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Physical Activity Measured by Accelerometry and its Associations With Cardiac Structure and Vascular Function in Young and Middle-Aged Adults

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***Background*—**Physical activity is associated with several health benefits, including lower cardiovascular disease risk. The independent influence of physical activity on cardiac and vascular function in the community, however, has been sparsely investigated.

***Measures and Results*—**We related objective measures of moderate- to vigorous-intensity physical activity (MVPA, assessed by accelerometry) to cardiac and vascular indices in 2376 participants of the Framingham Heart Study third generation cohort (54% women, mean age 47 years). Using multivariable regression models, we related MVPA to the following echocardiographic and vascular measures: left ventricular mass, left atrial and aortic root sizes, carotid–femoral pulse wave velocity, augmentation index, and forward pressure wave. Men and women engaged in MVPA 29.9±21.4 and 25.5±19.4 min/day, respectively. Higher values of MVPA (per 10-minute increment) were associated with lower carotid–femoral pulse wave velocity (estimate −0.53 ms/m; P=0.006) and lower forward pressure wave (estimate −0.23 mm Hg; P=0.03) but were not associated with augmentation index (estimate 0.13%; P=0.25). MVPA was associated positively with $\log_e$ left ventricular mass (estimate 0.006 $\log_e$ [g/m^2]; P=0.0003), left ventricular wall thickness (estimate 0.07 mm; P=0.0001), and left atrial dimension (estimate 0.10 mm; P=0.01). MVPA also tended to be positively associated with aortic root dimension (estimate 0.05 mm; P=0.052). Associations of MVPA with cardiovascular measures were similar, in general, for bouts lasting <10 versus ≥10 minutes.

***Conclusions*—**In our community-based sample, greater physical activity was associated with lower vascular stiffness but with higher echocardiographic left ventricular mass and left atrial size. These findings suggest complex relations of usual levels of physical activity and cardiovascular remodeling. **(*J Am Heart Assoc*. 2015;4:e001528 doi: 10.1161/JAHA.114.001528)**

Key Words: echocardiography • epidemiology • physical activity • vascular measures

Compared with other preventive strategies, physical activity may be a particularly efficient method of reducing the risk of future cardiovascular disease (CVD) at the population level because it modifies several key risk factors simultaneously and has independent favorable effects on the cardiovascular system.[1] Joint guidelines from the American College of Sports Medicine and the American Heart Association recommend that otherwise healthy persons aged 18 to 65 years should engage in moderate-intensity physical activity for at least 30 minutes 5 days per week (150 minutes per week) or vigorous-intensity activity for at least 20 minutes at least 3 times per week (60 minutes per week) to promote and maintain health.[2] The

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guidelines emphasize only bouts lasting ≥10 minutes (ie, bouts) in their recommendations. It is unknown whether bouts lasting <10 minutes per session (ie, nonbouts) have beneficial health effects. The guidelines acknowledge that increases in physical activity beyond recommendations may be associated with additional health benefits but conclude that little is currently known about whether there is an upper limit of physical activity at which benefits may level out.[2]

Although several studies have shown that physical activity is associated with improvement in several CVD risk factors and subclinical disease measures in various populations, some uncertainty remains.[3–5] Data on physical activity in relation to vascular and echocardiographic measures at the community level are sparse, and a majority of previous epidemiological studies have been limited by a lack of objective measures on physical activity. Furthermore, prior studies have not distinguished between nonbouts and bouts of exercise, the latter being emphasized in guidelines, as noted. Accordingly, we conducted a comprehensive analysis of the association between physical activity (assessed objectively by accelerometry) and cardiac structure and vascular function measures in a large community-based sample of young-adult to middle-aged men and women.

Methods

The study sample comprised participants from the third generation cohort of the Framingham Heart Study,[6] namely, children of the offspring cohort participants[7] and grandchildren of the original cohort.[8] In total, 4095 persons attended the first examination (2002–2005), and 3411 participated in the second examination (2008–2011). For the present investigation, we included those who attended the second examination and who had valid accelerometry data (validity is defined in "Physical Actvity"). Fasting blood samples, anthropometric measures, blood pressure, medical history update, smoking status, and medication use were obtained at examination cycle 2. We excluded participants without valid accelerometry data (n=952; these participants had slightly higher body mass index and a higher prevalence of diabetes than participants with valid accelerometry data; full characteristics of participants with and without accelerometry data are shown in Table 1), with prevalent CVD (defined as myocardial infarction, coronary insufficiency, heart failure, or stroke; n=57), prevalent valve disease (n=22), or missing covariates (n=2). All participants gave written informed consent, and the institutional review board at the Boston University Medical Center approved the study protocols.

Physical Activity

All participants were asked to wear an omnidirectional accelerometer on the hip for 8 days (Actical model no. 198-0200-00; Philips Respironics). In total, 2672 (78%) agreed to do so and had valid accelerometry measures. A thorough description of the ascertainment of these measures has been published.[9] In brief, participants were asked to wear the accelerometer throughout the day and night except when they were bathing. For calculations of sedentary time, we considered only wear time between 6 AM and 10 PM. The accelerometer recorded signals from nonvertical body movements within 0.5 to 3 Hz and recorded accelerations or decelerations within 0.05 to 2.0*g*. Recorded signals were grouped in "counts" by 30-second intervals and stored on the device.

