	-0.16 [‡]	0.06	-0.05	-0.19 [*]	-0.18 [*]
Insulin ^a , mU/dL	-0.30 ^{***}	0.24 ^{**}	-0.12	-0.29 ^{***}	-0.35 ^{***}

^a A square-root transformation was applied to normalize variable distribution

[‡] $p < .10$;

^{*} $p < .05$;

^{**} $p < .01$;

^{***} $p < .001$

Table 4

Unadjusted cardiovascular disease risk factors, medication use, and physical activity (PA) levels at the EBT1 and EBT4 Follow-up Visits by coronary artery calcification (CAC) group^d in the Healthy Women Study (n=148).

	EBT1 Follow-Up Visit				EBT4 Follow-Up Visit			
	No Detectable CAC	Incident CAC	Prevalent CAC	p value ^e	No Detectable CAC	Incident CAC	Prevalent CAC	p value ^e
	n=37	n=46	n=65		n=37	n=46	n=65	
Cardiovascular Risk Factors								
Age ^a , years	61.9 ± 1.7	61.8 ± 1.6	62.0 ± 1.9	.79	73.3 ± 1.5	73.4 ± 1.6	73.1 ± 1.8	.70
Body mass index ^a , kg/m ²	25.3 ± 3.0	26.4 ± 4.5	28.8 ± 6.1	.002*	25.7 ± 3.7	27.1 ± 5.1	28.4 ± 5.5	.03*
Waist circumference ^a , cm	79.8 ± 8.3	79.9 ± 9.9	87.2 ± 15.6	.002*	86.7 ± 9.8	88.0 ± 11.8	92.5 ± 15.3	.06
Systolic blood pressure ^a , mmHg	117.2 ± 18.1	120.8 ± 17.5	124.9 ± 18.6	.11	123.3 ± 15.5	121.6 ± 17.7	125.6 ± 24.3	.58
Diastolic blood pressure ^a , mmHg	70.8 ± 8.2	71.5 ± 9.6	71.5 ± 9.0	.92	68.0 ± 7.4	65.6 ± 10.5	63.8 ± 12.6	.16
Total cholesterol ^a , mg/dL	218.3 ± 34.1	213.8 ± 29.4	214.9 ± 38.8	.82	232.3 ± 44.9	224.8 ± 42.4	205.7 ± 46.3	.01*
Low density lipoprotein cholesterol ^a , mg/dL	133.8 ± 33.6	124.1 ± 27.4	129.8 ± 38.5	.44	139.3 ± 38.5	131.4 ± 37.7	116.1 ± 41.8	.01*
High density lipoprotein cholesterol ^a , mg/dL	62.6 ± 18.1	65.5 ± 17.2	58.2 ± 16.1	.08	71.3 ± 14.0	70.2 ± 14.6	63.8 ± 13.8	.02*
Triglycerides ^a , mg/dL	109.5 ± 50.0	121.7 ± 73.5	138.2 ± 84.8	.16	109.1 ± 40.9	114.2 ± 46.2	128.8 ± 56.9	.12
Glucose ^a , mg/dL	86.0 ± 6.0	89.9 ± 9.5	94.5 ± 18.5	.01*	98.8 ± 6.6	104.0 ± 14.1	105.5 ± 16.7	.07*
Insulin ^a , mU/dL	---	---	---	---	12.2 ± 4.1	12.6 ± 5.1	14.0 ± 5.6	.17
Medication Use								
Current lipid lowering medication use ^b	2.7 (0.0, 7.9)	2.0 (0.0, 6.4)	10.8 (3.2, 18.3)	.02	27.0 (12.7, 41.3)	37.0 (23.0, 50.9)	63.1 (51.3, 74.8)	.001
Current hypertension medication use ^b	5.4 (0.0, 12.7)	6.5 (0.0, 13.7)	15.4 (6.6, 24.2)	.01	40.5 (24.7, 56.4)	39.1 (25.0, 53.2)	60.0 (48.1, 71.9)	.05
Current diabetes medication use ^b	---	---	---	---	0.0 (0.0, 0.0)	4.4 (0.0, 10.2)	10.8 (3.2, 18.3)	.09
Physical Activity (PA)								
Self-reported physical activity ^c , kcal-wk ⁻¹	1772.2 ± 206.1	2000.0 ± 307.9	1787.0 ± 374.0	.72	---	---	---	---
Self-reported physical activity ^c , MET-hr-wk ⁻¹	---	---	---	---	24.0 ± 4.4	17.2 ± 4.3	15.4 ± 4.0	.07*
<i>Accelerometer-derived estimates</i>								

