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Joint associations of peripheral artery disease and accelerometry-based physical activity with mortality: the Hispanic Community Health Study / Study of Latinos (HCHS/SOL)

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Abstract

Background and aims: Peripheral artery disease (PAD) and lower levels of physical activity are both associated with higher mortality. Yet, their joint prognostic impact has not been systematically examined, especially in Hispanics/Latinos, and with objective measures. We aimed

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CRediT author statement

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Declaration of competing interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

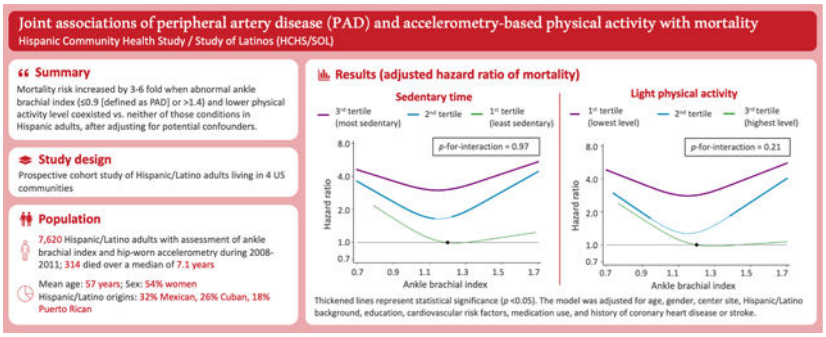
to examine the joint associations of PAD and physical activity with mortality in the Hispanic Community Health Study / Study of Latinos (HCHS/SOL).

Methods: We studied 7,620 Hispanic/Latino adults aged 45–74 years at baseline (2008–2011) who underwent assessment of PAD with ankle-brachial index (ABI) and physical activity with hip-worn accelerometry. We calculated four physical activity measures: sedentary time, light activity, moderate/vigorous activity, and total activity counts. We quantified the relationship between ABI and mortality overall, and by tertiles of activity measures in restricted cubic splines, using multivariable Cox models accounting for sampling weights. We also assessed cross-categories of ABI and activity measures with mortality.

Results: During a median follow up of 7.1 years, 314 participants died. We observed a U-shaped association of ABI with mortality overall (e.g., hazard ratio 1.80 [95%CI 1.20–2.80] at ABI 0.7 *vs* 1.2). This U-shaped association was generally consistent after stratifying by activity measures, but an elevated mortality risk for higher ABI was not evident in the most active tertile based on sedentary time, time in light activity, and total activity counts. In the cross-category analysis of ABI and physical activity, the highest mortality risk was consistently seen in abnormal ABI (≤0.9 or >1.4) plus the least active tertile (e.g., HR 5.61 [3.31–9.51] for light activity), compared to referent ABI (0.9–1.4) plus the other more active two tertiles, with no interactions between ABI and activity measure.

Conclusions: Abnormal ABI and lower accelerometry-based physical activity were independently and jointly associated with mortality in Hispanics, suggesting the importance of simultaneously evaluating leg vascular condition and physical activity.

Graphical Abstract



1. Introduction

Lower-extremity peripheral artery disease (PAD) affects approximately 8.5 million adults in the US[1] and increases the risk of mortality, mainly due to cardiovascular disease.[2,3] Given this, the American Heart Association (AHA) and the American College of Cardiology (ACC) 2016 PAD Guideline recommends screening for PAD using the ankle-brachial index (ABI) among asymptomatic individuals at high risk of PAD (e.g., older adults and middle age adults with PAD risk factors).[4] Moreover, the AHA/ACC 2018 Lipid Guideline recognizes low ABI (≤0.9) as a risk enhancer to guide decision making about use of lipid-lowering therapy.[5]

Reduced physical activity is another important manifestation of PAD and may partially contribute to elevated mortality with PAD.[6–11] However, to our best knowledge, only two studies with relatively small sample sizes (n<500) reported that lower physical activity predicts poor prognosis in PAD patients.[6,7] Since these two studies only investigated PAD patients, they were unable to quantify the joint prognostic value of PAD and physical activity in the community. In addition, the larger study only investigated PAD patients with intermittent claudication, a small subgroup of PAD, and relied on self-reported physical activity.[6] The other smaller PAD study used accelerometry-based physical activity, but only investigated 225 patients.[7] Reflecting limited evidence, the AHA/ACC 2016 PAD Guideline describes the potential value of objectively measuring physical activity in PAD patients for motivating behavioral changes but not for prognostication.[4]

To overcome these knowledge gaps, we quantified the independent and joint associations of ABI and accelerometry-based physical activity with all-cause mortality over a median of 7 years of follow up using data from the Hispanic Community Health Study/Study of Latinos (HCHS/SOL). This investigation specific in Hispanics is important since the prevalence of two major risk factors of PAD, smoking and diabetes, is high in this population[12] and unique physical activity patterns across Hispanic/Latino backgrounds have been reported[13].

