Atherosclerosis 230 (2013) 278–283

Contents lists available at ScienceDirect

Atherosclerosis

journal homepage: www.elsevier.com/locate/atherosclerosis

The association between physical activity and both incident coronary artery calcification and ankle brachial index progression: The Multi-Ethnic Study of Atherosclerosis

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ARTICLE INFO

Article history:
Received 14 February 2013
Received in revised form
11 June 2013
Accepted 24 July 2013
Available online 2 August 2013

Keywords:
Ankle brachial index
Coronary artery calcification
Physical activity
Epidemiology
Prospective cohort study

ABSTRACT

Objective: Both coronary artery calcification (CAC) and the ankle brachial index (ABI) are measures of subclinical atherosclerotic disease. The influence of physical activity on the longitudinal change in these measures remains unclear. To assess this relation we examined the association between these measures and self-reported physical activity in the Multi-Ethnic Study of Atherosclerosis (MESA).

Methods: At baseline, the MESA participants were free of clinically evident cardiovascular disease. We included all participants with an ABI between 0.90 and 1.40 ($n = 5656$). Predictor variables were based on self-reported measures with physical activity being assessed using the *Typical Week Physical Activity Survey* from which metabolic equivalent-minutes/week of activity were calculated. We focused on physical activity intensity, intentional exercise, sedentary behavior, and conditioning. Incident peripheral artery disease (PAD) was defined as the progression of ABI to values below 0.90 (given the baseline range of 0.90–1.40). Incident CAC was defined as a CAC score >0 Agatston units upon follow up with a baseline score of 0 Agatston units.

Results: Mean age of participants was 61 years, 53% were female, and mean body mass index was 28 kg/m^2. After adjusting for traditional cardiovascular risk factors and socioeconomic factors, intentional exercise was protective for incident peripheral artery disease (Relative Risk (RR) = 0.85, 95% Confidence Interval (CI): 0.74–0.98). After adjusting for traditional cardiovascular risk factors and socioeconomic factors, there was a significant association between vigorous PA and incident CAC (RR = 0.97, 95% CI: 0.94–1.00). There was also a significant association between sedentary behavior and increased amount of CAC among participants with CAC at baseline (Δlog (Agatston Units + 25) = 0.027, 95% CI 0.002, 0.052).

Conclusions: These data suggest that there is an association between physical activity/sedentary behavior and the progression of two different measures of subclinical atherosclerotic disease.

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1. Introduction

Both coronary artery calcification (CAC) and the ankle brachial index (ABI) are measures of subclinical cardiovascular disease (CVD) [1,2]. From a prevention perspective, it is important to monitor these subclinical CVD measures and determine which risk factors may contribute to their changes. In this regard, the direct effects of physical activity (PA) on the development or progression of subclinical atherosclerosis are not well established [3,4].

The ABI is used to detect peripheral artery disease (PAD), with a value <0.90 being indicative of significant flow limiting atherosclerotic disease in the lower extremity [5], which can lead to mobility loss [6] and mortality [7,8]. In patients with intermittent claudication, a decline to a lower ABI has been linked to decreased participation in moderate and vigorous PA [9]. However, it is unknown whether a population free of baseline CVD would show a similar association.

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http://dx.doi.org/10.1016/j.atherosclerosis.2013.07.045

CAC is a measure of atherosclerotic plaque evolution and provides an excellent marker of coronary artery disease. However, there are inconsistencies in the literature related to the association between PA and CAC. Prior research suggests that chronic exercise attenuates the presence and extent of CAC [10], while slower walking time is associated with more CAC [2,11] and higher levels of cardio-respiratory fitness at a particular age or age range? are associated with a lower risk of having CAC 15 years later [12]. Conversely, other studies have indicated that high intensity PA [13] and/or intentional exercise are unrelated to CAC [2]. To our knowledge, no studies have evaluated different types of PA and changes in CAC over follow-up.

It is important to determine what type and how much activity is most effective at reducing or preventing subclinical CVD. Additionally, since sedentary behaviors are significant CVD mortality predictors [14] and are associated with higher odds of metabolic syndrome and individual CVD risk factors [15], determining how sedentary behaviors influence both prevalent and incident subclinical CVD is also relevant to prevention. As such, the aim of this study was to determine the associations between different types of PA and the incidence and progression of both CAC and the ABI in the Multi-Ethnic Study of Atherosclerosis.

