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Ankle Brachial Index (ABI) Predicts Change over Time in Functional Status in the San Diego Population Study (SDPS)

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Abstract

Background—Peripheral artery disease (PAD) affects millions of people, both in the US and world-wide. Even when asymptomatic, PAD and the ankle brachial index (ABI), the major clinical diagnostic criterion for PAD, are associated with decreased functional status and quality of life, as well as mobility impairment. Whether the ABI or change in the ABI predicts decline in functional status over time has not been previously assessed in a population-based setting.

Methods—Participants were 812 non-Hispanic white, African-American, Hispanic and Asian men and women from the San Diego Population Study (SDPS) who attended a baseline exam (1994–98), and follow up clinic exam approximately 11 years later. The Medical Outcomes Study 36-item short form (SF-36) was obtained at both the baseline and follow-up exams, and the summary performance score (SPS) at the follow up exam. Associations of the baseline ABI and clinically relevant change in the ABI (<-0.15 vs ≥ -0.15) with change in SF-36 scores over time were assessed using growth curve models, a type of mixed model which accounts for within participant correlation of measurements over time, and using linear regression for SPS. Models were adjusted for baseline age, sex, race/ethnicity, body mass index, ever smoking, physical activity, hypertension, diabetes, and dyslipidemia.

Results—Mean±SD for the baseline ABI was 1.11±0.10, and 50.8±9.0 for the baseline PCS, 50.1±9.5 for the baseline MCS, and 11.2±1.9 for the SPS at the follow-up exam. In fully adjusted models, each SD lower of the baseline ABI was significantly associated with an average decrease over time of 0.6 (95% CI (−1.1, −0.1), p=0.02) units on SF-36 PCS. Each SD lower of the baseline ABI was also significantly associated with an average decrease over time of 1.2 units ((−2.3,

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−0.2), p=0.02) on the SF-36 physical functioning subscale, and a decrease of 1.3 units ((−2.3, −0.3), p=0.01) on the SF-36 energy/vitality subscale in fully adjusted models. Baseline ABI was not significantly associated with change in the SF-36 MCS over time, or the SPS at the follow-up exam. Change in the ABI was not associated with SF-36 PCS, MCS or the SPS.

Conclusions—In this multi-ethnic population of healthy middle-aged community-living men and women, we showed that participants with a lower baseline ABI had declines in functional status over 11 years. Findings suggest that small differences in the ABI, even within the normal range, may identify subclinical lower extremity PAD, which in turn may help to identify individuals at risk for declining functional status with age.

Introduction

Peripheral artery disease (PAD) affects 8.5 million people in the US[1] and over 200 million people globally[2]. Between 2000 and 2010, PAD increased by almost 29% in low and middle income countries and 13% in high income countries[2]. It is well known that both PAD and a low ankle-brachial index (ABI), the major clinical diagnostic criterion for PAD, are associated with risk of adverse cardiovascular events and mortality[3–7]. Less well-recognized, but equally important, is that PAD, even when asymptomatic, is associated with decreased functional status, mobility, and quality of life[8–11]. Even pre-clinical or asymptomatic PAD is associated with mobility impairment, including inability to walk ¼ mile or climb one flight of stairs, as well as inability to complete a 6 minute walk[10]. Furthermore, functional performance and functional status predict mortality in those with PAD[12–15].

Several studies have examined the cross-sectional associations of a low ABI with functional status, but primarily in participants with already existing PAD[16–21]. These studies have found consistent evidence that lower ABI was associated with worse physical functioning, including poorer walking endurance[19,21], slower walking velocity[18,20], and shorter walking distances[18,20,21]. The ABI was also significantly correlated with the SF-36 Physical Component Score[16,17]. Two longitudinal studies have also found the ABI associated with functional decline among those with known, prevalent PAD[22,23].

Far fewer studies have examined the role of the ABI in functional status in population-based settings of participants with and without PAD[24,25]. Whether the ABI predicts change in functional status over time has not been previously assessed in a population-based setting. Thus, in the San Diego Population Study, a multi-ethnic prospective cohort of men and women predominantly without PAD at baseline, we examined associations of the ABI from a baseline exam with change in functional status over 11 years of follow-up. We additionally examined whether change in the ABI predicted change in functional status between the baseline and follow-up exams.