According to a predefined protocol, all data were manually reviewed for spurious information; signals likely to be artifacts were deleted.[9] Data were analyzed at the Framingham Heart Study using customized software (KineSoft, version 3.3.63; KineSoft). Measures from the first day of wear were not included in analyses. Accelerometer data were considered valid if the accelerometer was worn >10 hours per day for at least 5 of 7 days including at least 1 weekend day.[10,11]

Based on the counts accrued and regression coefficients from previously published work,[12] *moderate-intensity* physical activity was defined as 435 to 2535 counts per 30 seconds (which corresponds to 3 to 6 metabolic equivalents), and *vigorous-intensity* physical activity was defined as ≥2536 counts per 30 seconds (corresponding to >6 metabolic equivalents). *Light* physical activity was defined as 100 to 434 counts per 30 seconds, and *sedentary time* was defined as <100 counts per 30 seconds. For the present analysis, data for moderate and vigorous physical activity were pooled and coded as total minutes per week (denoted as moderate- to vigorous-intensity physical activity [MVPA]) because very few people had a significant amount of vigorous activity. Consistent with current guidelines, MVPA sessions that lasted <10 minutes were considered nonbouts, and any session that lasted ≥10 minutes was considered a bout. We defined compliance with physical activity guidelines in 2 different ways: as ≥150 minutes of MVPA per week performed in bouts of ≥10 minutes and as ≥150 minutes total MVPA per week regardless of the duration. For people with <7 days of valid wear, we averaged the activity over the valid days and extrapolated to estimate the MVPA for 7 days (corresponding to 1 week).

Concomitant strength training (used in sensitivity analyses) was defined as at least 30 minutes of activities such as snow shoveling, moving heavy objects, or weight lifting at least 4 times per month during the past 12 months (home or work related) based on self-reported questionnaire data administered at examination cycle 2.

Vascular Measures

All study participants underwent arterial applanation tonometry investigation after an overnight fast during the second

Table 1. Characteristics of People With and Without Valid Accelerometry Data

	Valid Accelerometry (n=2455)	No Valid Accelerometry (n=952)
Age, y	47 (9)	46 (9)*
Sex, women, %	1312 (53)	495 (52)
Body mass index, kg/m^2	27.7 (5.5)	28.9 (6.7)**
Systolic blood pressure, mm Hg	116 (14)	116 (14)
Diastolic blood pressure, mm Hg	74 (9)	74 (9)
Total cholesterol, mg/dL	187 (35)	186 (35)
HDL cholesterol, mg/dL	60 (18)	58 (17)*
LDL cholesterol, mg/dL	105 (30)	104 (32)
Antihypertensive medication, %	403 (16)	183 (19)
Lipid-lowering medication, %	400 (16)	164 (17)
Diabetes, %	122 (5)	60 (6)
Current smoker, %	247 (10)	142 (15)**
Echocardiography measures		
Left ventricular mass, g/m^2	157 (42)	159 (43)
Left ventricular wall thickness (IVSTD+PWTD), mm	17.9 (2.4)	18.1 (2.4)
Left ventricular end-diastolic dimension, mm	49.3 (4.0)	49.3 (4.2)
Aortic root dimension, mm	31.2 (3.8)	31.2 (3.7)
E/e′ ratio	5.9 (1.5)	5.8 (1.4)
Left atrial dimension, mm	27.3 (4.5)	27.6 (4.8)
Tonometry measures		
CFPWV, m/s	7.1 (1.4)	7.1 (1.6)
−1000/CFPWV, ms/m	−146 (25)	−146 (27)
Augmentation index, %	9.9 (12.6)	10.0 (12.3)
Forward pressure wave, mm Hg	45.6 (10.9)	45.4 (11.2)

CFPWV indicates carotid–femoral pulse wave velocity; HDL, high-density lipoprotein cholesterol; IVSTD, end-diastolic interventricular septum thickness; LDL, low-density lipoprotein cholesterol; PWTD, end-diastolic posterior wall thickness.
*P<0.05 difference between groups. **P<0.001 difference between groups.

examination cycle. Measures were obtained with the participant in a supine position after approximately 5 minutes of rest. Pulse wave profiles were obtained by the use of a custom tonometer (Cardiovascular Engineering Inc). Tonometry and ECG data were digitally stored and analyzed in a core laboratory (Cardiovascular Engineering Inc) by trained analysts who were blinded to data on physical activity. The forward pressure wave and augmentation index were derived from carotid pressure waveform measures.[13] The augmentation index was calculated as the augmentation pressure (ie, the difference between first systolic inflection point and the peak waveform) divided by the total pulse pressure and multiplied by 100.[14] Carotid–femoral pulse wave velocity (CFPWV) was measured as the distance between the carotid and femoral sites (adjusted for parallel transmission) divided by the time delay between the foot of the carotid and femoral waveforms.[14]

During the first examination cycle, which was performed, on average, 6.1 (±0.6) years prior to the second examination cycle, assessments of endothelial function (by flow-mediated dilation) and shear stress (by baseline and hyperemic artery flow velocities) were undertaken on the brachial artery using a commercially available ultrasound system, as described in detail previously.[15,16] Baseline artery flow velocity was measured with the participants in a resting supine state, and then a cuff was placed on the upper arm and inflated for 5 minutes. At 15 seconds after cuff deflation, the artery flow velocity was measured again to derive the peak hyperemic artery flow velocity. Flow-mediated dilation (percentage) was calculated as the difference of the brachial artery dimension (60 seconds after cuff deflation) and the dimension at baseline divided by baseline dimension. These measures were included as secondary analyses to explore the relation of endothelial function in a medium-sized muscular artery to physical activity.

