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ORIGINAL RESEARCH

One-Year Change in Walking Performance and Subsequent Mobility Loss and Mortality Rates in Peripheral Artery Disease: Longitudinal Data From the WALCS

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BACKGROUND: Associations of 1-year change in functional performance measures with subsequent mobility loss and mortality in people with lower extremity peripheral artery disease are unknown.

METHODS AND RESULTS: Six-minute walk and 4-meter walking velocity (usual and fastest pace) were measured at baseline and 1 year later in 612 people with peripheral artery disease (mean age 71±9 years, 37% women). Participants were categorized into tertiles, based on 1-year changes in walking measures. Cox proportional hazards models were used to examine associations between 1-year change in each walking measure and subsequent mobility loss and mortality, respectively, adjusting for potential confounders. Compared with the best tertile, the worst tertile (ie, greatest decline) in 1-year change in each performance measure was associated with higher rates of mobility loss: 6-minute walk (Tertile 1 [T1] cumulative incidence rate [IR], 72/160; Tertile 3 [T3] IR, 47/160; hazard ratio [HR], 2.35; 95% CI, 1.47–3.74), usual-paced 4-meter walking velocity (T1 IR, 54/162; T3 IR, 57/162; HR, 2.21; 95% CI, 1.41–3.47), and fast-paced 4-meter walking velocity (T1 IR, 61/162; T3 IR, 58/162; HR, 1.81; 95% CI, 1.16–2.84). Compared with the best tertile, the worst tertiles in 1-year change in 6-minute walk (T1 IR, 66/163; T3 IR, 54/163; HR, 1.61; 95% CI, 1.07–2.43) and fast-paced 4-meter walking velocity (T1 IR, 63/166; T3 IR, 44/166; HR, 1.75; 95% CI, 1.16, 2.64) were associated with higher mortality.

CONCLUSIONS: In people with peripheral artery disease, greater 1-year decline in 6-minute walk or 4-meter walking velocity may help identify people with peripheral artery disease at highest risk for mobility loss and mortality.

Key Words: mobility loss ■ mortality ■ peripheral artery disease ■ walking performance

People with lower extremity peripheral artery disease (PAD) have poorer 6-minute walk distance and slower walking velocity than those without PAD.[1] Although poorer 6-minute walk and slower walking velocity measured at a single time point are associated with higher rates of adverse outcomes in PAD,[2] associations of 1-year change in these walking measures with subsequent adverse outcomes are unclear.

This study combined data from 3 longitudinal observational studies to assess the association of 1-year change in 6-minute walk distance, usual-paced 4-meter walking velocity, and fast-paced 4-meter walking velocity with subsequent mobility loss and all-cause mortality in people with PAD. The association of 1-year change in self-reported walking difficulty due to pain in the calves or buttocks and the association of 1-year change in self-reported walking difficulty due to pain in the thighs and subsequent mobility loss and all-cause mortality, respectively, were also examined. Study hypotheses were that greater 1-year worsening of each objective and subjective measure would be associated with higher rates of subsequent mobility loss and all-cause mortality.

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CLINICAL PERSPECTIVE

What Is New?

- In 612 people with peripheral artery disease, greater 1-year declines in 6-minute walk distance, usual-paced 4-meter walking velocity, and fast-paced 4-meter walking velocity were each associated with higher rates of subsequent mobility loss.
- Greater declines in 6-minute walk and fast-paced 4-meter walking velocity were associated with the highest rates of subsequent all-cause mortality.

What Are the Clinical Implications?

- Clinicians may potentially perform serial annual measures of 6-minute walk or 4-meter walking velocity to identify patients with peripheral artery disease at the highest risk of mobility loss and mortality.

Nonstandard Abbreviation and Acronym

WALCS Walking and Leg Circulation Study

METHODS

Study Population

Participants were part of the WALCS (Walking and Leg Circulation Study), WALCS II, and WALCS III longitudinal observational studies designed to study functional impairment and decline in people with PAD.[3–10] Methods of the 3 cohorts have been described[3–10] and are summarized in Table 1. The study was approved by the institutional review board at Northwestern University and all participating institutions. All participants provided written informed consent. Data that support the findings of this article are available from the corresponding author upon reasonable request.

Participant Identification

Participants with PAD were identified from noninvasive vascular laboratories or in vascular surgery, cardiology, and/or general medical practices and geriatric and endocrinology clinics from medical centers in Chicago.[3–10] Participants were assessed at baseline and annually, for up to 4 annual follow-up visits.

Inclusion and Exclusion Criteria

WALCS enrolled participants aged 55 years and older, and WALCS II enrolled participants aged 59 years and older. There was no age inclusion criterion for WALCS III. Participants with PAD from the 3 WALCS cohorts who had ankle brachial index (ABI) values <0.90 at baseline were included in these analyses.

For all cohorts, potential participants with dementia, recent major surgery, or above-or-below knee amputation; nursing home residents; and those wheelchair bound were excluded. Non-English speaking participants were excluded because the investigators were not fluent in non-English languages. Because WALCS III assessed the association between magnetic resonance imaging measured femoral artery plaque characteristics with mobility loss, participants with contraindications to magnetic resonance imaging testing were excluded from the WALCS III cohort. Additionally, for WALCS III, those who required oxygen or stopped a 6-minute walk test due to dyspnea and those with severe osteoarthritis of the knee were excluded.[3,4] For all 3 cohorts, participants with mobility impairment at baseline or 1-year follow-up and those who died between baseline and 1-year follow-up were excluded from these analyses.

Ankle Brachial Index Measurement

Following standardized methods, a hand-held Doppler probe (Nicolet Vascular Pocket Dop II, Nicolet Biomedical Inc., Golden, CO) was used to measure systolic pressures in the left and right brachial, dorsalis pedis, and posterior tibial arteries. The systolic pressures were measured twice. ABI was calculated by dividing the mean of the dorsalis pedis and posterior tibial pressures in each leg by the mean of the 4 brachial pressures.[11] The pressures in the arm with the highest pressures were used when one arm pressure was higher than the opposite arm pressure in both sets of pressure measurements, and the difference between the left and right brachial pressures was 10 mm Hg or more in at least 1 set of measurements. These individuals were likely to have subclavian stenosis.[12] The lowest leg ABI was used in analyses.

Six-Minute Walk

The 6-minute walk is a well-validated test in people with PAD that measures walking endurance.[13,14] The test was performed in a 100-foot hallway by trained and certified staff. Participants were instructed to walk back and forth in the 100-foot hallway, covering as much ground as possible in 6 minutes. Participants were allowed to rest if necessary, but the clock continued to run during resting periods. At the end of the test, the total distance walked was measured.[2,14,15]

Four-Meter Walking Velocity

Walking velocity over 4 meters was measured at usual and at fastest pace. For the “usual”-paced walk,

Table 1. Description of WALCS Cohorts

Study	Sample size	Study period	Study primary aim[3–10]
WALCS	339 participants aged 55 y and older.	Between 1998 and 2004	To examine the association between ankle brachial index and leg symptoms and annual decline in 6-minute walk distance over time.
WALCS II	177 participants aged 59 y and older	Between 2002 and 2009	To examine the association between calf skeletal muscle characteristics and nerve conduction velocity at baseline and decline in 6-minute walking distance over time.
WALCS III	261 participants*	Between 2007 and 2014	To examine the relationship between magnetic resonance imaging-measured atherosclerotic plaque characteristics in the superficial femoral artery and functional impairment and decline among people with peripheral artery disease

WALCS indicates Walking and Leg Circulation Study.
*No age inclusion criterion was used in WALCS III.

participants were instructed to walk at their usual pace, "as if going down the street to the store." For the fastest paced walk, participants were instructed to walk at their fastest pace. Each walk was performed twice, with the faster walking velocity in each pair used in analyses.

Walking Impairment Questionnaire

The Walking Impairment Questionnaire is a PAD-specific measure of self-reported walking limitations with 3 sections: walking distance, walking speed, and stair climbing.[17] This study focused on 2 questions from the Walking Impairment Questionnaire, because those directly focused on participant-reported walking difficulty due to leg symptoms. The questions were administered at baseline and 1-year follow-up, and responses were compared between these 2 periods. In the first question, participants were asked to rank on a Likert scale of 0 to 4 their perceived difficulty walking due to pain or aching in the calves or buttocks. For the second question, participants were asked to rank on a Likert scale of 0 to 4 their perceived difficulty walking due to pain or aching in the thighs. A score of 0 implied very much difficulty, whereas a score of 4 implied no walking difficulty due to pain in the calves or buttocks (question 1) or thighs (question 2).