Methods

Study Participants

The San Diego Population Study (SDPS) enrolled an ethnically diverse group of 2404 men and women between 1994 and 1998 to study lower extremity PAD and venous diseases. Participants were current or former employees of the University of California, San Diego

and significant others of these employees, and were randomly chosen within age, sex and ethnicity strata. Age strata were 40–49, 50–59, 60–69 and 70–79 years; however, the overall age range of the study was 29–91, due to inclusion of a small number of significant others and volunteers (see below). Women and ethnic minorities (African-American, Hispanic, Asian) were over-sampled in order to have adequate power for hypotheses involving these groups. Of the 2404 participants, a small number of volunteers and their significant others (n=193) heard about the study, asked to participate, and were enrolled. The baseline clinic exam included persons of all levels of education and varying occupations, as well as working, unemployed, and retired persons.

The follow-up clinic exam took place between 2007 and 2011, following the same procedures and protocols as the baseline exam, and included 1103 participants who returned an average of 11 years later. Every effort was made to schedule and examine the participants in approximately the same order as they were examined at the baseline visit. Further details of the study have been published elsewhere [26–28].

For all study procedures, participants provided signed informed consent after a detailed introduction and description of the study at both the baseline and follow-up examinations. The study received approval from the Institutional Review Board Committee on Investigations Involving Human Subjects at University of California-San Diego (UCSD).

Ankle Brachial Index (ABI)

At the baseline and follow-up examinations, systolic blood pressure was measured in both arms with the participant in a supine position. Continuous wave Doppler ultrasound was used to measure systolic blood pressure two times in the posterior tibial artery. If there was no obtainable signal in the posterior tibial artery, the dorsalis pedis was used; this occurred rarely. The ABI at both the baseline and follow-up exams was calculated as the average systolic blood pressure in the posterior tibial artery or dorsalis pedis divided by the higher of the SBP in the two arms. The higher arm SBP was used in these calculations due to previous studies showing a strong association between PAD and subclavian stenosis[29]. The overall ABI at both the baseline and follow-up exams for each individual was defined as the lower of the left and right ABI.

Measures of Physical and Mental Function

The Medical Outcomes Study 36-item short form (SF-36) questionnaire was used to measure health related quality of life and functional status at both the baseline and follow-up exams[30]. Administration of the SF-36 questionnaire began after the commencement of the baseline exam, so was not available in all participants at baseline. However, the 1793 participants who completed the SF-36 at the baseline exam did not appear to differ substantially from the 611 participants who did not (Supplemental Table I), with the exception of age and prevalence of hypertension. SF-36 Version 1 was used at the baseline exam, and Version 2 at the follow-up exam, but the slight differences between Versions 1 and 2 still results in comparable SF-36 scores[31,32]. From the questionnaire responses, the Physical Component Score (PCS), Mental Component Score (MCS) as well as the subscale scores (Physical Functioning, Role Physical, Bodily Pain, General Health, Energy/Vitality,

Social Functioning, Role Emotional, and Mental Health) were calculated, and the PCS and MCS were standardized[30]. The subscale scores range from 0–100 while the PCS and MCS are standardized to a t-distribution.

At the follow-up exam, participants also completed the three component measures of the summary performance score (SPS), including time to rise from a seated position 5 times, the standing balance, and usual 4-meter walking velocity[33]. Each component is scored from 0 and 4; a "0" on the components corresponds to an inability to complete the test, while a "4" corresponds to best performance. The three component scores are summed to calculate the overall SPS, which can range from 0–12. The scale is derived from normative data in 6,534 community-dwelling older men and women participating in the Established Populations for the Epidemiologic Study of the Elderly[33].

Covariates

Age, sex and race/ethnicity at baseline were determined via questionnaire. Current and past cigarette smoking habits were also ascertained via baseline questionnaire, smoking was defined as ever having smoked versus never smoked. Height (in centimeters) and weight (in kilograms) were measured, and the body mass index (BMI) was calculated as kg/m^2. Physical activity was assessed via self-report, with a question asking "Compared to other persons your age, how would you describe your level of physical activity: much less active, somewhat less active, about as active, somewhat more active, or much more active?" Much less and somewhat less categories were combined due to small numbers. Diabetes at baseline was defined as self-report, or use of anti-diabetic medications or insulin. Hypertension at baseline was defined as a systolic pressure ≥ 140 mm Hg or a diastolic pressure ≥ 90 mm Hg, or use of anti-hypertensive medications.