	EBT1 Follow-Up Visit				EBT4 Follow-Up Visit			
	No Detectable CAC	Incident CAC	Prevalent CAC	<i>p</i> value ^e	No Detectable CAC	Incident CAC	Prevalent CAC	<i>p</i> value ^e
	n=37	n=46	n=65		n=37	n=46	n=65	
Wear time ^a , min/d	---	---	---	---	1031.8 ± 95.1	1035.9 ± 112.2	1052.7 ± 126.5	.61
Total counts ^c , cts/d	---	---	---	---	195958.6 ± 5442.4	171724.8 ± 5282.6	161122.8 ± 10586.1	.08*
Sedentary ^a , min/d	---	---	---	---	719.6 ± 88.0	736.7 ± 100.9	776.3 ± 121.4	.09
Light Intensity PA ^c , min/d	---	---	---	---	233.5 ± 2.7	228.5 ± 2.6	223.6 ± 3.3	.64
Moderate- to Vigorous- Intensity PA ^c , min/d	---	---	---	---	73.7 ± 3.0	64.6 ± 3.6	53.5 ± 6.1	.01*
Moderate- to Vigorous- Intensity PA bouts ^c , min/d	---	---	---	---	23.4 ± 4.7	14.5 ± 5.9	9.9 ± 7.3	.006*

Presented as: ^amean ± standard deviation; ^b percent (95% confidence interval)

^c A square-root transformation was applied; data are back-transformed and presented as mean (standard deviation)

^d No Detectable CAC defined as CAC score = 0 at EBT1 and EBT4; Incident CAC defined as CAC score = 0 at EBT1 and >0 at EBT4; Prevalent CAC defined as CAC score >0 at EBT1 and EBT4.

^e ANOVA was used to test differences in cardiovascular disease risk factors and accelerometer-derived PA levels between CAC categories for normally-distributed variables. Chi-square or Freeman-Halton tests were used to determine differences in medication use between CAC categories

* Dunnett-Hsu post hoc tests were used to examine differences in accelerometer derived PA levels between the *no detectable* CAC group (referent) and *incident*- and *prevalent*- CAC groups; *no detectable* CAC group significantly different than *prevalent* CAC group (*p* .05)

Table 5

Adjusted^a mean $\pm$ standard error accelerometer-derived physical activity (PA) levels collected at the EBT4 visit by coronary artery calcification (CAC) group^b in the Healthy Women Study (n=148).

	No Detectable CAC (n=37)	Incident CAC (n=46)	Prevalent CAC (n=65)	No Detectable- vs. Incident- CAC <i>p</i> value	No Detectable- vs. Prevalent- CAC <i>p</i> value
Physical Activity (PA)					
<i>Self-reported estimates</i>					
Baseline ^c , kcal·wk ⁻¹	1226.8 $\pm$ 2.0	1215.8 $\pm$ 5.8	1350.5 $\pm$ 5.2	.71	.35
1 year post-menopausal ^c , kcal·wk ⁻¹	1430.6 $\pm$ 1.9	1562.8 $\pm$ 5.8	1546.1 $\pm$ 5.1	.53	.62
5 years post-menopausal ^c , kcal·wk ⁻¹	1665.8 $\pm$ 1.7	1668.2 $\pm$ 5.0	1635.0 $\pm$ 4.5	.84	.58
EBT1 ^c , kcal·wk ⁻¹	1859.3 $\pm$ 3.7	2013.0 $\pm$ 10.0	1872.2 $\pm$ 9.3	.52	.87
EBT4 ^c , MET·hr·wk ⁻¹	18.3 $\pm$.04	16.3 $\pm$.10	16.9 $\pm$.09	.48	.73
<i>Accelerometer- derived estimates</i>					
Total counts ^c , cts/d	179623.4 $\pm$ 86.4	160961.4 $\pm$ 240.1	157101.3 $\pm$ 216.4	.29	.11
Sedentary, min/d	737.3 $\pm$ 11.9	757.0 $\pm$ 19.8	767.9 $\pm$ 18.8	.55	.14
Light Intensity PA ^c , min/d	231.4 $\pm$.03	224.7 $\pm$.10	219.8 $\pm$.09	.71	.22
Moderate- to Vigorous- Intensity PA ^c , min/d	65.1 $\pm$.05	57.4 $\pm$.14	53.2 $\pm$.13	.45	.046
Moderate- to Vigorous- Intensity PA bouts ^c , min/d	16.5 $\pm$.07	10.4 $\pm$.19	9.2 $\pm$.17	.17	.035

^a Generalized linear mixed models were used to compare PA levels between the *no detectable* CAC group (referent group) and the *incident*- and *prevalent*- CAC groups after adjustment for age (years) and BMI (kg/m²) at relevant visit and reported lipid-lowering or anti-hypertensive medication use at EBT1 and EBT4.

^b No Detectable CAC defined as CAC score = 0 at EBT1 and EBT4; Incident CAC defined as CAC score = 0 at EBT1 and >0 at EBT4; Prevalent CAC defined as CAC score >0 at EBT1 and EBT4.

^c A square-root transformation was applied; data are back-transformed and presented as mean $\pm$ standard deviation