Walking Exercise

Data on participation in supervised exercise were not collected. Walking exercise was determined based on self-report of walking for exercise at baseline. Participants who reported walking for exercise for at least 3 days per week for at least 30 minutes per day were classified as "walking for exercise."[18]

Comorbidities

Comorbidities assessed at baseline were diabetes, angina, myocardial infarction, heart failure, cancer, pulmonary disease, hip and knee arthritis, spinal stenosis, and spinal disc disease. These comorbidities were ascertained and verified using disease-specific-algorithms that combined data from patient report, medical record review, medications, laboratory values, and a questionnaire completed by the participant's primary care physician.[19] Knee and hip osteoarthritis were diagnosed using the American College of Rheumatology criteria.[20,21]

Other Measures

Height and weight were measured at the baseline visit. Body mass index was calculated by dividing weight in kilograms by the square of height in meters. The other measures included age, sex, race/ethnicity, and smoking status, which were obtained from self-report. Statin use was determined by review of medication lists or bottles of medication brought to study visits, and adjudicated by the senior author (MMM). Lower extremity revascularization was determined by self-report and assessed at each follow-up visit using a questionnaire administered to all participants.

Mobility Loss

Associations between 1-year changes in objective or subjectively assessed walking performance and subsequent mobility loss were evaluated. At baseline and each follow-up visit, participants were asked whether they could walk one-quarter mile or walk up and down a flight of stairs, either on their own, with assistance, or not at all. Mobility impairment was defined as the inability to walk one-quarter mile or walk up and down a flight of stairs without assistance. Mobility loss was defined as becoming newly unable to walk one-quarter mile or walk up and down 1 flight of stairs without assistance after the 1-year follow-up period, among those able to walk one-quarter mile and walk up and down a flight of stairs at baseline and at 1-year follow-up.[22]

All-Cause Mortality

Deaths were systematically ascertained at the time of each follow-up visit from family members or primary

care physicians and subsequently confirmed with death certificates. For participants whose family members or primary care physicians could not be reached to ascertain vital status during follow-up, death was determined by searching the Social Security Administration Death Index.[2] A total of 206 of the 248 deaths (83%) identified during follow-up were confirmed with death certificates.

Statistical Analysis

One-year change in each objective measure of walking performance measure (6-minute walking distance, usual- and fast-paced 4-meter walking velocity) was calculated as the difference between the walking performance measure at 1-year follow-up and that at baseline. For each walking performance measure, participants were categorized into tertiles according to their 1-year change in walking performance between baseline and 1-year follow-up (Tertile 1: greatest decline). Baseline characteristics were compared between participants in the 3 walking performance tertiles using general linear models for continuous variables and chi-square tests/Fisher's exact test for categorical variables.

Based on changes in baseline to 1-year follow-up in self-reported walking difficulty due to pain in the calves or buttocks and pain in the thighs, participants' reports of walking difficulty were classified as "worse," "improved," or "no change." Participants who reported lower or higher Likert scale scores at the 1-year follow-up for each question, compared with baseline, were classified as "worse" and "improved," respectively. Participants who reported the same score at both baseline and 1-year follow-up were classified as "no change." Analyses of change in self-reported walking difficulty due to pain in the calves or buttocks were performed separately from analyses of change in walking difficulty due to pain in the thighs because in a previous study,[23] participant-reported change in walking difficulty due to pain in the calves or buttocks was not uniformly consistent with participant-reported change in walking difficulty due to pain in the thighs.

Chi-square tests were used to examine the association between 1-year change in self-reported walking difficulty due to pain in the calves or buttocks and 1-year change in self-reported walking difficulty due to pain in the thighs, respectively, with 1-year change in 6-minute walk tertiles.

Cumulative incidence curves were plotted to estimate cumulative rates of mobility loss across tertiles of 1-year change in walking performance for each functional measure. Death before developing mobility loss was treated as a competing risk and right-censored for studying the cause-specific hazard ratios (HR) associated with mobility loss. Cox proportional hazards analyses were performed to examine the association between 1-year change in functional performance tertiles and time to subsequent mobility loss and all-cause mortality, respectively, adjusting for potential confounders. Model 1 adjusted for WALCS cohort and baseline functional performance measure. Model 2 adjusted for variables in Model 1 and age, sex, race, baseline ABI, body mass index (BMI), smoking status, diabetes, heart failure, myocardial infarction, angina, pulmonary disease, hip arthritis, knee arthritis, spinal disc disease, spinal stenosis, cancer, statin use, and walking exercise. The Cox proportional hazards analyses were repeated for the association between 1-year change in self-reported walking difficulty due to pain in the calves or buttocks and due to pain in the thighs, respectively, and subsequent mobility loss and all-cause mortality, respectively, using the group that reported "improved" walking performance as reference. In additional analyses of self-reported walking difficulty due to pain in the calves or buttocks and pain in the thighs, the Cox models were additionally adjusted for tertiles of 1-year change in 6-minute walk and baseline 6-minute walk distance.

In sensitivity analyses, Cox models for the association of 1-year change in each functional performance measure with subsequent mobility loss and death were restricted to participants who did not undergo lower extremity revascularization during follow-up. Analyses were performed using SAS statistical software (version 9.4, SAS Institute, Cary, NC) and R statistical software (version 4.0.3, The R Foundation for Statistical Computing). Statistical significance was defined as $P<0.05$.

RESULTS

Of 1079 unique participants with PAD in WALCS, WALCS II, and WALCS III, 203 were excluded due to mobility impairment at baseline, 45 were excluded due to developing new mobility impairment or due to death before 1-year follow-up, and 180 were excluded due to missing data for mobility loss/impairment during follow-up. Of the 651 remaining, 604, 612, and 612 had both baseline and 1-year follow-up data for 6-minute walk, 4-meter walk usual pace, and 4-meter walk fast pace, respectively. For the self-reported walking difficulty questions, 555 and 554 participants had both baseline and 1-year follow-up data for the 2 Walking Impairment Questionnaire questions on walking difficulty due to leg symptoms, respectively. A total of 612 participants (mean age 71±9 years, 37% women, 19% Black race) were included. The mean follow-up from the baseline visit was 37±16 months. The mean follow-up after assessment of 1-year change in functional performance and self-reported walking difficulty was 28±15 months. Among the 612 participants with PAD

included, 162 (26%) developed mobility loss, and 77 (13%) died after 1-year follow-up.

Baseline Characteristics Across Tertiles

For the 6-minute walk tertiles, participants in Tertile 1 (greatest decline) were older, and had higher prevalence of heart failure and spinal stenosis compared with participants in Tertile 2 and Tertile 3 (Table 2). For usual-paced and fast-paced 4-meter walk velocity, participants in Tertile 1 had higher baseline usual-paced and fast-paced 4-meter velocity, compared with participants in Tertiles 2 and 3 (Tables S1 and S2).

At 1-year follow-up, participants in Tertile 1, indicating the greatest 1-year decline in 6-minute walk, had a higher rate of reporting greater difficulty walking due to pain in the calves or buttocks after 1 year, compared with participants in Tertile 2 and Tertile 3 (rates of reporting greater difficulty walking due to pain in the calves or buttocks: 59/180 [33%], 49/183 [27%], and 39/192 [20%] for Tertiles 1–3 of 1-year change in 6-minute walk), though the difference was not statistically significant (*P* value for trend: 0.09; Table 3). At 1-year follow-up, there was no significant association of tertiles of change in 6-minute walk with 1-year change in self-reported walking difficulty due to pain in the thighs (*P* value for trend: 0.30; Table 3).

Associations of 1-Year Change in 6-Minute Walk Distance With Subsequent Mobility Loss

Across tertiles of 1-year change in 6-minute walk distance, the cumulative mobility loss rates were 72/160 (45%), 41/160 (26%), and 47/160 (29%) respectively (*P* value for trend: 0.0021, Figure). Participants in Tertile 1 (greatest 1-year decline in 6-minute walk) had significantly higher rates of mobility loss compared with participants in Tertile 3 (HR, 2.44; 95% CI, 1.63–3.66; *P* value for trend: <0.0001), adjusting for WALCS cohort and baseline 6-minute walk (Model 1). After additional adjustment for age, sex, race, baseline ABI, BMI, smoking status, comorbidities, statin use, and walking exercise (Model 2), the HR was 2.35; 95% CI, 1.47–3.74; *P* value for trend: 0.0002 (Table 4). In analyses adjusting for covariates in Model 2 and excluding participants who underwent lower extremity revascularization during follow-up, the HR was 2.77; 95% CI, 1.58–4.88; *P* value for trend: 0.0002 (Table S3).