A blood sample was drawn, and total and HDL cholesterol were measured with standardized laboratory assays (Beckman Coulter analyzer). Dyslipidemia, which has consistently been found to be the best single lipid/lipoprotein parameter in assessing cardiovascular disease (CVD) risk[34], was defined as a ratio of total cholesterol to HDL cholesterol (TC/HDL) > 5.0 or use of lipid lowering medications at baseline.

Statistical Analysis

Univariate associations of baseline characteristics with tertiles of the SF-36 PCS were assessed using chi-square or ANOVA as appropriate. Baseline ABI was modeled per standard deviation increment *lower*. Clinically relevant change in the ABI was modeled as a binary variable, defined as change in the ABI<−0.15 versus ≥−0.15[35]. Baseline covariates were used in all models, with the ABI or clinically relevant change in the ABI as the independent variable and functional status measures as the outcomes. To examine associations of baseline ABI and change in the ABI with SPS at follow-up, linear regression was used. To examine the association of the baseline ABI and change in the ABI with change in the SF-36 PCS, MCS and subscales, growth curve models, a type of linear mixed model, were used with an unstructured correlation matrix to account for within participant correlation of the SF-36 PCS, MCS, and subscale outcomes measured at two time points. Growth curve models are often used to model changes over time in continuous outcomes.

Using raw change, as in the context of a standard linear regression model, can compound the measurement error from two time points rather than cancelling it out. Alternatively, growth curve models minimize the error normally encountered by using raw change scores as the outcome (in our case, the SF-36 PCS, MCS, and subscales), and ensure the greatest precision; thus we chose to use growth curve models to examine change in the SF-36 PCS, MCS, and subscale outcomes. Potential confounders were staged into the models as follows: unadjusted; then adding demographics (age, sex, race/ethnicity); then adding BMI, ever smoker, physical activity, diabetes, hypertension, and dyslipidemia. SAS Version 9.3 was used for modeling analysis, with figures created in Excel and Stata Version 12.

Results

A total of 812 participants had baseline ABI, change in the ABI, the SF-36 outcomes at both exams, and the SPS at the follow-up exam. An additional eight participants with ABI>1.4 at the baseline exam were excluded for multivariate analysis, as this generally indicates arterial stiffening and it is unknown whether these participants also have significant lower extremity obstructive or atherosclerotic disease[36,37]. Table I shows baseline participant characteristics by tertile of baseline SF-36 PCS. Participants differed significantly across tertiles in age, sex, race/ethnicity, BMI, physical activity, hypertension, systolic blood pressure, diabetes, and the ABI (Table I). In general, those in the highest tertile of the PCS, indicating better functional status, appeared to have the best overall CVD risk factor profile. The average ABI increased slightly from the baseline to the follow-up exam (Table II); however this was due to several participants who appeared to progress to a much higher ABI at the follow-up exam (Supplemental Figure 1). The average PCS and MCS decreased over approximately 11 years of follow-up, and the mean±SD SPS was 11.2 ± 1.9 at the follow-up exam (Table II).

In unadjusted models, the ABI at baseline was significantly associated with change over time in several SF-36 subscales, including physical functioning, role physical, bodily pain, general health, energy/vitality and social functioning (Table III). However, after adjustment for demographics, lifestyle factors and comorbidities, associations were somewhat attenuated. In fully adjusted models, each standard deviation (SD=0.095) lower of the ABI was significantly associated with an average decrease over time of 1.2 units on the physical functioning subscale, and a decrease of 1.3 units on the energy/vitality subscale (Table III). Each SD lower of the baseline ABI was significantly associated with an average decrease over time of 1.3 units (95% CI (−1.9, −0.8), p<0.001) in PCS and an average decrease of 0.9 units (95% CI (−1.5, −0.3), p=0.005) in MCS in unadjusted models (Figure 1). After adjustment, lower baseline ABI remained significantly associated with an average decreased in the PCS (−0.6, 95% CI (−1.1, −0.1), p=0.02), but not the MCS (Figure 1). Baseline ABI was not significantly associated with SPS at the follow-up exam (Figure 1). A clinically relevant decrease in the ABI of <−0.15 compared to ≥−0.15 was also not significantly associated with change over time in the PCS or MCS, or the SPS at follow-up in fully adjusted models (Table IV).