2. Materials and methods

2.1 Study Participants

The HCHS/SOL is a community-based prospective cohort study of 16,415 self-identified Hispanic/Latino adults aged 18–74 years living in four US communities (Bronx, New York; Chicago, Illinois; Miami, Florida; San Diego, California) at baseline (2008–2011). Details of the cohort design and sampling methods have been published previously.[14,15] Briefly, participants were recruited using a multi-stage probability sampling design.[14] Census block groups were first randomly selected in each of the four communities; households and individuals were then randomly selected in each sample block group. The 45–74 age group was oversampled to accrue endpoints of interest sooner. The HCHS/SOL included participants with Central American, Cuban, Dominican, Mexican, Puerto Rican, South American, or other/mixed Hispanic origins. Participants attended an in-person baseline examination and thereafter were contacted annually for a brief telephone questionnaire. The study was approved by the institutional review board of each participating institution and all study participants provided written informed consent.

At baseline, 9,705 participants met the eligibility criteria of age ≥45 years old to undergo the requisite blood pressure measurements to compute the ABI. Of these, we excluded participants with missing ABI values (n=65), missing covariates of interest (n=394), and non-adherence to wearing accelerometers (adherence defined as at least 10 hours per day for 3 days or more) (n=1,626), leaving a final sample size of 7,620 for the primary analysis. Compared to participants excluded due to non-adherence to accelerometers, our study population was slightly older, more likely to be in normal weight and never smokers but, overall, we did not recognize considerable differences between the two groups (Supplementary Table 1).

2.2 Assessment of ABI

After at least 5 minutes of rest, systolic blood pressures of bilateral brachial, posterior tibial, and dorsalis pedis arteries were measured in supine position using appropriate manual sphygmomanometer cuffs and a hand-held Doppler probe (Nicolet Elite 100R; Nicolet Biomedical Inc, Golden, CO). The ABI in each leg was calculated using the higher of the posterior tibial or dorsalis pedis blood pressure in each leg divided by the higher of left or right brachial pressure. In general, the lower ABI of the two legs was used in analyses. When one leg ABI was greater than 1.4 and another between 0.9 and 1.4 (referent ABI), we used the higher ABI value for the analysis since high ABI is often indicative of arterial incompressibility and can be prognostic of cardiovascular events and mortality.[3]

2.3 Accelerometry-based measures

At the baseline clinic examination, participants were instructed to wear an omnidirectional accelerometer (Actical, model 198-0200-03; Respironics Co. Inc., Bend, OR) on the iliac crest for 7 consecutive days. Participants were instructed to remove the accelerometer during swimming, bathing, and sleeping. The accelerometer was programmed to capture accelerations in counts in 1-minute epoch at a sampling rate of 32 Hz. Based on the validated Choi algorithm, we classified nonwear time as ≥90 minutes of consecutive zero counts, with an allowance of up to 2-min nonzero counts if no counts were detected in a 30-minute window upstream and downstream of the 90-minute period.[16] Any nonzero counts except the allowed up to 2-min nonzero count intervels were considered as wear time.

Accelerometry thresholds of the hip-worn Actical used in our study have been previously validated in adults aged 20 to 79 years old to objectively assess different phases of physical activity.[17–19] The following counts/min thresholds were applied: sedentary (physical inactivity) <100 counts/min; light 100–1,534 counts/min; and moderate or vigorous ≥1,535 counts/min. Sedentary time (hours/d) was determined by summing the daily wear time within the specified acceleration count range and then averaging across adherent days. Given that sedentary time and wear time were strongly correlated (r=0.80), we standardized sedentary time to the mean accelerometer wear time per day at each center site, using the residual from a regression model with wear time, center site, and their interaction predicting sedentary time, as was done previously.[20,21] After standardization, the correlation coefficient between sedentary time and wear time was down to 0.34. Time spent in light-intensity (hours/d) and moderate/vigorous-intensity (mins/d) were aggregated according to intensity thresholds and averaged across adherent days. Daily average activity counts (counts/d) were used to assess total physical activity volume. Light, moderate/vigorous, and total physical activity were not strongly correlated with accelerometer wear time (r<0.3).

2.4 Covariates

Age, gender, Hispanic/Latino background, education, smoking status, history of stroke, and use of anti-hypertensive and lipid-lowering medications were based on self-report. San Diego Claudication Questionnaire was administered by study staff to assess leg pain symptoms during participant interviews; leg pain symptoms were categorized into no pain on exertion *vs.* pain on exertion.[22,23] History of coronary heart diseae was ascertained

based on electrocardiography and self-reported heart attack, angina, or related prodecure (angioplasty, stent, bypass surgery).