Associations of 1-Year Change in Usual- and Fast-Paced 4-Meter Walking Velocity and Subsequent Mobility Loss

Across tertiles of 1-year change in usual-paced 4-meter walking velocity, cumulative mobility loss rates were 54/162 (33%), 51/162 (31%), and 57/162 (35%), respectively (*P* value for trend: 0.66). Participants in Tertile 1 (greatest decline in usual-paced 4-meter walking velocity) had higher rates of mobility loss (HR, 2.11; 95% CI, 1.41–3.16; *P* value for trend: 0.0004) compared with Tertile 3, adjusting for WALCS cohort and baseline usual-paced 4-meter walking velocity (Model 1). After additional adjustment for age, sex, race, baseline ABI, BMI, smoking status, comorbidities, statin use, and walking exercise (Model 2), the HR was 2.21; 95% CI, 1.41–3.47; *P* value for trend: 0.0005 (Table 4). After excluding participants who underwent lower extremity revascularization during follow-up in Model 2, the HR was 2.52; 95% CI, 1.43–4.45; *P* value for trend: 0.002 (Table S3).

Across tertiles of 1-year change in fast-paced 4-meter walking velocity, the cumulative mobility loss rates were 61/162 (38%), 43/162 (27%), and 58/162 (36%), respectively (*P* value for trend 0.64). Participants in Tertile 1 (indicating greatest decline in fast-paced 4-meter walking velocity) had higher rates of mobility loss (HR, 2.07; 95% CI, 1.38–3.10; *P* value for trend: 0.001) compared with Tertile 3, adjusting for WALCS cohort and baseline fast-paced 4-meter walking velocity (Model 1). After additional adjustment for age, sex, race, baseline ABI, BMI, smoking status, comorbidities, statin use, and walking exercise (Model 2), the HR was 1.81; 95% CI, 1.16–2.84; *P* value for trend: 0.01 (Table 4). After excluding participants who underwent lower extremity revascularization during follow-up in Model 2, the HR was 2.30; 95% CI, 1.33–3.98; *P* value for trend: 0.004 (Table S3).

Associations of 1-Year Change in Self-Reported Walking Difficulty and Subsequent Mobility Loss

Observed cumulative mobility loss rates were 42/145 (29%), 53/145 (37%), and 50/145 (34%) for participants who reported improvement, no change, or worse 1-year change in self-reported difficulty walking due to calf or buttock symptoms (*P* value for trend: 0.025). Participants who reported worse 1-year change in walking difficulty due to pain in the calves or buttocks had higher rates of subsequent mobility loss, compared with those who reported improvement in walking difficulty (HR, 2.66; 95% CI, 1.65–4.28; *P* value for trend: 0.0001), adjusting for WALCS cohort and baseline walking difficulty due to pain in the calves or buttocks (Model 1) (Table 5). The HR was 2.16; 95% CI, 1.26–3.69; *P* value for trend: 0.006 after additional adjustment for age, sex, race, baseline ABI, BMI, smoking status, comorbidities, statin use, and walking exercise (Model 2). The HR was 1.98; 95% CI, 1.19–3.31; *P* value for trend: 0.01, after additional adjustment for tertiles of change in 6-minute walk and baseline 6-minute walk

Table 2. Baseline Characteristics of Participants With Peripheral Artery Disease by 1-Year Change in 6-Minute Walk Distance

	Tertile 1* n=201	Tertile 2 n=202	Tertile 3 n=201	*P* value for trend
Age, y	72 (9)	70 (9)	70 (9)	0.002
Female sex, n (%)	73 (36.3)	79 (39.1)	71 (35.3)	0.84
Black race, n (%)	33 (16.4)	49 (24.3)	32 (15.9)	0.90
Baseline ankle brachial index	0.65 (0.14)	0.67 (0.14)	0.67 (0.15)	0.09
Body mass index, kg/m^2	27.7 (5.5)	27.3 (4.5)	28.1 (5.7)	0.54
Current smokers, n (%)	41 (20.4)	37 (18.3)	45 (22.4)	0.62
Diabetes, n (%)	65 (32.3)	55 (27.4)	69 (34.5)	0.64
Angina, n (%)	51 (26.0)	37 (18.5)	44 (22.2)	0.37
Cancer, n (%)	40 (19.9)	31 (15.4)	33 (16.4)	0.36
Congestive heart failure, n (%)	24 (12.2)	18 (8.9)	9 (4.6)	0.007
Myocardial infarction, n (%)	48 (24.1)	43 (21.5)	49 (24.8)	0.88
Pulmonary disease, n (%)	38 (19.0)	30 (14.9)	26 (13.1)	0.10
Hip arthritis, n (%)	21 (10.5)	21 (10.5)	14 (7.1)	0.24
Disc disease, n (%)	58 (29.0)	48 (23.9)	54 (27.3)	0.69
Knee arthritis, n (%)	24 (12.0)	33 (16.5)	34 (17.2)	0.15
Spinal stenosis, n (%)	22 (11.0)	12 (6.0)	10 (5.1)	0.02
Walking exercise, n (%)	40 (19.9)	54 (26.7)	34 (16.9)	0.46
Statin use, n (%)	114 (56.7)	111 (55.0)	101 (50.3)	0.19
Lower extremity revascularization, n (%)	59 (29.4)	62 (30.7)	72 (35.8)	0.16
Baseline 6-min walk, meters)	387.33 (94.69)	405.77 (93.81)	361.76 (112.20)	0.01
Baseline usual-paced 4-meter walk velocity, m/s	0.92 (0.18)	0.92 (0.16)	0.95 (0.21)	0.07
Baseline fast-paced 4-meter walk velocity, m/s	1.26 (0.23)	1.28 (0.24)	1.27 (0.26)	0.46

Walking exercise: Self-reported walking for ≥3 days per week for ≥30 minutes per day. Continuous variables are presented as mean (SD).
*Tertile 1 (−429.5 to −25.3 meters): greater 1-year decline in 6-minute walk; Tertile 3 (14.6 to 263.3 meters): 1-year improvement in 6-minute walk; Tertile 2 (−25.0 to 14.3 meters): change between Tertile 1 and Tertile 3.

(Table 5). After excluding participants who underwent lower extremity revascularization during follow-up in Model 3, the HR was 1.64; 95% CI, 0.81–3.29; *P* value for trend: 0.16 (Table S4).

Cumulative mobility loss rates were 42/145 (29%), 61/145 (42%), and 42/145 (29%) for participants who reported improvement, no change, and worse difficulty walking due to pain in the thighs, respectively, over 1-year follow-up (*P* value for trend: 0.60). Participants who reported worse walking difficulty due to pain in the thighs at 1-year follow-up had higher rates of subsequent mobility loss, compared with those who reported improvement in walking difficulty due to thigh pain (HR, 1.69; 95% CI, 1.05–2.72; *P* value for trend: 0.02) adjusting for WALCS cohort and baseline walking difficulty due to pain in the thighs (Model 1). The HR was 1.33; 95% CI, 0.78–2.27; *P* value for trend: 0.24 after additional adjustment for age, sex, race, baseline ABI, BMI, smoking status, comorbidities, statin use, and walking exercise (Model 2). The HR was 1.37; 95% CI, 0.79–2.38; *P* value for trend: 0.19, after additional adjustment for tertiles of change in 6-minute walk and baseline 6-minute walk (Model 3) (Table 5). After excluding participants who underwent lower extremity revascularization during follow-up in Model 3, the HR was 1.23; 95% CI, 0.63–2.42; *P* value for trend: 0.45 (Table S4).