Discussion

In a multi-ethnic prospective population-based cohort of men and women with predominantly normal range ABI, we found that a lower ABI at baseline significantly predicts decline in functional status over 11 years of follow-up as measured by the SF-36 physical component score (PCS). A lower baseline ABI also significantly predicted a decrease in the SF-36 physical functioning and energy/vitality subscale scores. However, after adjustment, a lower baseline ABI was not significantly predictive of a decline in SF-36 mental component score (MCS) over time. Baseline ABI was not significantly associated with the SPS measured 11 years later. Clinically relevant change in the ABI over time was also not significantly associated with the SF-36 PCS, SF-36 MCS or the SPS. The discrepancy in findings with the baseline ABI and change in the ABI is likely due in part to relatively lower power to detect associations with clinically relevant change in the ABI. In this population-based study of relatively healthy individuals, only 47 participants had what would be considered a clinically relevant decrease in the ABI over time of −0.15. It is also possible that an unknown confounding factor is present which varies with both change in the ABI and change in functional status measures.

Although previous studies have examined associations of the ABI with functional status, the majority of these studies have been in participants with existing PAD[16–19,21,22], have had small sample sizes[16,17,19,22], were cross-sectional study designs[16–18,20,21,24,25], or were not population-based[16–19,21,22]. In the current study, we showed that a lower baseline ABI predicts decline in functional status over 11 years in a multi-ethnic cohort of men and women. This association was evident even though the mean ABI was squarely within the normal range at baseline in our participants. Despite differences in study design and use of differing measures of functional status, results of previous studies have been largely consistent with the current study, showing that a lower ABI is significantly associated with worse functional status and in particular, worse physical function. McDermott et al[20] showed a lower ABI was associated with larger declines in 6 minute walk performance over a 2 year follow up among a cohort of 676 men and women with and without PAD. In a cross-sectional population-based study of 915 participants aged 45–70 years with at least one cardiovascular risk factor, both PAD (ABI≤0.90) and borderline PAD (0.91≤ABI≤1.00) were associated with worse functional status as measured by the SF-36 PCS[24]. In 1635 participants aged 70–89 from the Lifestyle Interventions and Independence for Elders (LIFE) study, lower ABI values were associated cross-sectionally with longer 400m walk times and slower walking velocity[25]. Similar to our study, ABI groups (<0.90, 0.90–0.99, 1.00–1.09, 1.10–1.4) were not associated with the short physical performance battery (SPPB), another name for the SPS, in the LIFE study[25].

Often there is some question as to whether the magnitudes of intra-individual change in the SF-36 scores over time are clinically relevant. The most commonly suggested metric, the minimal clinically important difference (MCID), which is closely approximated by one standard error of the mean (SEM) in the work of Wyrich et al[38–40], is largely based upon older populations with already existing significant comorbidities, i.e. heart failure and chronic obstructive pulmonary disease. However, the average age of our relatively healthy population is 57 years at baseline, so this criterion may not be appropriate. Additionally the

utility of the MCID or the SEM criterion has not been established in a population-based setting such as the current study. Our standard errors (SEs) of the beta estimates, or the average decline in SF-36 scores over time, are less than half the size of the beta estimates, and these estimates are *per standard deviation* decrease in the ABI. For example, the average decline in the physical functioning subscale over time is 1.2 units per standard deviation lower of the ABI, with an SE of 0.52. Additionally, in our study, each standard deviation increment lower of the ABI is associated with a decline in physical functioning which is about two times greater than the decline associated with each additional year of baseline age, i.e. each additional year of age was associated with a decrease of 0.65 units in the physical functioning subscale, while each SD lower of the baseline ABI was associated with a decrease of 1.2 units. Although these declines over time in functional status may seem small in terms of clinical relevance, in a population-based setting such as this, the main aim is ultimately to identify early declines in physical function which are likely due to pre-clinical or asymptomatic PAD, i.e. small differences in the ABI. Given the high cost and comorbid conditions associated with PAD and the high mortality risk among those with PAD, early detection of decline in functional status associated with lower extremity PAD may be relevant to early intervention and prevention.