Body mass index was calculated using weight in kilograms divided by height in meters squared (kg/m^2). Sitting blood pressure was calculated by averaging three readings obtained using an automatic sphygmomanometer. Serum total cholesterol was measured in mg/dL using a cholesterol oxidase enzymatic technique, and high-density lipoprotein (HDL) cholesterol was measured in mg/dL by a direct magnesium/dextran sulfate method (Roche Diagnostics, Indianapolis, IN) (to convert total and HDL cholesterol from mg/dL to mmol/L, multiply by 0.02586).[24] Glucose was measured in ethylenediaminetetraacetic acid (EDTA) plasma using a hexokinase enzymatic method (Roche Diagnostics, Indianapolis, IN) and hemoglobin A1c was measured in EDTA whole blood using a Tosoh G7 Automated HPLC Analyzer (Tosoh Bioscience, Inc, South San Francisco, CA).[24] Prediabetes (fasting glucose 100–125 mg/dL [to convert glucose from mg/dl to mmol/L, multiply by 0.0555], 2-h post oral glucose tolerance 140–199 mg/dL, or hemoglobin A1c 5.7–6.5%) and diabetes (fasting glucose ≥126 mg/dL, non-fasting glucose ≥200 mg/dL, 2-h post oral glucose tolerance test ≥200 mg/dL, hemoglobin A1c ≥6.5% or self-reported use of anti-diabetic medications) were defined based on American Diabetes Association standard.[25] Details about the actual assessment and definition of all covariatesare summarized in Supplementary Table 2.

2.5 Outcome

The outcome of interest was all-cause mortality, identified from annual follow-up interviews (with responses from family members or other proxy). Participants were followed until December 31, 2018, date of death, or date of last completed annual follow up interview (whichever came first).

2.6 Statistical analysis

All statistical analyses incorporated the survey weights to account for the 2-stage probability sampling design. ABI was grouped into three categories: ≤0.9 (indicative of PAD),[26] 0.9–1.4 (reference),[27,28] and >1.4 (arterial incompressibility with potential PAD).[29] Accelerometry-based measures were categorized according to unweighted tertiles, with the theoretically healthiest tertile as reference (i.e., 1st tertile for sedentary time and 3rd tertile for other physical activity measures). Baseline characteristics were summarized by ABI categories as mean (standard error, SE) or median [interquartile interval, IQI] for continuous variables and percentage (SE) for categorical variables. We also explored baseline characteristics across tertiles of physical activity measures.

Using Cox proportional hazards models, we first examined the associations of ABI with all-cause mortality in restricted cubic splines overall and after stratifying by tertiles of accelerometry-based measures. We prespecified three knots for ABI at 0.9, 1.15, and 1.4 and set 1.2 as the referent. We adjusted the following potential confounders: age, gender, center site, Hispanic/Latino background, education, smoking status, body mass index, total and HDL cholesterol, diabetes status, systolic blood pressure, anti-hypertensive, lipid-lowering drugs, accelerometer wear time, and history of coronary heart disease or stroke.

We also ran Cox models for cross-categories of ABI and physical activity. To obtain reliable estimates, instead of modeling nine cross-categories we created four cross-categories from two categories of ABI (merging ≤0.9 and >1.4 [abnormal ABI] *vs.* 0.9–1.4 [referent ABI][28]) and two categories of accelerometry-based measures (the least active tertile *vs.* the remaining tertiles). We also estimated mortality risk using the Kaplan-Meier method.

We further conducted analyses in subgroups of age, gender, smoking status, diabetes, history of coronary heart disease or stroke, and leg pain symptoms. All statistical interactions were evaluated using the likelihood ratio test. All analyses were performed using Stata, version 15.1 (StataCorp, College Station, TX), and a *p*-value <0.05 was considered statistically significant.

3. Results

3.1 Baseline characteristics

At baseline, the mean age of our study population was 56.6 years, and 54.4% were women. In terms of Hispanic origins, 32.2% were Mexican, 26.3% were Cuban, 17.8% were Puerto Rican, 9.7% were Dominican, 6.4% were Central American, 5.4% were South American, and the remaining 2.0% reported other/mixed origins. The mean ABI was 1.07 (SE, 0.003); 5.4% and 2.8% of the population had ABI ≤0.9 and >1.4, respectively. The mean accelerometer wear time was 15.9 (SE, 0.08) hours/d (median 15.6 [IQI 13.6–18.5]). The mean sedentary time was 12.0 (SE, 0.07) hours/d (median 11.9 [IQI 10.5–13.6]). Overall individuals engaged in, on average, 3.6 (SE, 0.03) hours/d (median 3.5 [IQI 2.6–4.6]) of light physical activity and 19.6 (SE, 0.54) mins/d (median 12.0 [IQI 4.3–26.2]) of moderate/vigorous physical activity. Mean total physical activity was 146,049 (SE, 2,491) counts/d (median 118,109 [IQI 77,683–180,257]). Among individuals who reported leg pain symptoms, 43.2% (49.0% for women *vs.* 36.4% for men) reported pain on exertion.