Associations of 1-Year Change in Objectively Measured Walking Performance and Subsequent Mortality

Across tertiles of 1-year change in 6-minute walk distance, the cumulative all-cause mortality rates were 66/163 (40%), 43/163 (26%), and 54/163 (33%) respectively (*P* value for trend: 0.012). In analyses of change in 6-minute walk and all-cause mortality, participants in Tertile 1 (greatest 1-year decline in 6-minute walk) had higher rates of all-cause mortality compared with those in Tertile 3 (HR, 1.92; 95% CI, 1.32–2.78; *P* value for trend=0.001), adjusting for WALCS cohort and baseline 6-minute walk distance (Model 1). After additional adjustment for age, sex, race, baseline ABI, BMI, smoking status, comorbidities, statin use, and walking exercise, the HR was 1.61; 95% CI, 1.07–2.43; *P* value for trend: 0.04 (Model 2) (Table 6). The association

Table 3. Associations of 1-Year Change in 6-Minute Walk Distance With Change in Participant-Reported Change in Difficulty Walking Due to Pain in the Calves or Buttocks or Pain in the Thighs

	One-year change in 6-min walk		
One-year change in walking difficulty due to pain in the calves or buttocks	**Tertile 1* (worst) n=180 N (%)**	**Tertile 2 n=183 N (%)**	**Tertile 3 (best) n=192 N (%)**
Worse	59 (32.8)	49 (26.8)	39 (20.3)
No change	68 (37.8)	70 (38.3)	79 (41.2)
Improved	53 (29.4)	64 (35.0)	74 (38.5)
P value for trend: 0.09			
One-year change in walking difficulty due to pain in the thighs	**Tertile 1 (worst) n=180 N (%)**	**Tertile 2 n=183 N (%)**	**Tertile 3 (best) n=191 N (%)**
Worse	46 (25.6)	43 (23.5)	35 (18.3)
No change	89 (49.4)	100 (54.6)	100 (52.4)
Improved	45 (25.0)	40 (21.9)	56 (29.3)
P value for trend: 0.30			

*Tertile 1 (−429.5 to −25.3 meters): greater 1-year decline in 6-minute walk; Tertile 3 (14.6 to 263.3 meters): 1-year improvement in 6-minute walk; Tertile 2 (−25.0 to 14.3 meters): change between Tertile 1 and Tertile 3.

between 1-year change in 6-minute walk tertiles and all-cause mortality was no longer significant in Model 2 after excluding participants who underwent lower extremity revascularization during follow-up (Table S5).

Across tertiles of 1-year change in usual-paced 4-meter walking velocity, the cumulative all-cause mortality rates were 62/168 (37%), 53/168 (32%), and 53/168 (32%), respectively (*P* value for trend: 0.66). Participants in Tertile 1 (greatest 1-year decline in usual-paced 4-meter walking velocity) had higher rates of mortality compared with participants in Tertile 3 (HR, 1.78; 95% CI, 1.19–2.66; *P* value for trend: 0.007), adjusting for WALCS cohort and baseline usual-paced 4-meter walking velocity (Model 1). The association was no longer significant after adjusting for additional confounders in Model 2 (HR, 1.41; 95% CI, 0.94–2.13; *P* value for trend: 0.11) (Table 6).

Across tertiles of 1-year change in fast-paced 4-meter walking velocity, the cumulative all-cause mortality rates were 63/166 (38%), 59/166 (36%), and 44/166 (27%) (*P* value for trend: 0.76). Participants in Tertile 1 (greatest 1-year decline in fast-paced 4-meter walking velocity) had higher rates of mortality compared with participants in Tertile 3 (HR, 2.11; 95% CI, 1.43–3.10; *P* value for trend: 0.0003), adjusting for WALCS cohort and baseline fast-paced 4-meter walking velocity (Model 1). After additional adjustment for age, sex, race, baseline ABI, BMI, smoking status, diabetes, heart failure, myocardial infarction, angina, pulmonary disease, hip arthritis, knee arthritis, spinal disc disease, spinal stenosis, cancer, statin use, and walking exercise (Model 2), the HR was 1.75; 95% CI, 1.16–2.64; *P* value for trend: 0.007 (Table 6).

Associations of 1-Year Change in Self-Reported Walking Difficulty and All-Cause Mortality

Across the 3 categories of self-reported walking difficulty due to pain in the calves or buttocks, all-cause mortality rates were 47/146 (32%), 61/146 (42%), and 38/146 (26%), respectively, for participants who reported improvement, no change, or worse difficulty walking due to calf or buttock symptoms (*P* value for trend: 0.90). There were no significant associations between self-reported walking difficulty due to pain in the calves or buttocks with all-cause mortality either adjusting for WALCS cohort and baseline self-reported walking difficulty (*P* value for trend: 0.07) (Model 1), or after additional adjustment for age, sex, race, baseline ABI, BMI, smoking status, diabetes, heart failure, myocardial infarction, angina, pulmonary disease, hip arthritis, knee arthritis, spinal disc disease, spinal stenosis, cancer, statin use, and walking exercise (*P* value for trend: 0.58) (Model 2), or after additional adjustment for tertiles of change in 6-minute walk and baseline 6-minute walk distance (*P* value for trend: 0.997) (Model 3; Table 7). After excluding participants who underwent lower extremity revascularization during follow-up in Model 3, the HR was 1.14; 95% CI, 0.64–2.27; *P* value for trend: 0.66 (Table S6).

Across the 3 categories of self-reported walking difficulty due to pain in the thighs, the cumulative all-cause mortality rates were 33/146 (23%), 79/146 (54%), and 34/146 (23%), respectively, for participants who reported improvement, no change, and worse pain, respectively, over 1-year follow-up (*P* value for trend: 0.74).

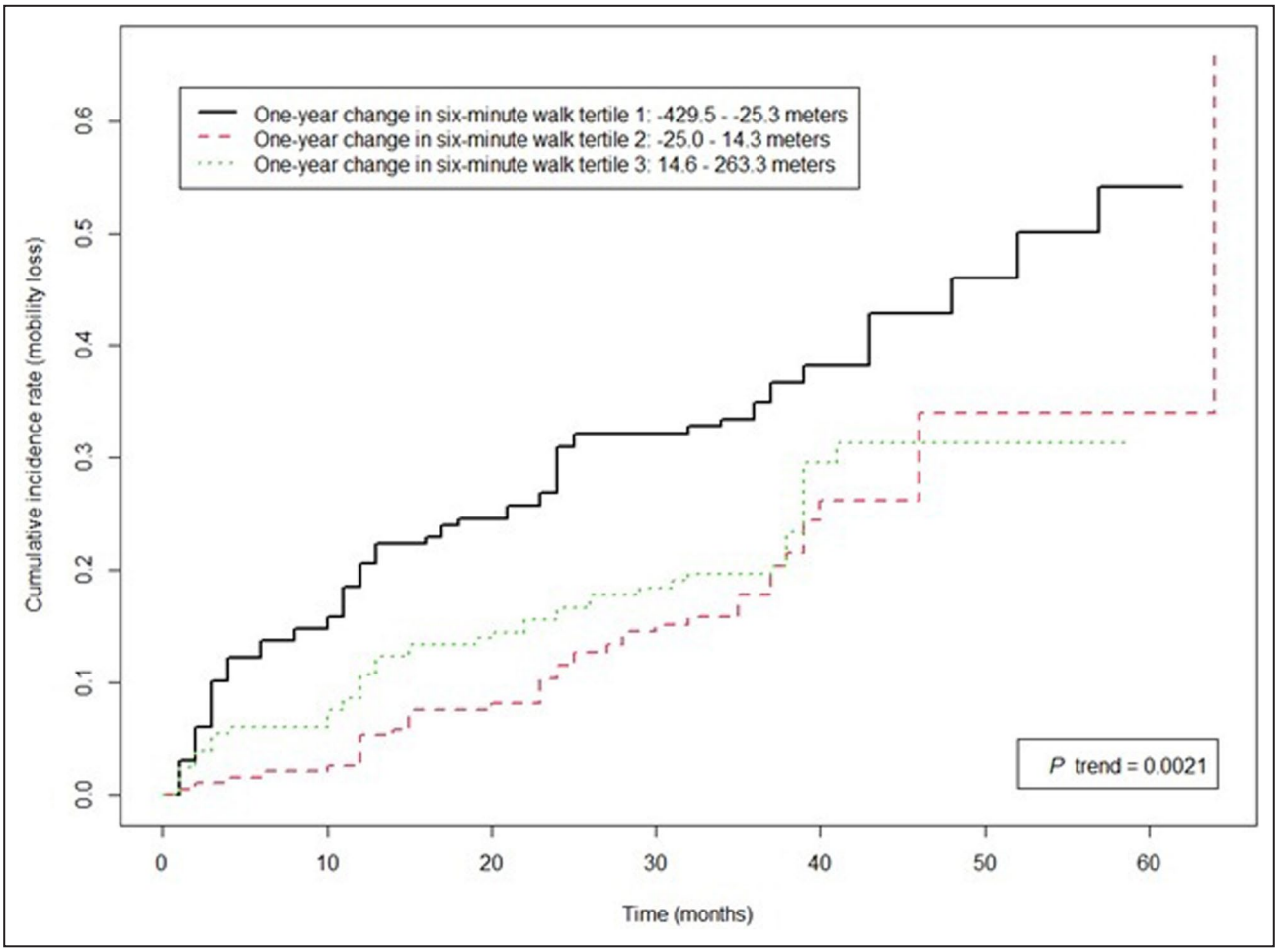

Figure 1. Cumulative incidence curves of mobility loss rates by 1-y change in 6-min walk tertiles among 612 people with peripheral artery disease.