Our study has several strengths. The SDPS is a multi-ethnic prospective cohort of men and women specifically designed to study lower extremity disease. The current analysis makes use of the 11 years of follow-up time of the cohort, and the repeated measurements of the SF-36. We were able to determine whether the ABI is associated with measures of functional status in a relatively healthy population, likely in the earlier stages of the lower extremity disease process. Most previous studies have concentrated on those with existing PAD or much older populations.

The study also has some important limitations. The SPS was only available at the follow-up exam, so we could not examine decline over time for this measurement. We did not have enough participants with ABI<0.90 in this population to adequately examine associations of ABI groupings and/or prevalent and incident PAD. A loss to follow-up between exams could have resulted in a healthy survivor bias in our results; however, our aim was to study the ABI in relatively healthy individuals at baseline, with the goal of early detection of decline in functional status associated which may be associated with lower extremity PAD. We observed relatively small declines in functional status over time, which are statistically significant in this population-based study of relatively healthy individuals, but may not be relevant to a clinical study or setting in which many of the participants have a significant level of disease. Additionally, our main goal was to identify early declines in physical function in a population-based setting which are likely due to pre-clinical or asymptomatic PAD.

Conclusions

In this multi-ethnic population of predominantly healthy middle-aged community-living men and women, we showed that participants with lower ABI had declines in functional status over 11 years. The association was primarily driven by declines in the physical performance score, but not the mental component score of the SF-36. These findings suggest

that subtle decreases in the ABI, even within the normal range, may identify sub-clinical lower extremity PAD, and this, in turn may identify individuals at risk for loss of physical function with age.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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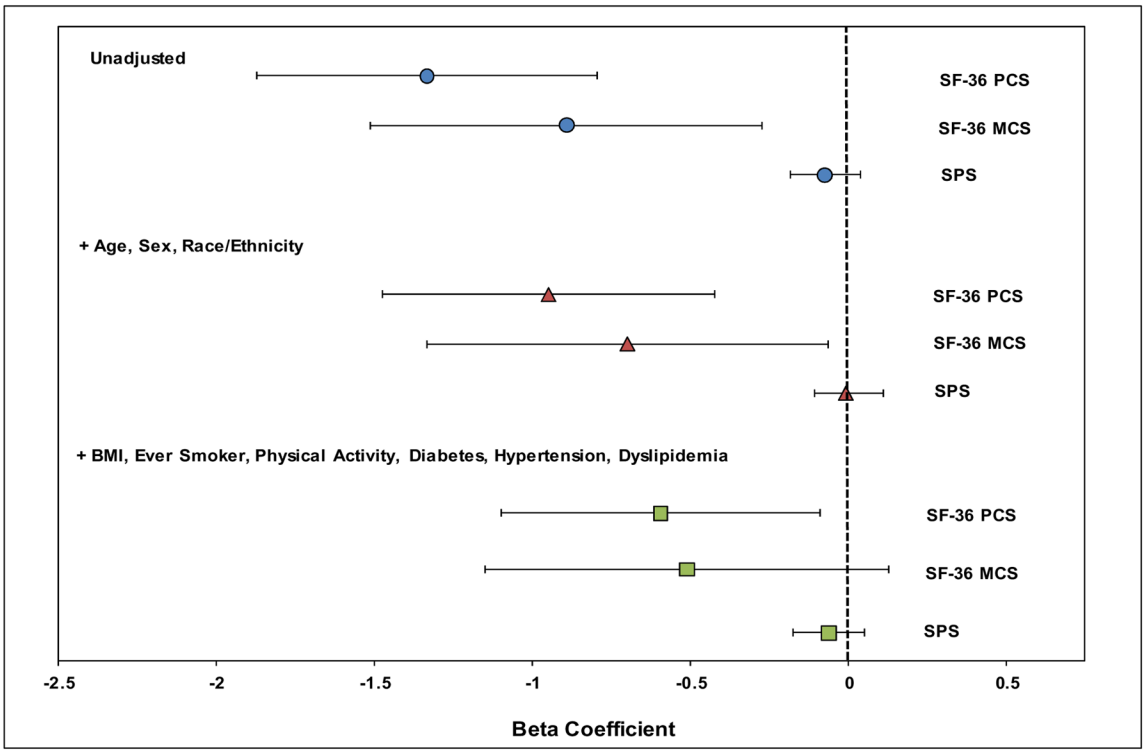