As compared with the referent ABI (0.9–1.4), individuals with low (≤0.9) or high ABI (>1.4) were more likely to be older, be diabetic, have higher systolic blood pressure, engage in more sedentary behavior and less physical activity, and experience more leg pain on exertion (Table 1). The prevalence of current smoking was highest among those with low ABI, followed by referent ABI and high ABI. When we compared baseline characteristics across tertiles of sedentary time, longer sedentary time was associated with a higher risk factor profile (e.g., older age, higher body mass index, higher blood pressure, and higher prevalence of diabetes) and more leg pain. However, the prevalence of current smoking was lowest in the 3rd tertile of sedentary time. Similarly, a more unfavorable comorbidity profile was observed with lower activity level across light, moderate/vigorous, and total physical activity measures. ABI values were weakly correlated with each physical activity variable (|r|=~0.1 when we focus on ABI <1.4) (Supplementary Table 3).

3.2 ABI, physical activity, and mortality

During a median follow up of 7.1 years (IQI, 7.0–7.3 and maximum 10.1 years), 314 participants died. Overall, we observed a U-shaped association between ABI and mortality (e.g., hazard ratio 1.80 [95%CI 1.20–2.70] and 1.41 [1.20–1.66] at ABI 0.7 and 1.5 [vs 1.2],

respectively) (Figure 1). This U-shaped association was generally consistent after stratifying by activity level, but the elevated mortality risk with higher ABI was not evident in the most active tertile based on sedentary time, light activity, and total physical activity (green lines in Figure 2 and Supplementary Figure 1). At a given level of ABI, the least active tertile generally demonstrated the highest mortality (purple lines in Figure 2 and Supplementary Figure 1), regardless of physical activity measures. The most active tertile had the lowest mortality in general, except for moderate/vigorous activity. The interaction between ABI and physical activity measures did not reach statistical significance (p >0.1) in all models.

When we explored cross-categories of ABI and physical activity, the highest mortality risk was generally seen in abnormal ABI (≤0.9 or >1.4) plus the least active tertile, with no significant interactions (Table 2). For example, the hazard ratio of mortality was 5.61 (95% CI 3.31–9.51) for abnormal ABI among those in the 1st tertile of light activity compared to the referent ABI 0.9–1.4 among those in the 2nd and 3rd tertiles of light activity. In this specific example, the two intermediate groups (i.e., abnormal ABI but top two light activity tertiles or the least light activity tertile but ABI 0.9–1.4) demonstrated hazard ratio around 2.1–2.4. Based on the Kaplan-Meier estimate, the highest risk in abnormal ABI (≤0.9 or >1.4) plus the least active tertile was translated into the 7-year cumulative mortality of ~20%, compared to of ~3% in the group with ABI 0.9–1.4 plus the top two active tertiles (red lines and purple lines, respectively, in Figure 3).

The associations for cross-categories of ABI and accelerometry-based measures with mortality were largely consistent in subgroups of age, gender, smoking status, diabetes, history of coronary heart disease or stroke, and leg pain symptoms (Supplementary Figures 2–5). In almost all comparisons, the highest mortality was observed in abnormal ABI plus the least active tertile. We did not observe any statistically significant interactions in these analyses except for diabetic status. Specifically, the main difference was seen in the cross-category of abnormal ABI plus the more active tertiles, with elevated mortality risk more evident in diabetes (even similar to the cross-category of abnormal ABI plus the least active tertile) than no diabetes (e.g., Supplementary Figure 4).

4. Discussion

To our knowledge, this is the first study evaluating the joint associations of ABI and accelerometry-based physical activity measures with all-cause mortality. We observed a U-shaped association between ABI and mortality in this Hispanic cohort, and ABI and physical activity were independently associated with mortality. More specifically, when cross-categories of ABI and physical activity were assessed, the highest mortality was generally seen in abnormal ABI (≤0.9 or >1.4) plus the least active tertile regardless of activity measures, with hazard ratios of 3–6, compared to ABI 0.9–1.4 plus top two active tertiles. These results suggest that even for those with poor leg vascular condition, less sedentary time or more physical activity (regardless of activity intensity) appeared to show improved prognosis.

The observed U-shaped association of ABI with mortality is generally consistent with previous studies[3,28,30] and likely reflects low ABI as an indicator of PAD and high ABI

representing non-compressible arteries typically due to medial arterial calcification.[4,31] Notably, ABI >1.4 showed largely similar or worse prognosis than ABI ≤0.9 in our study, which highlights the importance of recognizing high ABI as a risk factor for mortality. Some studies have reported high prevalence of PAD (~85%) in individuals with ABI>1.4.[32] As a result, the AHA/ACC 2016 PAD Guideline recommends using toe-brachial index to diagnose PAD among persons with ABI >1.4 since toe arteries are rarely calcified.[4] Conversely, the AHA/ACC 2018 Lipid Guidelines acknowledge low ABI, but not high ABI, as a factor that increases cardiovascular risk.[5] Whether high ABI is particularly prognostic in Hispanics would require further investigation.