Echocardiography Measures

Data on transthoracic echocardiograms were carried forward from examination cycle 1 for analysis in relation to physical activity (no echocardiography was performed contemporaneously with accelerometry). Echocardiograms were performed according to a specified protocol by trained sonographers. Images were stored on a local hard drive and analyzed by a sonographer and/or a cardiologist blinded to clinical information. Measures of left ventricular (LV) structure (interventricular septum and LV posterior wall thicknesses at end diastole and LV end-diastolic and end-systolic dimensions) were obtained from M-mode images, according to American Society of Echocardiography guidelines, using a leading-edge technique.[8] End-diastolic measurements of the aortic root and end-systolic dimension of the left atrium were also measured from M-mode images. LV mass (LVM) was calculated using the American Society of Echocardiography formula applied by Devereux et al[17]:

$$\text{LVM} = 0.8\{1.04([\text{LVIDD+PWTD+IVSTD}]^3 - [\text{LVIDD}]^3)\} + 0.6g$$

In this equation, LVIDD denotes LV end-diastolic dimension, and PWTD and IVSTD indicate the end-diastolic thicknesses of the posterior wall and the interventricular septum, respectively. We previously reported excellent reproducibility of echocardiographic measurements at the Framingham Heart Study.[18] LV diastolic function was assessed by the E/e′ ratio obtained from Doppler tissue imaging, estimated from the apical 4-chamber view with the transducer placed immediately apical to the mitral valve (E) and at the LV lateral wall (e′).

Statistical Analyses

Linear regression models were used to assess the relationships between different vascular and echocardiographic measures (dependent measures) and physical activity (independent variable). LVM was naturally log-transformed because of its skewed distribution, and this reduced differences in variance between men and women.[19] CFPWV was inverse-transformed and multiplied by −1000 (to reduce heteroscedasticity and to maintain directionality).[20] All models were adjusted for total wear time (in min/day), sex, age, height, weight, systolic blood pressure, use of antihypertensive and lipid-lowering medications, current smoking status, serum total and high-density lipoprotein cholesterol concentrations, and diabetes. To ensure that strength training did not influence the associations of physical activity (as measured with accelerometry) with LVM and CFPWV, we performed a sensitivity analysis with additional adjustment of concomitant strength training assessed with a questionnaire. Because echocardiographic measures were not obtained contemporaneously with the other variables, we estimated additional multivariable models that also adjusted for measurements of systolic blood pressure and weight at the time of echocardiographic measurements (in addition to adjusting for these variables at the time of accelerometry) as sensitivity analyses. We calculated estimated changes in LVM associated with physical activity measures as percentage change in LVM=100×[exp(regression estimate×increment in physical activity)−1]. We compared estimates for MVPA in bouts versus nonbouts using the "test" statement in SAS *proc reg* (SAS Institute Inc). Multivariable-adjusted cubic splines were created to graphically display linearity of the observed associations.[21] Because graphic analyses did not reveal major deviations from linear analyses, we used a linear model for simpler interpretation. All analyses were performed in SAS version 9.3. A 2-sided P value <0.05 was considered significant for all analyses. Given the exploratory nature of the study, we did not make adjustments for multiple testing.

The authors had full access to the data and take responsibility for its integrity. All authors read and agreed with the study as written.

Results

Characteristics of our sample are provided in Table 2. On average, men and women accumulated 29.9±21.4 and 25.5±19.4 min/day in MVPA, but there were large differences among participants; total daily MVPA accrued varied from 0.4 to 192 minutes for men and from 0.2 to 157 minutes for women. Most MVPA was carried out in

Table 2. Participant Characteristics

	Men (n=1096)	Women (n=1280)
Age, y	47 (8)	47 (9)
Body mass index, kg/m^2	28.7 (4.6)	26.7 (6.0)
Systolic blood pressure, mm Hg	121 (13)	112 (14)
Diastolic blood pressure, mm Hg	78 (9)	72 (9)
Total cholesterol, mg/dL	188 (36)	187 (35)
HDL cholesterol, mg/dL	51 (14)	68 (18)
LDL cholesterol, mg/dL	111 (29)	101 (30)
Antihypertensive medication, %	207 (19)	160 (12)
Lipid-lowering medication, %	234 (21)	126 (10)
Diabetes, %	58 (5)	47 (4)
Current smoker, %	124 (11)	111 (9)
Echocardiography measures		
Left ventricular mass, g/m^2	187 (35)	130 (25)
Left ventricular wall thickness (IVSTD+PWTD), mm	19.5 (2.0)	16.5 (1.7)
Left ventricular end diastolic dimension, mm	51.6 (3.6)	47.3 (3.2)
Aortic root dimension, mm	33.7 (3.2)	28.9 (2.6)
E/e′ ratio	5.7 (1.4)	6.0 (1.6)
Left atrial dimension, mm	29.1 (4.2)	25.5 (3.9)
Tonometry measures		
CFPWV, m/s	7.4 (1.4)	6.8 (1.3)
−1000/CFPWV, ms/m	−139 (23)	−152 (25)
Augmentation index, %	5.2 (12.5)	13.8 (11.3)
Forward pressure wave, mm Hg	47.2 (10.4)	44.1 (10.8)
Activity measures		
Total MVPA per week, min	199 (146)	169 (130)
Sedentary time, min/day	657 (71)	670 (65)
Light PA, min/day	143 (54)	132 (45)
Moderate PA, min/day	28.0 (19.6)	22.9 (17.0)
Vigorous PA, min/day	1.9 (5.2)	2.5 (6.4)
MVPA, min/day	29.9 (21.4)	25.5 (19.4)
MVPA ≥10, min/day*	12.6 (12.4)	15.6 (14.1)
MVPA <10 min/day	22.8 (15.9)	16.0 (10.8)
PA guidelines compliance any MVPA, %	651 (59.4)	618 (48.3)
PA guidelines compliance MVPA ≥10 only, %	116 (10.6)	194 (15.2)
Leisure time strength training, %	381 (35)	247 (19)
Work time strength training, %	271 (25)	102 (8)