Figure 1. Associations of Baseline ABI per standard deviation with Change in PCS and MCS, and SPS at Follow-up*

Figure 1 displays associations of the baseline ankle brachial index (ABI) measurement with change in SF-36 physical component score (PCS) and mental component score (MCS) over time, as well as summary performance score (SPS) at follow-up. The x-axis denotes the beta coefficients for the models. The dashed black line represents a null value of zero, or no association. The blue circles represent the beta coefficients for unadjusted models, the red triangles represent beta coefficients in models adjusted for age, sex and race/ethnicity, while the green squares represent beta coefficients for fully adjusted models with age, sex, race/ethnicity, ever smoker, BMI, physical activity, diabetes, hypertension and dyslipidemia. The error bars are the 95% confidence intervals around the beta coefficients.

*Among those with ABI<1.4 at baseline; standard deviation for ABI = 0.095

J Vasc Surg. Author manuscript; available in PMC 2017 September 01.

Table I

Baseline Participant Characteristics by Tertile of SF-36 Physical Component Score (PCS)*

	SF-36 PCS			
	Tertile 1 ≤50.11 n=273	**Tertile 2 50.12–56.10 n=274**	**Tertile 3 ≥56.11 n=265**	**p-value**
Age, years	60 ± 10	57 ± 9	55 ± 9	<0.001
Female Sex, n(%)	200 (73%)	182 (66%)	148 (56%)	<0.001
Race/Ethnicity, n(%)				
Non-Hispanic White	148 (54%)	178 (65%)	167 (63%)	0.002
Hispanic	36 (13%)	35 (13%)	38 (14%)	
African-American	52 (19%)	17 (6%)	27 (10%)	
Asian	32 (12%)	40 (15%)	30 (11%)	
Other	5 (2%)	4 (2%)	3 (1%)	
Ever Smoker, n(%)	130 (48%)	117 (43%)	114 (43%)	0.43
Body Mass Index, kg/m^2	28 ± 6	26 ± 4	25 ± 4	<0.001
Physical Activity, n(%)†				
Less active	56 (21%)	31 (12%)	23 (9%)	<0.001
Same active	65 (25%)	73 (27%)	46 (17%)	
More active	147 (55%)	164 (61%)	195 (74%)	
Prevalent Hypertension, n(%)	144 (53%)	97 (35%)	84 (32%)	<0.001
Systolic Blood Pressure, mmHg	131 ± 21	128 ± 18	126 ± 18	0.01
Diastolic Blood Pressure, mmHg	77 ± 11	77 ± 10	77 ± 10	0.62
Prevalent Diabetes, n(%)	26 (10%)	13 (5%)	5 (2%)	<0.001
Total Cholesterol, mg/dL	212 ± 36	212 ± 39	206 ± 41	0.18
HDL Cholesterol, mg/dL	54 ± 17	56 ± 17	56 ± 17	0.36
Dyslipidemia, n(%)‡	84 (31%)	78 (28%)	65 (25%)	0.27
Ankle Brachial Index	1.10 ± 0.11	1.12 ± 0.10	1.13 ± 0.09	0.008

*Only for 812 participants with *both baseline and follow-up data* on the ABI, SF-36 physical component score (PCS), mental component score (MCS), and follow-up data on the summary performance score (SPS)

† Compared to other persons your age, how would you describe your level of physical activity: much less active, somewhat less active, about as active, somewhat more active, or much more active? Much less and somewhat less categories were combined.