The lack of association between high ABI and mortality in the most active tertile based on sedentary time, light activity, and total physical activity deserves discussion. Although we are not sure about potential mechanisms, our observation may be related to the effect of aerobic exercise on reducing vascular stiffness,[33] since as noted above, high ABI may serve as an indicator for vascular stiffness. Interestingly, a prior study showed that aerobic exercise could partially restore arterial stiffness in sedentary middle-aged adults.[34] Nonetheless, future studies are needed to confirm our observation, and if so, to explore potential biological mechanisms.

There seem to be a few potential mechanisms linking lower physical activity with elevated mortality risk. For example, lower levels of physical activity may be caused by comorbidities (e.g., stroke), which can increase the risk of adverse outcomes. On the other hand, higher physical activity can promote better health (e.g., maintaining normal weight). Whether there is a threshold of physical activity to improve health and prognosis is still controversial although several studies have shown that any physical activity may improve prognosis. Indeed, our study and a few others demonstrated a dose-response relationship between accelerometry-based physical activity and mortality.[35]

There are a few potential clinical implications of the present study. First, given our finding of 3–6-fold increased mortality risk for individuals with abnormal ABI and lower physical activity level *vs.* those with neither, it seems worth discussing whether accelerometry-based measures should be utilized for risk stratification in patients with PAD or high ABI. Of importance, the AHA/ACC 2016 PAD Guidelines already acknowledge the value of physical activity assessment for behavioral changes in the context of exercise therapy and thus the data should be available in some patients.[4] Moreover, the number of people using personal devices with accelerometers (e.g., smartphones and smartwatches) is increasing, and indeed, a study has confirmed that lower step counts assessed by a commerical device were associated with health-related adverse outcomes.[36] Nonetheless, a standardized approach for the objective evalution of free-living physical activity would be necessary for this measure to be taken into account clinically. Second, we observed that even mild physical activity was associated with a significant reduction in mortality risk for persons with PAD. This observation seems to further support the coverage of supervised exercise therapy for symptomatic PAD patients by the Center for Medicare & Medicaid Services.[37] Whether similar exercise programs are also beneficial for asymptomatic PAD or those with high ABI requires further studies. Lastly, the interaction by diabetes (i.e., greater activity did not necessarily result in lower mortality in individuals with abnormal ABI and diabetes) should

be confirmed in future studies since we have conducted our subgroup analysis without *a priori* hypothesis. If confirmed, this observation will have clinical implications on exercise programs in patients with diabetes.

A few limitations of this study should also be acknowledged. The Hispanic adults aged 45–74 years included in our study may not be representative to the overall Hispanics in the US. Nevertheless, the center sites from HCHS/SOL are among the largest in concentrations of Hispanics based on consensus; thus, our study results should be relatively generalizable for Hispanic population. Whether the results in our study can be generalizable to other racial/ethnic groups should be examined in future studies. Because this is still a young cohort that has only been followed for fewer years, we were unable to analyze cause-specific mortality. Also, our study is based on participants who adhered to wearing accelerometers, which might potentially influence our estimates. Nevertheless, this approach has been commonly done in the literature and characteristics were largely similar between our study population and those who were excluded due to non-adherence. Lastly, additional measures that assess the severity of PAD such as toe-brachial index or post-exercise ABI were not available in any study participants.

In summary, abnormal ABI (≤0.9 or >1.4) and lower accelerometry-based activity level were both independently and jointly associated with increased mortality risk even after controlling for potential confounders. Our results suggest the importance of objectively evaluating leg vascular health and physical activity. Although the clinical use of accelerometry-based measurement has yet to be established, this measurement may be especially valuable for persons with PAD.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- Peripheral artery disease (PAD) and physical activity were each associated with mortality
- Mortality risk increased greatly when PAD and low physical activity coexist
- No interactions between PAD and physical activity were observed
- Simultaneously evaluating leg vasculature and physical activity improves prognosis