2. Materials and methods

2.1. Study design

The Multi-Ethnic Study of Atherosclerosis (MESA) is a population-based sample of 6814 men and women from 4 ethnic groups. Details regarding design, recruitment, and objectives of MESA have been published previously [16]. Briefly, eligible MESA participants were defined as persons living within the defined geographic boundaries of each of the six field centers (Baltimore, MD; Chicago, IL; Forsyth County, NC; Los Angeles County, CA; northern Manhattan, NY; and St. Paul, MN) who were aged 45–84 years at enumeration via a phone interview. Participants did not meet any of the exclusion criteria including a self-reported medical history of heart attack, angina, cardiovascular procedures, heart failure, cerebrovascular disease, active treatment for cancer, pregnancy or amputation at follow up exam.

2.2. Data collection

Eligible participants were invited to a clinic for further examination. During the baseline examination (2000–2002) and follow up examinations (exam 3, 2004–2005 and exam 4, 2005–2007), standardized questionnaires and calibrated devices were utilized to obtain demographic data, tobacco use data, information on medical conditions, current prescription medication usage, weight, and height. Resting, seated blood pressure was measured 3 times using a Dinamap automated oscillometric sphygmomanometer (model Pro 100; Critikon, Tampa, Florida); the last 2 measurements were averaged for analysis. Hypertension was defined as use of an antihypertensive medication, systolic blood pressure $\geq$140 or diastolic blood pressure $\geq$90 mm Hg.

2.3. Laboratory measures

Fasting blood samples were drawn and were sent to a central laboratory for measurement of glucose and lipids [17]. Participants were considered to have diabetes if they used hypoglycemic drugs or if their fasting blood glucose was $\geq$7.0 mmol/L (126 mg/dL). Participants were considered to have impaired fasting glucose if they did not have diabetes according to the preceding criteria but their fasting blood glucose level was $\geq$100–<126 mg/dL in accordance with the 2004 American Diabetes Association definition [18]. Individuals with total:high-density lipoprotein cholesterol ratio >5 or those who reported the use of a medication to treat high cholesterol were classified as dyslipidemic.

2.4. Electron beam computed tomography

Chest computed tomography was performed by using either a cardiac-gated electron-beam scanner or a prospectively electrocardiogram-triggered scan acquisition at 50% of the R–R interval with a multi-detector system, acquiring a block of 4 2.5-mm slices for each cardiac cycle in a sequential or axial scan mode. Phantoms of known physical calcium concentration in participants were scanned twice. Scans were read at a central reading center. The measurement of CAC was calibrated against the phantom. For each scan, a total phantom-adjusted Agatston score, defined as the sum of calcium measures from the left main, left anterior descending, circumflex, and right coronary arteries, was calculated. The mean score was used in these analyses. We defined CAC progression as a continuous change in CAC from baseline to exam 3. For incident CAC analysis, we excluded participants with CAC >0 at baseline. Incident CAC was a binary variable, defined as those without CAC at baseline but had a CAC score greater then zero at follow up.

2.5. Ankle brachial index

To obtain the ABI, participants rested supine for 5 min, and then systolic blood pressures were measured in both arms and legs with the appropriate-sized cuffs. For each leg, the systolic blood pressure in each posterior tibial and dorsalis pedis artery was measured. All pressures were detected with a continuous-wave Doppler ultrasound probe. The leg-specific ABI was calculated as the higher systolic blood pressure in the posterior tibial or dorsalis pedis divided by the higher of the 2 systolic blood pressures in the arms. For this analysis, the lower of the two leg specific ABIs was utilized. We defined ABI progression as a change in ABI from baseline to exam 3, measured as a continuous variable. We defined incident PAD as a binary variable where the ABI was between 0.90 and 1.40 (a normal ABI) [19] at baseline and decreased to $\leq$0.90 at follow up (exam 3) [5].

2.6. Physical activity survey

The MESA Typical Week Physical Activity Survey (TWPAS), adapted from the Cross Cultural Activity Participation Study [20], was designed to identify time spent in and frequency of various PA during a typical week in the past month. The rationale for the selected time frame was the intention to capture the typical activity patterns in a participant's daily life. The survey includes 28 items in categories of household chores, lawn/yard/garden/farm, care of children/adults, transportation, walking (not at work), dancing and sport activities, conditioning activities, leisure activities, and occupational and volunteer activities. Participants were first asked if they participated in these categories of activity (yes/no), and if yes, they answered the questions regarding the average number of days per week and time per day engaged in these activities. If appropriate, questions also differentiated the intensity of activities as light, moderate and vigorous.

The sum of minutes spent in all activity types was multiplied by the metabolic equivalent (MET) level assigned to each activity [21]. Summary measures include total minutes/day and total MET-min/day for nine physical activity categories and three intensity levels (light, moderate and vigorous). After reviewing the patterns of response regarding PA intensity, we grouped no and low PA into one intensity level. Moderate and vigorous PA were combined as another variable since approximately 64% of the participants reported no vigorous PA.

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