‡ Total Cholesterol/HDL>5.0 or use of lipid-lowering medications

Table II

Baseline and Follow-up Ankle Brachial Index, Peripheral Artery Disease, SF-36 and SPS

	Baseline Exam 1994–98	Follow-Up Exam 2007–11	Unadjusted Change Between Exams
SF-36 PCS *	51.0 ± 8.8	50.3 ± 9.2	−0.72 ± 9.0
SF-36 MCS *	51.2 ± 10.1	49.9 ± 10.9	−1.22 ± 11.0
SPS *	--	11.2 ± 1.9	--
Ankle Brachial Index *	1.12 ± 0.10	1.14 ± 0.15	0.02 ± 0.16
Peripheral Artery Disease †	15 (1.8%)	23 (2.8%)	--
Clinically Relevant Change ABI †	--	--	47 (5.8%)

*Mean ± SD for n=812 participants with both baseline and follow-up data for the physical component score (PCS), mental component score (MCS), and the ankle brachial index (ABI), as well as summary performance score (SPS) at follow-up

†n(%) for n=812 participants with both baseline and follow-up data; PAD defined as ABI<0.90; a clinically relevant change is defined as a change in the ABI of <−0.15 versus >−0.15

Table III

Associations of baseline ABI per standard deviation with change in SF-36 Subscales*

Subscale	Unadjusted β (95% CI); p	Demographic Adjusted† β (95% CI); p	Fully Adjusted‡ β (95% CI); p
Physical Functioning	**−3.0 (−4.2, −1.9); <0.001**	**−2.1 (−3.2, −1.0); <0.001**	**−1.2 (−2.3, −0.2); 0.02**
Role Physical	**−2.4 (3.9, −1.0); 0.001**	**−1.9 (−3.3, −0.4); 0.01**	−1.3 (−2.8, 0.1); 0.07
Bodily Pain	**−2.1 (−3.3, −1.0); <0.001**	**−1.5 (−2.6, −0.3); 0.01**	−1.0 (−2.2, 0.2); 0.09
General Health	**−1.4 (−2.5, −0.4); 0.008**	**−1.2 (−2.3, −0.1); 0.03**	−0.5 (−1.5, 0.6); 0.36
Energy/Vitality	**−1.9 (−2.9, −0.9); <0.001**	**−1.7 (−2.7, −0.6); 0.002**	**−1.3 (−2.3, −0.3); 0.01**
Social Functioning	**−1.3 (−2.2, −0.3); 0.008**	**−1.0 (−2.1, −0.1); 0.04**	−1.0 (−2.0, 0.05); 0.06
Role Emotional	0.8 (−1.9, 0.3); 0.17	−0.5 (−1.6, 0.7); 0.43	−0.3 (−15.9, 9.3); 0.61
Mental Health	−0.4 (−1.2, 0.3); 0.27	−0.4 (−1.2, 0.4); 0.29	−0.3 (−1.1, 0.6); 0.53

*Among those with ABI<1.4 at baseline; standard deviation for ABI = 0.095

†Adjusted for age, sex, race/ethnicity

‡Adjusted for age, sex, race/ethnicity, BMI, ever smoker, physical activity, diabetes, hypertension, dyslipidemia

Table IV

Associations of Clinically Relevant Change in the ABI over time with the SF-36 and SPS*

	Change in SF-36 PCS β (95% CI); p	Change in SF-36 MCS β (95% CI); p	SPS at Follow-Up β (95% CI); p
Unadjusted	−1.0 (−3.6, 1.6); 0.47	−2.3 (−5.3, 0.6); 0.12	−0.6 (−1.1, −0.1); 0.01
+Demographics†	−0.3 (−2.7, 2.2); 0.84	−2.4 (−5.3, 0.6) 0.12	−0.3 (−0.8, 0.1); 0.17
+Lifestyle/Comorbidities/Lipids‡	−0.16 (−2.4, 2.1); 0.89	−2.6 (−5.4, 0.3); 0.07	−0.3 (−0.8, 0.2); 0.22

*Among those with ABI<1.4 at baseline; clinically relevant change in the ABI is defined as <−0.15 compared to ≥−0.15

†Adjusted for age, sex, race/ethnicity

‡Adjusted for age, sex, race/ethnicity, BMI, ever smoker, physical activity, diabetes, hypertension, dyslipidemia

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