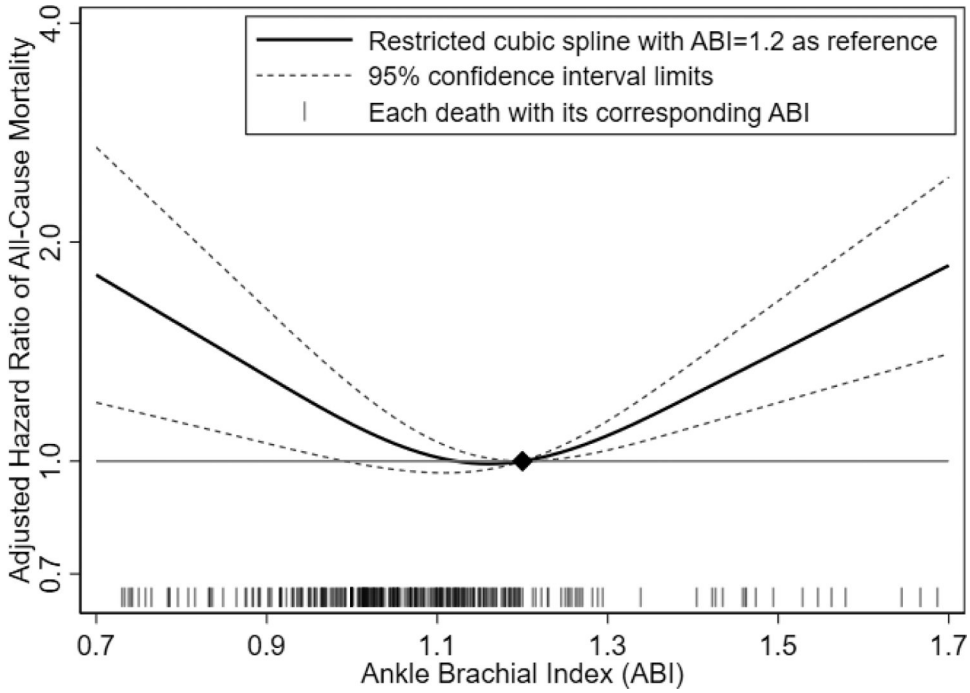

Figure 1.

Dose-response association of ABI with all-cause mortality, HCHS/SOL.

Three knots at 0.9, 1.15, and 1.4 for restricted cubic splines were specified, with ABI=1.2 as reference. The model was adjusted for age, gender, center site, Hispanic/Latino background, education, smoking status, body mass index, total and HDL cholesterol, diabetes status, systolic blood pressure, anti-hypertensive use, use of lipid-lowering drugs, accelerometer wear time, and history of coronary heart disease or stroke. All estimates accounted for the complex sample design. ABI, ankle-brachial index; HCHS/SOL, the Hispanic Community Health Study / Study of Latinos; HDL, high-density lipoprotein.

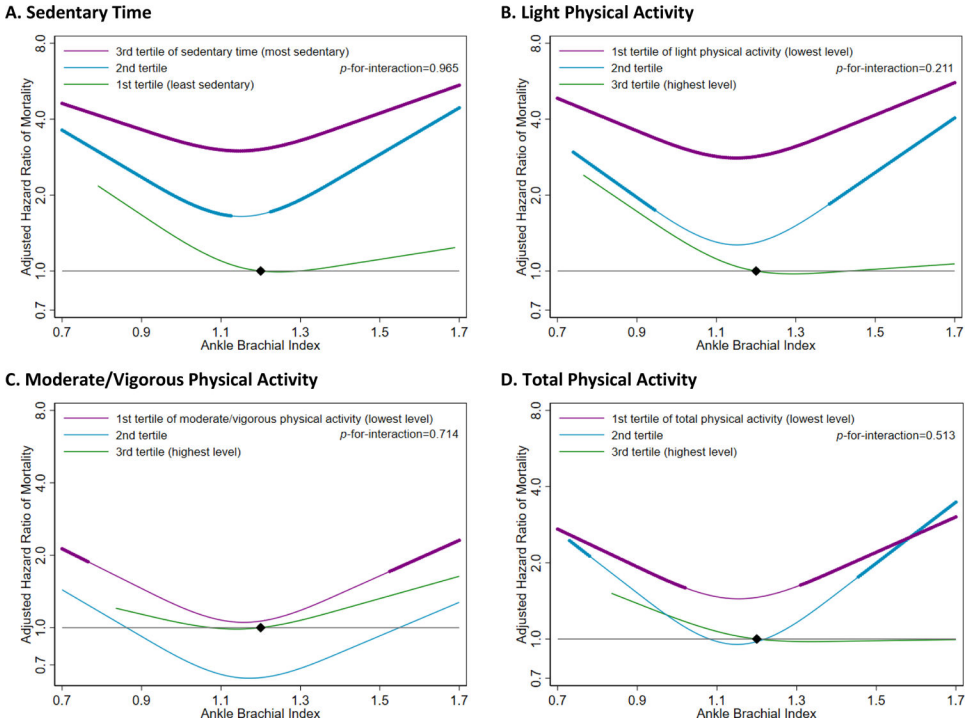

Figure 2.

Associations of ABI with all-cause mortality by accelerometry-based measures.

Dots on each plotted line (thickened line segments) represent statistical significance (p <0.05). Three knots at 0.9, 1.15, and 1.4 for restricted cubic splines were specified, with ankle brachial index=1.2 as reference. The 33rd percentile (1st – 2nd tertiles) and 67th percentile (2nd – 3rd tertiles) cutoffs were 11.0 and 12.9 hours/d for sedentary time, 2.9 and 4.2 hours/d for light physical activity, 6.3 and 20.2 mins/d for moderate/vigorous physical activity, and 90,911 and 156,033 counts/d for total physical activity, respectively. The model was adjusted for age, gender, center site, Hispanic/Latino background, education, smoking status, body mass index, total and HDL cholesterol, diabetes status, systolic blood pressure, anti-hypertensive use, use of lipid-lowering drugs, accelerometer wear time, and history of coronary heart disease or stroke. HDL, high-density lipoprotein.