Values are mean (SD) for continuous measures or percentage as indicated. CFPWV indicates carotid–femoral pulse wave velocity; HDL, high-density lipoprotein cholesterol; IVSTD, end-diastolic interventricular septum thickness; LDL, low-density lipoprotein cholesterol; MVPA, moderate- to vigorous-intensity physical activity; PA, physical activity; PWTD, end-diastolic posterior wall thickness.

*Calculated for those who had at least 1 bout per day (n=613 men and 774 women); therefore, the sum of MVPA <10 and MVPA ≥10 min/day does not equal total MVPA.

nonbouts (ie, bouts lasting <10 minutes). The average sedentary time was 657±71 and 670±65 min/day among men and women (minimum to maximum 385 to 816 min/day for men and 379 to 835 min/day for women), respectively.

Associations Between Physical Activity and Vascular Stiffness Measures

The relation of MVPA and CFPWV is depicted in Figure A. Higher values of MVPA were associated with lower CFPWV

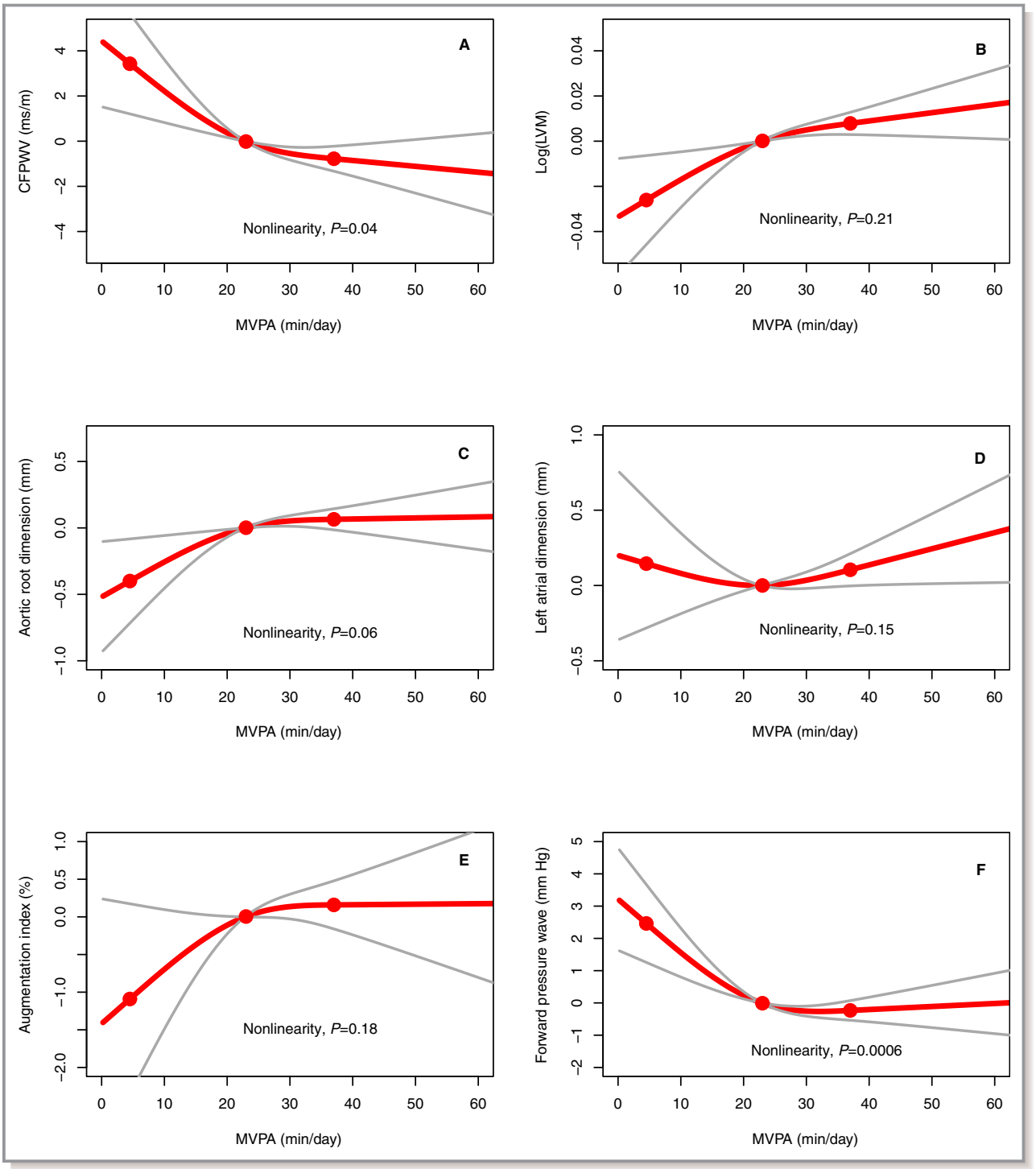

Figure. Adjusted splines of the association between MVPA in min/day (*x*-axis) and different cardiovascular measures (*y*-axis): A, CFPWV; B, $\log_e$ (LVM); C, aortic root dimension; and D, left atrial dimension. Knots were placed at MVPA 25th, 50th, and 75th percentiles (4.5, 23, 37 minutes). The *y*-axis illustrates deviations from the quantity estimated at the middle knot value. CFPWV indicates carotid–femoral pulse wave velocity; LVM, left ventricular mass; MVPA, moderate- to vigorous-intensity physical activity. The grey lines represent 95% confidence intervals.