There were no significant associations between self-reported walking difficulty due to pain in the thighs with all-cause mortality either adjusting for WALCS cohort and baseline self-reported walking difficulty (*P* value for trend: 0.07) (Model 1), or after additional adjustment for age, sex, race, baseline ABI, BMI, smoking status, diabetes, heart failure, myocardial infarction, angina, pulmonary disease, hip arthritis, knee arthritis, spinal disc disease, spinal stenosis, cancer, statin use, and walking exercise (*P* value for trend: 0.18) (Model 2), or after additional adjustment for tertiles of change in 6-minute walk and baseline 6-minute walk distance (*P* value for trend: 0.40) (Model 3; Table 7). After excluding participants who underwent lower extremity revascularization during follow-up in Model 3, the HR was 1.99; 95% CI, 0.91–4.35; *P* value for trend: 0.08 (Table S6).

DISCUSSION

Among 612 patients with PAD followed for a mean of 37 months, greater 1-year declines in 6-minute walk distance, usual-paced 4-meter walking velocity, and fast-paced 4-meter walking velocity were each associated with significantly higher rates of subsequent mobility loss, adjusting for known and potential confounders. Greater 1-year declines in 6-minute walk distance and fast-paced 4-meter walking speed were significantly associated with higher mortality rates, adjusting for confounders. Participants who reported greater difficulty walking due to calf or buttock pain at 1-year follow-up had significantly higher rates of mobility loss compared with those who reported improved symptoms. In contrast, in fully adjusted analyses, there were no significant associations of participant-reported change in difficulty walking due to thigh pain with subsequent mobility loss or mortality.

To our knowledge, no previous studies have assessed the association between 1-year change in walking performance measures or in 1-year change in participant-reported symptoms of walking difficulty and subsequent risk of mobility loss or all-cause mortality in people with PAD. McDermott et al previously

Table 4. Association Between 1-Year Change in Objective Walking Performance Measures and Subsequent Mobility Loss Among People With Peripheral Artery Disease (n=612)

Walking performance measures	Tertiles†	Rate of mobility loss	Hazard ratio (95% CI)	*P* value for trend
Model 1*				
6-min walk	Tertile 1 (n=201)	72/160 (45%)	2.44 (1.63–3.66)	<0.0001
	Tertile 2 (n=202)	41/160 (26%)	1.30 (0.85–2.00)	
	Tertile 3 (Reference) (n=201)	47/160 (29%)	1.00	
		Total events 160		
4-m velocity (usual pace)	Tertile 1 (n=204)	54/162 (33%)	2.11 (1.41–3.16)	0.0004
	Tertile 2 (n=204)	51/162 (31%)	1.30 (0.88–1.93)	
	Tertile 3 (Reference) (n=204)	57/162 (35%)	1.00	
		Total events 162		
4-m velocity (fast pace)	Tertile 1 (n=204)	61/162 (38%)	2.07 (1.38–3.10)	0.001
	Tertile 2 (n=204)	43/162 (27%)	0.93 (0.63–1.38)	
	Tertile 3 (Reference) (n=204)	58/162 (36%)	1.00	
		Total events 162		
Model 2				
6-min walk	Tertile 1		2.35 (1.47–3.74)	0.0002
	Tertile 2		1.20 (0.74–1.95)	
	Tertile 3 (Reference)		1.00	
4-m velocity (usual pace)	Tertile 1		2.21 (1.41–3.47)	0.0005
	Tertile 2		1.35 (0.87–2.08)	
	Tertile 3 (Reference)		1.00	
4-m velocity (fast pace)	Tertile 1		1.81 (1.16–2.84)	0.01
	Tertile 2		0.78 (0.50–1.23)	
	Tertile 3 (Reference)		1.00	

*Model 1: adjusted for WALCS (Walking and Leg Circulation Study) cohort and baseline functional performance; Model 2: adjusted for WALCS cohort, baseline functional performance, age, sex, race, baseline ankle brachial index, body mass index, smoking status, diabetes, heart failure, myocardial infarction, angina, pulmonary disease, disc disease, hip arthritis, knee arthritis, spinal stenosis, cancer, statin use, and walking exercise.

†Tertile 1: greater 1-year decline in functional performance; Tertile 3: 1-year improvement in functional performance; Tertile 2: change between Tertile 1 and Tertile 3.

reported that poorer baseline 6-minute walking performance and slower usual- and fast-paced 4-meter walking velocity were each associated with higher rates of mobility loss among people with PAD and that greater 2-year declines in 6-minute walk and fast-paced 4-meter walking velocity were associated with higher rates of subsequent mobility loss, all-cause mortality, and cardiovascular disease mortality.[2,22] Compared with the previous report of 2-year change in functional performance measures,[2,22] data reported here may be more relevant to clinical practice, because 1-year changes in 6-minute walk and 4-meter walking velocity are more feasible to obtain from patients who are typically evaluated in a clinical setting every 3 to 6 months. One-year change is also more practical to obtain than a variable that requires 2 years to obtain. Furthermore, compared with the prior reports,[2,22] data reported here are more current, with follow-up to 2014, and included a larger sample size than these prior reports. In addition, to our knowledge, no prior reports have evaluated change in participant reported difficulty walking due to calf or buttock symptoms and subsequent mobility loss or all-cause mortality.

Similar to prior findings from the WALCS and WALCS II cohorts,[2] in this report, 1-year changes in 6-minute walk and fast-paced 4-meter walking velocity were associated with subsequent mobility loss and with mortality. However, despite the larger sample size by inclusion of participants from WALCS III in this study, usual-paced 4-meter walking velocity was associated with subsequent mobility loss but not mortality. Although the reasons for lack of significant association of usual-paced walking velocity with mortality are unclear, data reported here suggest that 1-year changes in walking endurance and fast-paced walking speed may be more sensitive measures of future risk of both mobility loss and mortality, whereas 1-year change in usual-paced walking speed may be helpful for identifying people at increased risk for mobility loss but not mortality.

Table 5. Association Between 1-Year Change in Self-Reported Walking Difficulty and Subsequent Mobility Loss Among People With Peripheral Artery Disease (n=555)

Model 1*				
	Change in symptom	**Rate of mobility loss**	**Hazard ratio (95%CI)**	***P* value for trend**
Self-reported walking difficulty due to pain in calves or buttocks	Worse (n=147)	50/145 (34%)	2.66 (1.65–4.28)	0.0001
	No change (n=217)	53/145 (37%)	1.43 (0.95–2.16)	
	Improved (n=191)	42/145 (29%)	1.00	
		Total events 145		
Self-reported walking difficulty due to pain in thighs	Worse (n=124)	42/145 (29%)	1.69 (1.05–2.72)	0.02
	No change (n=289)	61/145 (42%)	1.02 (0.64–1.64)	
	Improved (n=141)	42/145 (29%)	1.00	
		Total events 145		
Model 2†				
Self-reported walking difficulty due to pain in calves or buttocks	Worse		2.16 (1.26–3.69)	0.006
	No change		1.32 (0.84–2.07)	
	Improved		1.00	
Self-reported walking difficulty due to pain in thighs	Worse		1.33 (0.78–2.27)	0.24
	No change		0.93 (0.56–1.53)	
	Improved		1.00	
Model 3‡				
Self-reported walking difficulty due to pain in calves or buttocks	Worse		1.98 (1.19–3.31)	0.01
	No change		1.13 (0.70–1.81)	
	Improved		1.00	
Self-reported walking difficulty due to pain in thighs	Worse		1.37 (0.79–2.38)	0.19
	No change		0.99 (0.60–1.64)	
	Improved		1.00	

*Model 1: adjusted for WALCS (Walking and Leg Circulation Study) cohort and baseline self-reported walking difficulty.

†Model 2: adjusted for WALCS cohort, baseline self-reported walking difficulty, age, sex, race, baseline ankle brachial index, body mass index, smoking status, diabetes, heart failure, myocardial infarction, angina, pulmonary disease, disc disease, hip arthritis, knee arthritis, spinal stenosis, cancer, statin use, and walking exercise.