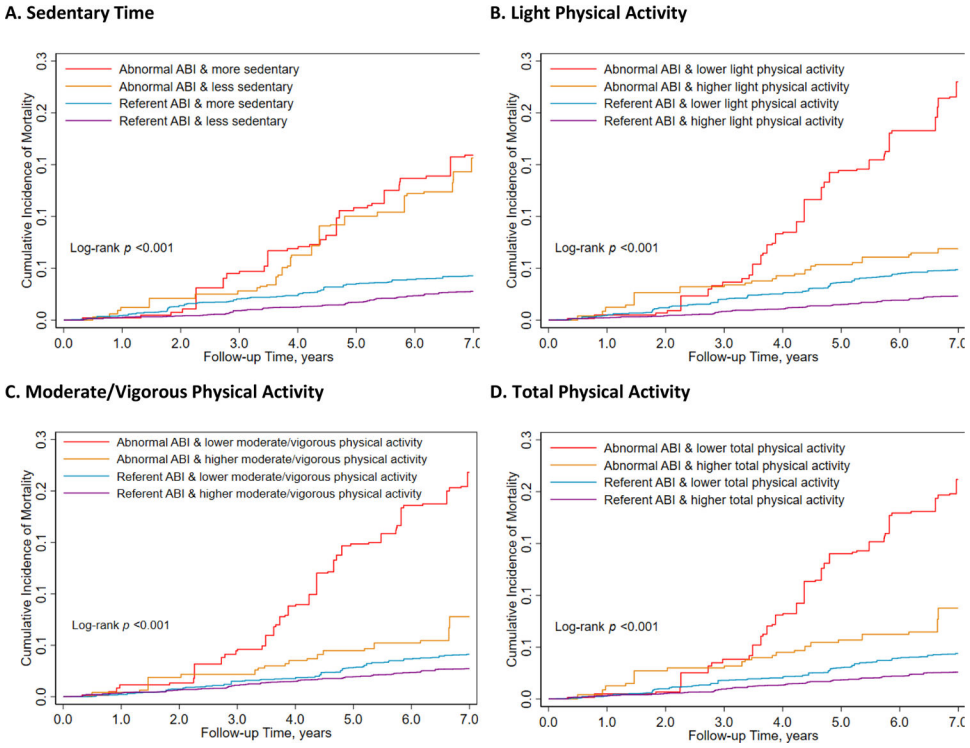

Figure 3.

Cumulative incidence of mortality by cross-categories of ABI and accelerometry-based measures

The accelerometry cutoff was 12.9 hours/d for less *vs.* more sedentary; 2.9 hours/d for lower *vs.* higher light physical activity; 6.3 mins/d for lower *vs.* higher moderate/vigorous physical activity, and 90,911 counts/d for lower *vs.* higher total physical activity. ABI, ankle-brachial index; PAD, peripheral artery disease.

Table 1.

Baseline characteristics of participants by ABI categories, HCHS/SOL (2008–2011)

	Ankle-Brachial Index		
Characteristic	**ABI≤0.9**	**0.9<ABI≤1.4**	**ABI>1.4**
Total participants, No. (unweighted)	364	7091	165
Age, y	61.2 (0.61)	56.2 (0.17)	61.5 (0.97)
Female, %	34.7 (3.2)	45.4 (0.8)	71.3 (5.3)
Hispanic/Latino background, %			
Dominican	8.5 (1.8)	9.9 (0.8)	6.1 (1.9)
Central American	5.1 (1.2)	6.6 (0.4)	4.0 (1.6)
Cuban	44.2 (3.9)	25.1 (2.0)	32.1 (5.6)
Mexican	19.5 (3.5)	33.1 (1.7)	29.7 (5.3)
Puerto Rican	16.3 (2.4)	17.8 (1.0)	20.6 (3.7)
South American	4.0 (1.0)	5.5 (0.4)	7.4 (2.2)
Other/mixed	2.4 (1.0)	2.0 (0.2)	0.2 (0.2)
Education status, %			
Less than high school	47.9 (3.6)	39.7 (1.0)	39.5 (5.5)
High school or equivalent	18.0 (3.2)	20.9 (0.7)	21.5 (4.3)
Greater than high school	34.1 (3.2)	39.4 (1.0)	39.0 (5.6)
Body mass index (kg/m^2)			
<25	24.5 (3.3)	16.9 (0.7)	16.7 (3.7)
25–30	35.0 (3.1)	41.7 (0.9)	26.4 (4.8)
≥30	40.4 (3.2)	41.4 (0.8)	56.9 (5.1)
Smoking status, %			
Never smoker	41.7 (3.6)	55.1 (0.9)	64.8 (5.4)
Former smoker	26.2 (3.0)	25.9 (0.9)	29.1 (5.3)
Current smoker	32.1 (3.4)	19.0 (0.8)	6.1 (1.8)
Prediabetes, %	38.3 (3.4)	47.6 (0.9)	42.9 (5.9)
Diabetes, %	44.4 (3.5)	26.5 (0.8)	47.6 (5.6)
Systolic blood pressure, mmHg	137.3 (1.40)	128.3 (0.33)	136.4 (2.09)
Use of anti-hypertensives, %	41.3 (3.5)	25.2 (0.8)	46.4 (5.8)
Total cholesterol, mg/dL	214.8 (3.21)	208.8 (0.85)	200.8 (4.78)
HDL-cholesterol, mg/dL	49.8 (0.91)	49.7 (0.23)	48.9 (1.20)
Use of lipid-lowering drugs, %	27.0 (3.3)	19.4 (0.8)	40.4 (5.9)
History of coronary heart disease, %	17.8 (2.8)	9.2 (0.5)	20.6 (5.1)
History of stroke, %	8.4 (2.2)	3.6 (0.3)	3.2 (1.8)
Accelerometer wear time, hours/d	15.4 [13.5–18.4]	15.5 [13.6–18.5]	16.9 [14.2–19.3]
Ankle-brachial index	0.85 [0.79–0.88]	1.07 [1.01–1.13]	1.66 [1.46–2.00]
Sedentary time, hours/d	12.1 [10.9–14.4]	11.8 [10.5–13.6]	13.2 [11.6–14.6]
Light physical activity, hours/d	2.9 [2.1–4.2]	3.5 [2.6–4.6]	2.9 [2.0–4.2]