(estimate±SE −0.53±0.19 ms/m [*P*=0.006] per 10 minutes of MVPA per day; 1 SD of MVPA is ≈20 minutes) (Table 3). The inverse association between MVPA and CFPWV was not statistically different for MVPA performed as bouts versus nonbouts (−0.80±0.30 ms/m [*P*=0.008] versus −0.45±0.29 ms/m [*P*=0.32] per 10 minutes of MVPA per day; *P*>0.05 for difference) (Table 3). Adjustment for strength training did not alter the associations of MVPA with CFPWV (data not shown). Compliance with guidelines, including both bout and nonbout activity, was significantly associated with lower CFPWV (estimate −2.05±0.78 ms/m [*P*=0.008], corresponding to ≈1.8 years of age effect; the adjusted estimate was 1.12±0.05 ms/m per 1-year older age). There was no statistically significant association between light physical activity or sedentary time and CFPWV (Table 3).

MVPA was significantly and inversely associated with the forward pressure wave (−0.23±0.11 mm Hg per 10 minutes higher MVPA per day; *P*=0.03) (Table 3). In addition, light physical activity was inversely associated with forward pressure wave (estimate −0.16±0.05 mm Hg per 10 minutes; *P*=0.0004), whereas sedentary time was not (Table 3). There were no statistically significant associations between compliance with physical activity guidelines and forward wave pressure (Table 3).

For the augmentation index, MVPA in nonbouts was associated with higher values, but MVPA in bouts was not (0.38±0.17% per 10 min/day for bouts [*P*=0.02] versus −0.09±0.17% per 10 min/day for nonbouts [*P*=0.31]; *P*=0.03 for difference between associations with augmentation index for MVPA in bouts versus nonbouts). Light physical activity was also associated with higher augmentation index values (0.18±0.05% [*P*=0.0002] per 10 minutes of light physical activity). Compliance with the guidelines and sedentary time were not associated with the augmentation index (Table 3). In an exploratory analysis additionally adjusting for resting heart rate (Table 4), the association of MVPA performed in nonbouts and augmentation index became statistically nonsignificant, whereas the association between MVPA performed in bouts and augmentation index became statistically significant (−0.45±0.16% [*P*=0.006] per 10 minutes of MVPA; *P*=0.02 for difference in association between bouts and nonbouts). Similarly, compliance with the guidelines including only bouts was significantly associated with a lower augmentation index after adjustment for heart rate (−1.24±0.60%; *P*=0.04).

Associations Between Physical Activity and Echocardiographic Measures

The relations between MVPA and $\log_e$ LVM, aortic root dimension, and left atrial dimension are depicted in Figure – Panel B through D. Higher mean levels of MVPA were associated with greater $\log_e$ LVM (0.006±0.002 $\log_e$ [g/m^2] per 10 min/day; *P*=0.0003) (Table 5), corresponding to approximately a 0.6% change in LVM per 10 minutes of MVPA per day. In additional analyses focused on the 2 components of LVM, the association between MVPA and LVM appeared to be largely secondary to the association of MVPA with LV wall thickness (0.07±0.02 mm per 10 min/day; *P*=0.0001) as opposed to LV internal dimensions (0.05±0.03 mm per 10 min/day; *P*=0.13). Light physical activity and

Table 3. Relations of Physical Activity to Tonometric Measures of Vascular Stiffness

	Carotid–Femoral Pulse Wave Velocity (ms/m)	Augmentation Index (%)	Forward Pressure Wave (mm Hg)
MVPA			
MVPA, per 10 min/day	−0.53 (0.19)**	0.13 (0.11)	−0.23 (0.11)*
MVPA ≥10 min (bouts), per 10 min/day	−0.80 (0.30)**	−0.09 (0.17)	−0.10 (0.17)
MVPA <10 min (nonbouts), per 10 min/day	−0.45 (0.29)	0.38 (0.17)*	−0.44 (0.16)**
PA guideline compliance, any MVPA (bouts or nonbouts)	−2.05 (0.78)**	0.40 (0.45)	−0.68 (0.43)
PA guideline compliance (only bouts of MVPA considered)	−1.82 (1.10)	−0.14 (0.63)	−0.61 (0.61)
Light activity			
Per 10 min/day	−0.13 (0.09)	0.18 (0.05)***	−0.16 (0.05)***
Sedentary time			
Per 10 min/day	0.07 (0.06)	−0.06 (0.03)	0.04 (0.03)

All association estimates are presented as estimates (SE). All models were performed with tonometry measures as the dependent variables and were adjusted for total wear time, sex, age, height, weight, systolic blood pressure, use of antihypertensive and lipid-lowering medications, current smoking status, serum total and high-density lipoprotein cholesterol concentrations, and diabetes. Tests for differences in association between MVPA in bouts vs nonbouts were not significant for all measures except for augmentation index (*P*=0.03). MVPA indicates moderate- to vigorous-intensity physical activity; PA, physical activity.
*P<0.05, **P<0.01, ***P<0.001.