‡Model 3: adjusted for WALCS cohort, baseline self-reported walking difficulty, change in 6-minute walk tertiles, baseline 6-minute walk distance, age, sex, race, baseline ankle brachial index, body mass index, smoking status, diabetes, heart failure, myocardial infarction, angina, pulmonary disease, disc disease, hip arthritis, knee arthritis, spinal stenosis, cancer, statin use, and walking exercise.

This study was not designed to delineate the biologic pathways for associations of greater declines in functional performance measures with subsequent mobility loss or with mortality. It is possible that comorbidities such as pulmonary disease or heart failure may have contributed to greater decline in 6-minute walk and 4-meter walking speed and subsequent increased rates of subsequent mobility loss or mortality in participants with PAD. However, the finding that greater 1-year changes in these objective functional performance measures were associated with higher rates of mobility loss and with mortality, regardless of what specifically caused the mobility loss or mortality, is useful for clinicians, patients, and scientists. Furthermore, data reported here reflect patients with PAD in the real world who have multiple comorbidities and may develop mobility loss either from PAD or from a comorbidity.

In fully adjusted models, although participant-reported increases in change in difficulty walking due to pain in the calves or buttocks were associated with subsequent mobility loss, participant-reported increases in difficulty walking due to pain in the thighs were not associated with subsequent mobility loss, and neither participant-reported measure of greater difficulty walking due to leg symptoms was associated with increased mortality. Furthermore, in sensitivity analyses restricted to participants who did not undergo lower extremity revascularization during follow-up, the

Table 6. Association Between 1-Year Change in Objective Walking Performance Measures and All-Cause Mortality Among People With Peripheral Artery Disease (n=702)

Walking performance measure	Tertiles†	Rate of all-cause mortality	Hazard ratio (95% CI)	*P* value for trend
Model 1*				
6-min walk	Tertile 1 (n=230)	66/163 (40%)	1.92 (1.32–2.78)	0.001
	Tertile 2 (n=231)	43/163 (26%)	1.06 (0.70–1.61)	
	Tertile 3 (Reference) (n=230)	54/163 (33%)	1.00	
		Total events163		
4-m velocity (usual pace)	Tertile 1 (n=234)	62/168 (37%)	1.78 (1.19–2.66)	0.007
	Tertile 2 (n=234)	53/168 (32%)	1.44 (1.01–2.06)	
	Tertile 3 (Reference) (n=234)	53/168 (32%)	1.00	
		Total events 168		
4-m velocity (fast pace)	Tertile 1 (n=232)	63/166 (38%)	2.11 (1.43–3.10)	0.0003
	Tertile 2 (n=234)	59/166 (36%)	1.42 (0.97–2.07)	
	Tertile 3 (Reference) (n=233)	44/166 (27%)	1.00	
		Total events 166		
Model 2				
6-min walk	Tertile 1		1.61 (1.07–2.43)	0.04
	Tertile 2		0.98 (0.65–1.49)	
	Tertile 3 (Reference)		1.00	
4-m velocity (usual pace)	Tertile 1		1.41 (0.94–2.13)	0.11
	Tertile 2		1.32 (0.89–1.97)	
	Tertile 3 (Reference)		1.00	
4-m velocity (fast pace)	Tertile 1		1.75 (1.16–2.64)	0.007
	Tertile 2		1.24 (0.83–1.86)	
	Tertile 3 (Reference)		1.00	

*Model 1: adjusted for WALCS (Walking and Leg Circulation Study) cohort and baseline functional performance; Model 2: adjusted for WALCS cohort, baseline functional performance, age, sex, race, baseline ankle brachial index, body mass index, smoking status, diabetes, heart failure, myocardial infarction, angina, pulmonary disease, disc disease, hip arthritis, knee arthritis, spinal stenosis, cancer, statin use, and walking exercise.

†Tertile 1: greater 1-year decline in functional performance; Tertile 3: 1-year improvement in functional performance; Tertile 2: change between Tertile 1 and Tertile 3.

association of participant-reported increased difficulty in walking due to pain in the calves or buttocks with subsequent mobility loss was no longer statistically significant after adjusting for baseline 6-minute walk and tertiles of change in 6-minute walk. Overall, findings reported here suggest that objective measures of performance were much more consistently significantly associated with mobility loss and mortality than participant-reported difficulty walking due to ischemic leg symptoms. These findings are consistent with prior work demonstrating some discordance between objectively measured versus participant reported outcomes in people with PAD and underscore the importance of objective assessment of walking performance in people with PAD.[23,24]

The 6-minute walk and 4-meter walking velocity can be ascertained relatively easily in clinical settings. These measures could potentially be used to identify individuals with PAD who are at highest risk for future mobility loss or mortality. In people without PAD, mobility loss was associated with higher rates of falls, poor psychological health, negative health outcomes, death, and higher health care costs.[25,26] Further study is needed to determine whether routine measurement of annual change in objective measures of functioning, such as the 6-minute walk and 4-meter walking velocities followed by implementation of interventions such as exercise therapy for those with greatest declines, can lead to lower rates of mobility loss in people with PAD. However, a prior randomized trial of 194 participants with PAD showed that a home-based walking exercise intervention prevented mobility loss, compared with a control group, at 6-month and 12-month follow-up.[27]

This study has some limitations. First, the study was observational. No causal inferences can be made. Second, unmeasured and residual confounding may account for findings reported here. Third, mobility loss was assessed at annual visits and thus the precise point of mobility loss was not defined. Fourth, findings

Table 7. Association Between 1-Year Change in Self-Reported Walking Difficulty and All-Cause Mortality Among People With Peripheral Artery Disease (n=636)

Model 1*				
	Change in symptom	**Rate of all-cause mortality**	**Hazard ratio (95% CI)**	***P* value for trend**
Self-reported walking difficulty due to pain in calves or buttocks	Worse (n=171)	38/146 (26%)	1.52 (0.93–2.48)	0.07
	No change (n=252)	61/146 (42%)	1.44 (0.96–2.17)	
	Improved (n=213)	47/146 (32%)	1.00	
		Total events 146		
Self-reported walking difficulty due to pain in thighs	Worse (n=144)	34/146 (23%)	1.76 (1.02–3.03)	0.07
	No change (n=326)	79/146 (54%)	1.75 (1.08–2.83)	
	Improved (n=166)	33/146 (23%)	1.00	
		Total events 146		
Model 2†				
Self-reported walking difficulty due to pain in calves or buttocks	Worse		1.15 (0.64–2.06)	0.58
	No change		1.28 (0.82–1.98)	
	Improved		1.00	
Self-reported walking difficulty due to pain in thighs	Worse		1.62 (0.89–2.94)	0.18
	No change		1.59 (0.93–2.69)	
	Improved		1.00	
Model 3‡				
Self-reported walking difficulty due to pain in calves or buttocks	Worse		0.99 (0.56–1.75)	0.997
	No change		1.15 (0.73–1.83)	
	Improved		1.00	
Self-reported walking difficulty due to pain in thighs	Worse		1.36 (0.75–2.48)	0.40
	No change		1.34 (0.80–2.25)	
	Improved		1.00	

*Model 1: adjusted for WALCS (Walking and Leg Circulation Study) cohort and baseline self-reported walking difficulty.

†Model 2: adjusted for WALCS cohort, baseline self-reported walking difficulty, age, sex, race, baseline ankle brachial index, body mass index, smoking status, diabetes, heart failure, myocardial infarction, angina, pulmonary disease, disc disease, hip arthritis, knee arthritis, spinal stenosis, cancer, statin use, and walking exercise.

‡Model 3: adjusted for WALCS cohort, baseline self-reported walking difficulty, change in 6-minute walk tertiles, baseline 6-minute walk distance, age, sex, race, baseline ankle brachial index, body mass index, smoking status, diabetes, heart failure, myocardial infarction, angina, pulmonary disease, disc disease, hip arthritis, knee arthritis, spinal stenosis, cancer, statin use, and walking exercise.

may not be generalizable to people with PAD who were not eligible for the WALCS cohorts.

CONCLUSIONS

Greater 1-year declines in 6-minute walk distance and greater 1-year declines in usual- and fast-paced 4-meter walking speed were associated with higher rates of subsequent mobility loss. Greater 1-year declines in 6-minute walk and fast-paced 4-meter walking velocity were associated with increased rates of all-cause mortality in people with PAD. Although these results suggest that 1-year change in objective measures may help clinicians to identify patients with PAD at highest risk of mobility loss or mortality, further study is needed to determine whether implementing interventions in individuals with the greatest 1-year declines in objective performance measures can prevent mobility loss and mortality in PAD.