	Ankle-Brachial Index		
Characteristic	**ABI≤0.9**	**0.9<ABI≤1.4**	**ABI>1.4**
Moderate/vigorous activity, mins/d	6.0 [1.6–15.3]	12.4 [4.5–26.8]	8.0 [1.7–24.3]
Total physical activity, counts/d	88822 [57826–133526]	120437 [79515–183118]	95746 [57951–162175]
Leg pain on exertion[a], %	56.4 (4.2)	42.0 (1.1)	54.6 (5.3)

[a]Reported data on leg pain symptoms were only available for 6,816 participants.

Continuous variables are given as mean (SE) or median [IQI]; categorical variables are given as percentage (SE). All estimates accounted for the complex sampling design. To convert total and HDL cholesterol from mg/dL to mmol/L, multiply by 0.02586.

ABI, ankle-brachial index; HCHS/SOL, the Hispanic Community Health Study / Study of Latinos; HDL, high-density lipoprotein; IQI, interquartile interval; SE, standard error.

Table 2.

Adjusted hazard ratios (95% CI) of mortality by cross-categories of ABI and accelerometry-based measures

ABI Categories	Sedentary Time		*p*-for-Interaction
	Less Sedentary (1st and 2nd tertiles)	More sedentary (3rd tertile)	
Referent ABI (0.9–1.4)	1 (Reference)	2.12 (1.32–3.41)[a]	0.26
Abnormal ABI (≤0.9 [PAD] or >1.4)	3.47 (1.96–6.16)[a]	3.59 (1.90–6.80)[a]	
	Light Physical Activity		
	Lower light physical activity (1st tertile)	Higher light physical activity (2nd and 3rd tertiles)	
Referent ABI (0.9–1.4)	2.14 (1.49–3.07)[a]	1 (Reference)	0.18
Abnormal ABI (≤0.9 [PAD] or >1.4)	5.61 (3.31–9.51)[a]	2.43 (1.37–4.31)[a]	
	Moderate/Vigorous Physical Activity		
	Lower moderate/vigorous activity (1st tertile)	Higher moderate/vigorous activity (2nd and 3rd tertiles)	
Referent ABI (0.9–1.4)	1.30 (0.91–1.86)	1 (Reference)	0.36
Abnormal ABI (≤0.9 [PAD] or >1.4)	3.91 (2.29–6.66)[a]	2.00 (1.14–3.49)[a]	
	Total Physical Activity		
	Lower total physical activity (1st tertile)	Higher total physical activity (2nd and 3rd tertiles)	
Referent ABI (0.9–1.4)	1.34 (0.92–1.95)	1 (Reference)	0.50
Abnormal ABI (≤0.9 [PAD] or >1.4)	3.86 (2.22–6.73)[a]	2.25 (1.27–3.99)[a]	

[a] $p < 0.05$

The 33rd percentile (1st – 2nd tertiles) and 67th percentile (2nd – 3rd tertiles) cutoffs were 11.0 and 12.9 hours/d for sedentary time, 2.9 and 4.2 hours/d for light physical activity, 6.3 and 20.2 mins/d for moderate/vigorous physical activity, and 90911 and 156033 counts/d for total physical activity, respectively. The model was adjusted for age, gender, center site, Hispanic/Latino background, education, smoking status, body mass index, total and HDL cholesterol, diabetes status, systolic blood pressure, anti-hypertensive use, use of lipid-lowering drugs, accelerometer wear time, and history of coronary heart disease or stroke. All estimates accounted for the complex sample design.

ABI, ankle-brachial index; CI, confidence interval; HDL, high-density lipoprotein; PAD, peripheral artery disease.