Table 4. Association of Different Measures of Physical Activity With Augmentation Index

	Augmentation Index (%)	
	Without HR	With HR
MVPA, per 10 min/day	0.13 (0.11)	−0.12 (0.10)
MVPA ≥10 min (bouts), per 10 min/day	−0.09 (0.17)	−0.45 (0.16)**
MVPA <10 min (nonbouts), per 10 min/day	0.38 (0.17)*	0.15 (0.16)
PA guideline compliance, any MVPA (bouts or nonbouts)	0.40 (0.45)	−0.58 (0.43)
PA guideline compliance (only bouts of MVPA considered)	−0.14 (0.63)	−1.24 (0.60)*
Light PA, per 10 min/day	0.18 (0.05)***	0.15 (0.05)***
Sedentary time, per 10 min/day	−0.06 (0.03)	−0.04 (0.03)

All association estimates are presented as β values (SE). All models were performed with augmentation index as the dependent variables and were adjusted for total wear time, sex, age, height, weight, systolic blood pressure, use of antihypertensive and lipid-lowering medications, current smoking status, serum total and high-density lipoprotein cholesterol concentrations, and diabetes. HR indicates heart rate; MVPA, moderate- to vigorous-intensity physical activity; PA, physical activity.
*P<0.05, **P<0.01, ***P<0.001.

Table 5. Relations of Physical Activity and Echocardiographic Measurements

	$\log_e$ Left Ventricular Mass (g/m^2)	LV End-Diastolic Dimension (mm)	LV Wall Thickness (mm)	Aortic Root Dimension (mm)	Left Atrial Dimension (mm)	E/e′ Ratio
Moderate to vigorous PA						
MVPA, per 10 min/day	0.006 (0.002)***	0.05 (0.03)	0.07 (0.02)***	0.05 (0.03)	0.10 (0.04)*	−0.01 (0.01)
MVPA ≥10 min (bouts), per 10 min/day	0.009 (0.003)**	0.11 (0.05)*	0.07 (0.03)**	0.03 (0.04)	0.13 (0.06)*	−0.02 (0.02)
MVPA <10 min (nonbouts), per 10 min/day	0.007 (0.003)*	0.01 (0.05)	0.09 (0.03)**	0.09 (0.04)*	0.11 (0.06)	−0.01 (0.02)
PA guideline compliance, any MVPA (bouts or nonbouts)	0.019 (0.007)**	0.19 (0.14)	0.18 (0.07)**	0.21 (0.11)	0.12 (0.15)	−0.03 (0.06)
PA guideline compliance (only bouts of MVPA considered)	0.018 (0.010)	0.31 (0.19)	0.10 (0.10)	0.03 (0.16)	0.20 (0.22)	−0.14 (0.08)
Light activity						
Per 10 min/day	0.002 (0.0008)**	0.04 (0.02)**	0.01 (0.008)	0.03 (0.01)**	0.02 (0.02)	0.001 (0.006)
Sedentary time						
Per 10 min/day	−0.002 (0.0005)***	−0.004 (0.01)	−0.03 (0.005)***	−0.026 (0.09)**	−0.01 (0.01)	−0.003 (0.005)

All association estimates are presented as estimates (SE). All models were performed with echocardiographic measures as the dependent variables and were adjusted for total wear time, sex, age, height, weight, systolic blood pressure, use of antihypertensive and lipid-lowering medications, current smoking status, serum total and high-density lipoprotein cholesterol concentrations, and diabetes. Because left ventricular mass was log-transformed (base e), the association of physical activity on untransformed left ventricular mass is multiplicative, estimated by an exponentiated regression coefficient. Tests for difference in association between MVPA in bouts vs nonbouts were not significant for all measures (P>0.05). MVPA indicates moderate- to vigorous-intensity physical activity; PA, physical activity.
*P<0.05, **P<0.01, ***P<0.001.

compliance with the guidelines were also associated with greater $\log_e$ LVM (Table 5). Sedentary behavior was associated with lower LV wall thickness and $\log_e$ LVM (−0.002 g/m^2 changes in $\log_e$ LVM, corresponding to 0.2% lower LVM, per 10 minutes of sedentary behavior).

MVPA was borderline significantly and positively associated with aortic root size and left atrial dimension, whereas compliance with guidelines was not associated with either measure (Table 5). Light physical activity was also positively associated with higher aortic root size, whereas sedentary time was associated with lower aortic root size. Adjustment for strength training did not alter the associations of MVPA with echocardiographic measures (data not shown). Further adjustment for weight and systolic blood pressure at time of echocardiography yielded similar results (data not shown).

No significant association was noted between physical activity or sedentary time and E/e′ ratio.

Secondary Analyses

Hyperemic flow velocity and flow-mediated dilation were not significantly associated with any of the physical activity measures (Table 6). Baseline flow velocity was significantly and inversely associated with MVPA performed in bouts (−0.16±0.07 cm/s per 10 minutes of MVPA; P=0.016) and with sedentary time (−0.04±0.01 cm/s per 10 minutes of sedentary behavior; P=0.007).