ARTICLE INFORMATION

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Supplemental Material

Tables S1–S6

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Supplemental Material

Table S1. Baseline characteristics of participants with peripheral artery disease by 1-year change in usual paced 4-meter walking velocity.

	Tertile 1* N= 204	Tertile 2 N = 204	Tertile 3 N = 204	p-value for trend
Age (years)	71 (8)	71 (9)	70 (9)	0.62
Female n (%)	77 (37.8)	61 (29.9)	86 (42.2)	0.36
African American n (%)	39 (19.1)	32 (15.7)	46 (22.6)	0.38
Baseline Ankle brachial index	0.67 (0.14)	0.66 (0.14)	0.66 (0.15)	0.62
Body mass index (kg/m^2)	27.5 (5.5)	27.7 (4.3)	28.1 (6.0)	0.21
Current smokers n (%)	42 (20.6)	39 (19.1)	42 (20.6)	1.00
Diabetes n (%)	60 (29.4)	64 (31.4)	66 (32.7)	0.48
Angina n (%)	42 (20.9)	41 (20.6)	50 (24.8)	0.35
Cancer n (%)	37 (18.1)	32 (15.7)	35 (17.2)	0.81
Congestive Heart Failure n (%)	20 (10.0)	14 (6.9)	19 (9.5)	0.87
Myocardial infarction n (%)	44 (22.0)	48 (23.8)	50 (24.6)	0.53
Pulmonary disease n (%)	40 (19.7)	24 (11.9)	32 (15.8)	0.28
Hip Arthritis n (%)	15 (7.4)	20 (9.8)	21 (10.5)	0.29
Disc disease n (%)	61 (30.1)	47 (23.4)	54 (26.6)	0.43
Knee arthritis n (%)	28 (13.7)	32 (15.8)	31 (15.5)	0.62
Spinal stenosis n (%)	16 (8.0)	16 (7.9)	12 (5.9)	0.43
Walking exercise n (%)	48 (23.5)	40 (19.6)	42 (20.6)	0.47
Statin use n (%)	103 (50.5)	122 (59.8)	106 (52.0)	0.77
Lower extremity revascularization n (%)	60 (29.4)	68 (33.3)	68 (33.3)	0.40
Baseline 6-minute walk (meters)	384.46 (100.85)	384.31(106.37)	383.27 (100.98)	0.91
Baseline Usual pace 4-meter walk velocity (meters/second)	1.02 (0.20)	0.92 (0.15)	0.85 (0.15)	<.0001
Baseline Fast pace 4-meter walk velocity (meters/second)	1.33 (0.26)	1.24 (0.23)	1.23 (0.24)	<.0001

*Tertile 1 (-0.63 - - 0.06 meters/second): greater 1-year decline in usual paced 4-meter walking velocity; Tertile 3 (0.06 – 0.59): 1-year improvement in usual paced 4-meter walking velocity; Tertile 2 (-0.06 – 0.05 meters/second): change between tertile 1 and tertile 3.

Walking exercise: Self-reported walking for ≥ 3days per week for ≥30 minutes per day

Continuous variables are presented as mean (standard deviation)

Table S2. Baseline characteristics of participants with peripheral artery disease by 1-year change in fast paced 4-meter walking velocity.

	Tertile 1* N= 204	Tertile 2 N = 204	Tertile 3 N = 204	p-value for trend
Age (years)	71 (9)	71 (9)	70 (9)	0.03
Female n (%)	63 (30.9)	82 (40.2)	79 (38.7)	0.10
African American n (%)	41 (20.1)	33 (16.2)	43 (21.1)	0.80
Baseline Ankle brachial index	0.67 (0.14)	0.65 (0.15)	0.67 (0.14)	0.67
Body mass index (kg/m^2)	27.7 (4.9)	27.7 (4.9)	27.9 (6.0)	0.69
Current smokers n (%)	41 (20.1)	36 (17.7)	46 (22.6)	0.54
Diabetes n (%)	62 (30.5)	62 (30.5)	66 (32.4)	0.69
Angina n (%)	45 (22.4)	44 (21.7)	44 (22.2)	0.97
Cancer n (%)	39 (19.1)	38 (18.6)	27 (13.3)	0.12
Congestive Heart Failure n (%)	17 (8.5)	19 (9.4)	17 (8.5)	0.98
Myocardial infarction n (%)	47 (23.2)	50 (24.8)	45 (22.5)	0.88
Pulmonary disease n (%)	37 (18.2)	34 (16.8)	25 (12.4)	0.11
Hip Arthritis n (%)	13 (6.4)	26 (12.8)	17 (8.5)	0.48
Disc disease n (%)	55 (27.0)	54 (26.7)	53 (26.4)	0.89
Knee arthritis n (%)	30 (14.8)	32 (15.8)	29 (14.4)	0.92
Spinal stenosis n (%)	12 (6.0)	22 (10.8)	10 (5.0)	0.68
Walking exercise n (%)	39 (19.1)	44 (21.6)	47 (23.0)	0.33
Statin use n (%)	109 (53.4)	110 (53.9)	112 (54.9)	0.77
Lower extremity revascularization n (%)	72 (35.3)	56 (27.5)	68 (33.3)	0.67
Baseline 6-minute walk (meters)	383.32 (105.88)	380.46 (99.98)	388.26 (102.20)	0.63
Baseline Usual pace 4-meter walk velocity (meters/second)	0.96 (0.18)	0.91 (0.17)	0.91 (0.20)	0.008
Baseline Fast pace 4-meter walk velocity (meters/second)	1.36 (0.26)	1.25 (0.22)	1.20 (0.24)	<.0001

*Tertile 1 (-1.01 - -0.08): greater 1-year decline in fast paced 4-meter walking velocity; Tertile 3 (0.07 – 0.65): 1-year improvement in fast paced 4-meter walking velocity; Tertile 2 (-0.08 – 0.07) : change between tertile 1 and tertile 3.

Walking exercise: Self-reported walking for ≥ 3days per week for ≥30 minutes per day

Continuous variables are presented as mean (standard deviation)

Table S3. Association between 1-year change in objective walking performance measures and subsequent mobility loss among people with peripheral artery disease (N= 394) after excluding participants who underwent lower extremity revascularization.

		Model 1*		
Walking performance measure	**Tertiles†**	**Rate of mobility loss**	**Hazard Ratio (95% Confidence Interval)**	**p-value for trend**
		Events		
6-minute walk	Tertile 1(N=129)	50/108 (46%)	2.55 (1.55, 4.19)	0.0001
	Tertile 2 (N=131)	28/108 (26%)	1.32 (0.78, 2.45)	
	Tertile 3 (Ref) (N=129)	30/108 (28%)	1.00	
		Total events 108		
4-meter velocity (usual pace)	Tertile 1 (N=131)	38/110 (35%)	2.38 (1.46, 3.87)	0.0007
	Tertile 2 (N=132)	33/110 (30%)	1.29 (0.78, 2.11)	
	Tertile 3 (Ref) (N=131)	39/110 (35%)	1.00	
		Total events 110		
4-meter velocity (fast pace)	Tertile 1 (N=131)	41/110 (37%)	2.60 (1.56, 4.31)	0.0006
	Tertile 2 (N=133)	30/110 (27%)	1.16 (0.72, 1.88)	
	Tertile 3 (Ref) (N=130)	39/110 (35%)	1.00	
		Total events 110		
		Model 2		
Walking performance measure	Tertiles		**Hazard Ratio (95% Confidence Interval)**	**p-value for trend**
6-minute walk	Tertile 1		2.77 (1.58, 4.88)	0.0002
	Tertile 2		1.24 (0.68, 2.27)	
	Tertile 3 (Ref)		1.00	
4-meter velocity (usual pace)	Tertile 1		2.52 (1.43, 4.45)	0.002
	Tertile 2		1.25 (0.73, 2.16)	
	Tertile 3 (Ref)		1.00	
4-meter velocity (fast pace)	Tertile 1		2.30 (1.33, 3.98)	0.004
	Tertile 2		0.98 (0.56, 1.71)	
	Tertile 3 (Ref)		1.00	

*Model 1: adjusted for Walking And Leg Circulation Study (WALCS) cohort and baseline functional performance; Model 2: adjusted for WALCS cohort, baseline functional performance, age, sex, race, baseline ankle brachial index, body mass index, smoking status, diabetes, heart failure, myocardial infarction, angina, pulmonary disease, disc disease, hip arthritis, knee arthritis, spinal stenosis, cancer, statin use, and walking exercise. †Tertile 1: greater 1-year decline in functional performance; Tertile 3: 1-year improvement in functional performance; Tertile 2: change between tertile 1 and tertile 3.