Discussion

In our large study of middle-aged ambulatory community-dwelling participants, higher mean levels of MVPA were associated with lower arterial stiffness, greater LVM, and greater aortic root and left atrial sizes compared with physical inactivity after adjustment for potential confounders. Compliance with current guidelines (ie, engaging in at least 150 minutes per week of MVPA) was associated with 1% lower CFPWV, corresponding to a reduction in vascular aging of ≈1.8 years. Sedentary behavior was associated inversely with LVM and aortic root but not with vascular stiffness measures.

Consistent with our study, smaller observational studies (also cross-sectional) in the general population and in patients with type 2 diabetes[22–24] and short-term interventional studies of postmenopausal women[25] and middle-aged men have reported lower central arterial stiffness with increasing levels of physical activity.[23] Because CFPWV has been reported to be a strong predictor of hypertension and CVD in the community,[20,26] the associations of compliance with guidelines and lower CFPWV may have important implications for reducing long-term cardiovascular risk.

Increased arterial stiffness is usually considered the result of exposure to several hemodynamic and systemic adverse factors such as hypertension, advancing age, diabetes, atherosclerosis, and inflammation. Arterial stiffening may result from both passive (increased intima-media thickness) and active (smooth vascular muscle tone) components, both of which can be altered by physical activity.[27] Typically, intima-media thickness increases by 2- to 3-fold during the adult life course.[28] Some observational studies have reported previously that questionnaire-based measurement of physical activity is associated with attenuated age-related increases in intima-media thickness in adolescent,[29] middle-aged, and elderly persons,[30] although not all studies have yielded consistent results.[31,32] The active component responsible for increases in arterial stiffness relates to heightened smooth vascular muscle tone and endothelial dysfunction.[27] Triggers for high muscular tone include mechanical stimulation, endocrine factors such as angiotensin, and oxidative stress.[27] Physical activity has been associated previously with healthier endothelial function in a cross-sectional study of middle-aged men.[33] Furthermore, a recent study of 114 previously sedentary older adults aged ≥50 years demonstrated improved flow-mediated dilation (a marker of endothelial function) among those who increased moderate physical activity levels in bouts of ≥10 minutes for at least ≥20 minutes per day over a 12-week period.[34] In our analyses, however, MVPA was not associated with endothelial-dependent measures (ie, flow-mediated dilation). It is conceivable that the temporal difference between accelerometry and forearm vascular measures may have introduced misclassification that could have masked a true positive association between flow-mediated dilation and MVPA in our study.

Table 6. Association of Different Measures of Physical Activity With Brachial Artery Measures

	Baseline Flow Velocity (cm/s)	Hyperemic Flow Velocity (cm/s)	Flow-Mediated Dilation (%)
MVPA, per 10 min/day	−0.05 (0.04)	−0.19 (0.20)	0.002 (0.04)
MVPA ≥10 min (bouts), per 10 min/day	−0.16 (0.07)*†	−0.26 (0.31)	0.04 (0.06)
MVPA <10 min (nonbouts), per 10 min/day	0.03 (0.07)†	−0.19 (0. 30)	−0.03 (0.06)
PA guideline compliance, any MVPA (bouts or nonbouts)	−0.28 (0.17)	−0.51 (1.13)	−0.11 (0.15)
PA guideline compliance (only bouts of MVPA considered)	−0.25 (0.24)	−0.86 (0.81)	0.25 (0.21)
Light PA, per 10 min/day	0.009 (0.02)	0.033 (0.088)	−0.0007 (0.02)
Sedentary time, per 10 min/day	−0.04 (0.01)**	−0.03 (0.06)	0.007 (0.01)

All association estimates are presented as β values (SE). All models were performed with vascular measures as the dependent variables and were adjusted for total wear time, sex, age, height, weight, systolic blood pressure, use of antihypertensive and lipid-lowering medications, current smoking, serum total and high-density lipoprotein cholesterol concentrations, and diabetes. MVPA, moderate- to vigorous-intensity physical activity; PA,physical activity.

†P=0.01 for difference between MVPA performed as bouts vs nonbouts.

*P<0.05, **P<0.01, ***P<0.001.

Cardiac remodeling secondary to physical activity has predominantly been studied in trained athletes. Endurance athletes often have eccentric hypertrophy (ie, increased LV internal dimension and stroke volume), whereas strength-trained athletes develop concentric hypertrophy[35]; however, LV area was also reported to increase by approximately 5.5% in a 12-week program of moderate exercise (ie, brisk walk or jogging at a heart rate ≥120 beats per minute) in young and middle-aged sedentary men and women.[36] In contrast, periods of physical inactivity, as tested in bed-rest trials, have been shown to cause significant reductions in LVM (ranging on average between 8% and 16% for 6 and 12 weeks of bed rest, respectively).[37,38] In the present study, we confirmed that typical levels of physical activity (of a magnitude much lower than that of athletes) were associated with overall modest increments in LVM. Compared with the average MVPA of 30 minutes per day, the participant with the highest accrued MVPA per day (192 minutes per day) would have an estimated increase in LVM, based on our estimates, of $100\times(\exp(0.006\times(192-30\ \text{min})/10\ \text{min}^{-1})=10.2\%$. In contrast, compared with the average sedentary time of 657 min/day, the person with highest sedentary time (835 sedentary min/day) would have estimated lower LVM of $100\times(\exp(-0.002\times(835-657\ \text{min})/10\ \text{min}^{-1})=3.5\%$. A significant positive association of LVM with a questionnaire-based measure of leisure time physical activity was reported nearly 25 years ago from the Framingham Heart Study offspring cohort (although the association was statistically significant only in men in that study), but given the temporal and methodological differences, it is challenging to compare the results of the present investigation with the findings in the previous study.[39]