Table S4. Association between one-year change in self-reported walking difficulty and subsequent mobility loss among people with peripheral artery disease (N=355) excluding those who underwent lower extremity revascularization.

		Model 1*		
	Change in symptom	**Rate of mobility loss**	**Hazard Ratio (95% Confidence Interval)**	**p-value for trend**
		Events		
Self-reported walking difficulty due to pain in calves or buttocks	Worse (N=102)	37/94 (39%)	2.51 (1.39, 4.53)	0.004
	No change (N=136)	34/94 (36%)	1.54 (0.90, 2.64)	
	Improved (N=117)	23/94 (24%)	1.00	
		Total events 94		
Self-reported walking difficulty due to pain in thighs	Worse (N=79)	28/94 (30%)	1.74 (0.97, 3.11)	0.03
	No change (N=190)	40/94 (43%)	1.05 (0.58, 1.93)	
	Improved (N=86)	26/94 (28%)	1.00	
		Total events 94		
		Model 2 †		
	Change in symptom		**Hazard Ratio (95% Confidence Interval)**	**p-value for trend**
Self-reported walking difficulty due to pain in calves or buttocks	Worse		2.31 (1.07, 4.25)	0.04
	No change		1.51 (0.85, 2.68)	
	Improved		1.00	
Self-reported walking difficulty due to pain in thighs	Worse		1.37 (0.71, 2.66)	0.26
	No change		0.99 (0.51, 1.93)	
	Improved		1.00	
		Model 3‡		
Self-reported walking difficulty due to pain in calves or buttocks	Worse		1.64 (0.81, 3.29)	0.16
	No change		1.24 (0.66, 2.34)	
	Improved		1.00	
Self-reported walking difficulty due to pain in thighs	Worse		1.23 (0.63, 2.42)	0.45
	No change		1.08 (0.55, 2.11)	
	Improved		1.00	

*Model 1: adjusted for Walking And Leg Circulation Study (WALCS) cohort and baseline self-reported walking difficulty; †Model 2: adjusted for WALCS cohort, baseline self-reported walking difficulty, age, sex, race, baseline ankle brachial index, body mass index, smoking status, diabetes, heart failure, myocardial infarction, angina, pulmonary disease, disc disease, hip arthritis, knee arthritis, spinal stenosis, cancer, statin use, and walking exercise. ‡Model 3: adjusted for change in six-minute walk tertiles ‡Model 3: adjusted for WALCS cohort, baseline self-reported walking difficulty, change in six-minute walk tertiles, baseline six-minute walk distance, age, sex, race, baseline ankle brachial index, body mass index, smoking status, diabetes, heart failure, myocardial infarction, angina, pulmonary disease, disc disease, hip arthritis, knee arthritis, spinal stenosis, cancer, statin use, and walking exercise.

Table S5. Association between 1-year change in objective walking performance measures and all-cause mortality among people with peripheral artery disease (N= 435) excluding participants who underwent lower extremity revascularization.

		Model 1*		
Walking performance measure	**Tertiles**	**~~Rate of~~ mobility loss**	**Hazard Ratio (95% Confidence Interval)**	**p-value for trend**
		Events		
6-minute walk	Tertile 1†(N=143)	40/92 (43%)	1.66 (1.02, 2.68)	0.04
	Tertile 2 (N=143)	25/92 (27%)	1.05 (0.60, 1.85)	
	Tertile 3 (Ref) (N=143)	27/92 (29%)	1.00	
		Total events 92		
4-meter velocity (usual pace)	Tertile 1 (N=144)	36/94 (38%)	1.86 (1.12, 3.09)	0.02
	Tertile 2 (N=146)	29/94 (31%)	1.38 (0.84, 2.27)	
	Tertile 3 (Ref) (N=145)	29/94 (31%)	1.00	
		Total events 94		
4-meter velocity (fast pace)	Tertile 1 (N=144)	31/93 (33%)	1.49 (0.90, 2.46)	0.14
	Tertile 2 (N=145)	32/93 (34%)	1.22 (0.75, 1.97)	
	Tertile 3 (Ref) (N=144)	30/93 (32%)	1.00	
		Total events 93		
		Model 2		
Walking performance measure	Tertiles		**Hazard Ratio (95% Confidence Interval)**	**p-value for trend**
6-minute walk	Tertile 1		1.38 (0.80, 2.37)	0.30
	Tertile 2		1.12 (0.65, 1.93)	
	Tertile 3 (Ref)		1.00	
4-meter velocity (usual pace)	Tertile 1		1.59 (0.96, 2.62)	0.06
	Tertile 2		1.35 (0.77, 2.37)	
	Tertile 3 (Ref)		1.00	
4-meter velocity (fast pace)	Tertile 1		1.32 (0.76, 2.31)	0.30
	Tertile 2		1.20 (0.71, 2.03)	
	Tertile 3 (Ref)		1.00	

*Model 1: adjusted for Walking And Leg Circulation Study (WALCS) cohort and baseline functional performance; Model 2: adjusted for WALCS cohort, baseline functional performance, age, sex, race, baseline ankle brachial index, body mass index, smoking status, diabetes, heart failure, myocardial infarction, angina, pulmonary disease, disc disease, hip arthritis, knee arthritis, spinal stenosis, cancer, statin use, and walking exercise. †Tertile 1: greater 1-year decline in functional performance; Tertile 3: 1-year improvement in functional performance; Tertile 2: change between tertile 1 and tertile 3.

Table S6. Association between one-year change in self-reported walking difficulty and all-cause mortality among people with peripheral artery disease (N=392) excluding participants who underwent lower extremity revascularization.

		Model 1*		
	Change in symptom	**~~Rate of mobility loss~~**	**Hazard Ratio (95% Confidence Interval)**	**p-value for trend**
		Events		
Self-reported walking difficulty due to pain in calves or buttocks	Worse (N=114)	24/84 (29%)	1.41 (0.74, 2.70)	0.25
	No change (N=151)	35/84 (42%)	1.40 (0.81, 2.41)	
	Improved (N=127)	25/84 (30%)	1.00	
		Total events 84		
Self-reported walking difficulty due to pain in thighs	Worse (N=88)	22/84 (26%)	2.62 (1.28, 5.37)	0.02
	No change (N=209)	46/84 (55%)	2.03 (1.09, 3.78)	
	Improved (N=96)	16/84 (19%)	1.00	
		Total events 84		
		Model 2 †		
	Change in symptom		**Hazard Ratio (95% Confidence Interval)**	**p-value for trend**
Self-reported walking difficulty due to pain in calves or buttocks	Worse		1.33 (0.61, 2.88)	0.43
	No change		1.41 (0.76, 2.62)	
	Improved		1.00	
Self-reported walking difficulty due to pain in thighs	Worse		2.28 (1.09, 4.81)	0.04
	No change		1.58 (0.80, 3.11)	
	Improved		1.00	
		Model 3‡		
Self-reported walking difficulty due to pain in calves or buttocks	Worse		1.14 (0.54, 2.41)	0.66
	No change		1.20 (0.64, 2.27)	
	Improved		1.00	
Self-reported walking difficulty due to pain in thighs	Worse		1.99 (0.91, 4.35)	0.08
	No change		1.30 (0.66, 2.55)	
	Improved		1.00	

*Model 1: adjusted for Walking And Leg Circulation Study (WALCS) cohort and baseline self-reported walking difficulty; †Model 2: adjusted for WALCS cohort, baseline self-reported walking difficulty, age, sex, race, baseline ankle brachial index, body mass index, smoking status, diabetes, heart failure, myocardial infarction, angina, pulmonary disease, disc disease, hip arthritis, knee arthritis, spinal stenosis, cancer, statin use, and walking exercise. ‡Model 3: adjusted for WALCS cohort, baseline self-reported walking difficulty, change in six-minute walk tertiles, baseline six-minute walk distance, age, sex, race, baseline ankle brachial index, body mass index, smoking status, diabetes, heart failure, myocardial infarction, angina, pulmonary disease, disc disease, hip arthritis, knee arthritis, spinal stenosis, cancer, statin use, and walking exercise.