In the present study, the cardiac remodeling associated with greater MVPA was driven by the association with greater increases in LV wall thickness (ie, concentric remodeling) rather than increases in LV end-diastolic dimensions (ie, eccentric remodeling). Such a remodeling pattern may also be apparent under pathological conditions like hypertension, but under these conditions, vascular stiffness is likely to be increased, and LV diastolic function is also likely to be impaired. In the present study, MVPA was inversely related to vascular stiffness, and there was no association with LV diastolic function as measured by the E/e′ ratio, suggesting that the pattern of LV remodeling seen in physical activity at levels typically observed in the community is likely benign.[40] Other studies have even indicated that, despite increases in LVM following physical activity, LV diastolic function assessed by sensitive tissue Doppler measures may be supranormal.[41,42]

We observed a significant association between higher levels of physical activity and greater dimension of left atrium and borderline significant associations of physical activity with aortic root dimension. To the best of our knowledge, this result has not been reported previously in people in the community engaging in nonextreme ranges of physical activity. Studies of very well-trained athletes have reported increases in both atrial and aortic root dimensions, especially in endurance-trained athletes, who experience greater hemodynamic loads compared with strength-trained athletes.[43–45] The magnitude of the association between physical activity and aortic root dimensions was very modest and was unlikely to be associated with any clinical consequence. Even in very well-trained athletes, aortic root dimensions very rarely exceeded >40 mm in male athletes and >34 mm in female athletes.[44] Left atrial size has been shown to be increased in endurance-trained athletes and may increase the risk of lone atrial fibrillation[46]; however, we observed very modest increases in left atrial dimensions with greater physical activity, and these were likely of little clinical relevance. Additional studies are needed to evaluate the long-term consequences of the modest increments in LVM, aortic root size, and left atrial dimensions observed with increasing MVPA.

Impact of Bout Duration on the Cardiovascular System

The importance of bouts versus nonbouts of physical activity for cardiovascular health has not been well investigated. Among previously sedentary, overweight women, a randomized trial demonstrated that those randomized to long bouts of exercise had similar improvements in cardiorespiratory fitness as those randomized to equivalent amounts of exercise in short bouts over an 18-month period.[47,48] It has been speculated that long bouts of physical activity may generate more free oxygen radicals than what the endogenous antioxidant system can neutralize[49,50] and thus may increase arterial stiffness (as suggested by a study of physical activity in patients with established CVD).[51] In contrast, in a recent study of previously sedentary adults aged ≥50 years, Suboc et al observed improved flow-mediated dilation for those who engaged for ≥20 min/day in moderate physical activity with bouts lasting ≥10 minutes but not for those who engaged in moderate physical activity with bouts lasting <10 minutes.[34] The authors of that report did not observe a statistically significant association of moderate physical activity with CFPWV or augmentation index.[34] In our study, we found no evidence of differential associations of short versus long bout duration on arterial stiffness, suggesting that physical activity of any duration may have beneficial effects on vascular stiffness.

Strengths and Limitations

The large community-based sample, comprehensive assessment of physical activity (including sedentary time and light physical activity) and vascular stiffness, and echocardiographic

measurements (including diastolic function) strengthen our investigations. Nonetheless, several limitations merit comment. The present study was observational and cross-sectional in design and thus precludes causal inferences. Although we adjusted all models for multiple variables, the influence of residual confounding cannot be excluded. In addition, accelerometry does not capture resistance training. The study sample was mainly composed of white participants of European descent, thereby limiting generalizability to other ethnicities. Furthermore, the echocardiographic measurements were obtained prior to accelerometry, and that can result in an underestimation of the strength of the associations between MVPA and cardiac measurements (regression dilution bias). Although we performed multiple analyses, we did not account for multiple statistical testing in our reporting of our results; several of our findings may be considered hypothesis generating and warrant replication in subsequent studies. Finally, notwithstanding the statistical significance of selected associations noted in our analyses, the effect sizes observed (for LVM and left atrial and aortic root dimensions) are modest and may not be clinically important.

Conclusions and Clinical Perspective

Physical activity was associated with favorable effects on arterial stiffness and with very modest increments in LVM and aortic root and left atrial size. Compliance with the guidelines was associated with 1% lower CFPWV comparable to having vascular stiffness that is 1.8 years younger than actual chronological age. Bouts lasting ≥10 and <10 minutes of duration were shown to have no overall differential effects on our subclinical vascular and cardiac measures, suggesting that physical activity, regardless of duration, may have similar associated beneficial effects on the cardiovascular system. A recent study estimated that the population life expectancy in the United States will increase by 2 years if adults reduce their time sitting to <3 hours per day.[52] Our results demonstrated that sedentary behavior was associated with an adjusted inverse relation with LVM. Although we did not observe any statistically significant inverse associations between sedentary time and arterial stiffness measures, other studies have suggested that physical inactivity is a significant risk factor for CVD independent of physical activity levels.[53,54] Consequently, physical inactivity should be considered as a CVD risk factor, notwithstanding the lack of association with vascular stiffness measures in the present report.

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Disclosures

Dr Mitchell is the owner of Cardiovascular Engineering Inc, a company that develops and manufactures devices to measure vascular stiffness. He has also served as consultant for and received honoraria from Merck and Novartis.

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