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The Walking Impairment Questionnaire Stair-Climbing Score predicts mortality in men and women with peripheral arterial disease

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Abstract

Objectives—The Walking Impairment Questionnaire (WIQ) measures self-reported walking distance, walking speed, and stair-climbing ability in men and women with lower extremity peripheral arterial disease (PAD). We determined whether poorer WIQ scores are associated with higher all-cause and cardiovascular disease (CVD) mortality in individuals with and without PAD.

Methods—1048 men and women with and without PAD were identified from Chicago-area medical centers. Participants completed the WIQ at baseline and were followed for a median of 4.5 years. Cox proportional hazards models were used to relate baseline WIQ scores with mortality, adjusting for age, sex, race, the ankle brachial index (ABI), comorbidities, and other covariates.

Results—461 participants (44.0%) died during follow-up, including 158 deaths from cardiovascular disease. PAD participants in the lowest baseline quartile of the WIQ stair-climbing scores had higher all-cause mortality (HR = 1.70 [95% Confidence Interval (CI) 1.08-2.66, p=0.02] and higher CVD mortality (HR = 3.11 [95% CI 1.30 – 7.47, p=0.01]) compared to those with the highest baseline WIQ stair climbing score. Among PAD participants there were no significant associations of lower baseline WIQ distance or speed scores with rates of all-cause mortality (*p* for trend = 0.20 and 0.07, respectively) or CVD mortality (*p* for trend = 0.51 and *p* for trend = 0.33, respectively). Among non-PAD participants there were no significant associations of lower baseline WIQ stair climbing, distance, or speed score with rates of all-cause mortality (*p* for trend = 0.94, 0.69, and 0.26, respectively) or CVD mortality (*p* for trend = 0.28, 0.68, and 0.78, respectively).

Conclusions—Among participants with PAD, lower WIQ stair climbing scores are associated with higher all-cause and CVD mortality, independently of the ABI and other covariates.

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INTRODUCTION

Lower extremity peripheral arterial disease (PAD) is a common condition that affects more than 8 million Americans(1). Compared to persons without PAD, affected individuals are at significantly increased risk for all-cause and cardiovascular mortality(2). Objective measures that predict survival in men and women with PAD include the ankle brachial index (ABI)(3) and functional performance measures, such as the six-minute walk test and four-meter walking velocity (4).

Subjective measures of overall health status that include assessment of general mobility, such as the EuroQol Questionnaire, have been used in recent studies to predict survival in participants with PAD(5). The Walking Impairment Questionnaire (WIQ) was developed as a simple self-administered instrument to measure self-reported walking distance, walking speed, and stair climbing limitations in patients with PAD in the outpatient setting (6). We investigated associations of the WIQ distance, speed, and stair-climbing scores with all-cause and cardiovascular disease mortality in individuals with PAD and without PAD. We hypothesized that lower WIQ scores would be associated with higher all-cause and CVD mortality among participants with PAD and without PAD. If our hypotheses are correct, the WIQ could potentially be used by clinicians to assess mortality risk in patients with PAD and without PAD.

METHODS

Participant Identification

Participants for this analysis were identified from the Walking and Leg Circulation Study (WALCS) and WALCS II studies. The WALCS and WALCS II are prospective, observational studies designed to identify clinical characteristics associated with functional impairment, functional decline, and mortality in men and women with PAD (7, 8). The WALCS cohort was assembled from October 1998 to March 2000. The WALCS II cohort was assembled from November 2002 to April 2004. WALCS II included WALCS participants who were alive and consented to participation in WALCS II as well as newly identified participants. WALCS participants were followed for up to eight years, while newly identified participants for WALCS II were followed for up to four years. For both WALCS and WALCS II, PAD participants were identified consecutively from among patients diagnosed with PAD in three Chicago-area non-invasive vascular diagnostic laboratories. Participants without PAD were identified from among consecutive patients in a general medicine practice at Northwestern University and had an ABI of 0.90 and greater and less than 1.40. The institutional review boards of Northwestern University and collaborating sites approved the study protocol. Written informed consent was obtained.

Exclusion criteria

For participants with PAD, we excluded individuals with an ABI ≥ 0.90 at baseline because they either did not have PAD or because they had non-compressible arteries which did not allow accurate assessment of PAD severity. At enrollment for WALCS and WALCS II, PAD and non-PAD persons with above- or below-knee amputations or ulcers, nursing home residents and wheelchair-bound patients were excluded due to severely limited functional capacity at baseline. Participants with prior lower extremity revascularization procedures were not excluded. Non-English-speaking participants were excluded as the data collectors were fluent only in the English language. At baseline, participants with recent major surgery and self-identified or physician-identified dementia as well as those unlikely to return for 12-month follow-up because of medical illness or logistical issues were excluded (Figure 1).

Walking Impairment Questionnaire

Participants self-administered the WIQ forms at baseline. In the WIQ distance score, the participant is asked to assess the degree of difficulty in walking specific distances (ranging from walking indoors to 1500 feet, or 5 blocks) on a graded scale from zero to four. A score of zero represents the inability to walk the distance in question and a score of four represents no difficulty. In the WIQ speed score, the participant is asked to assess the degree of difficulty in walking one block at specific speeds ranging from walking slowly to jogging on a graded scale ranging from zero to four. In the WIQ stair-climbing score, the participant is asked to report the degree of difficulty climbing specific numbers of flights of stairs ranging from one to three flights of stairs on a graded scale ranging from zero to four. This graded score is multiplied by a pre-specified weight for each distance, speed, or number of stair flights. The products are summed and divided by the maximum possible score to obtain a percent score, ranging from 0 (representing the inability to perform any of the tasks) to 100 (representing no difficult with any of the tasks) (9). The WIQ scores have been shown to improve in response to lower extremity revascularization (10) and supervised exercise therapy(11).

ABI measurement

Using a handheld Doppler probe (Nicolet Vascular Pocket Dop II, Nicolet Biomedical, Golden, Colorado), systolic pressures were measured in the right and left brachial, posterior tibial, and dorsalis pedis arteries and then again in reverse order. The ABI was calculated by dividing the mean of the posterior tibial and dorsalis pedis pressures in each leg by the mean of the four brachial pressures (12). Average brachial pressures in the arm with highest pressure were used when one brachial pressure was higher than the opposite brachial pressure in both measurement sets and the two brachial pressures differed by 10 or more mmHg in at least one measurement set, because in such cases, subclavian stenosis is possible (13). The lowest leg ABI was used in the analyses. This method was used as it has been shown to be the most closely associated with impaired lower extremity functioning (12).

Comorbidities

We measured and verified baseline comorbidities that would potentially influence WIQ scores and mortality: history of congestive heart failure, angina, myocardial infarction, diabetes, cancer and chronic pulmonary disease. This was done using algorithms developed for the Women's Health and Aging Study(17) which combine data from medical record review, medications, patient self-report, selected laboratory values, and a questionnaire completed by the participant's primary care provider.

Participant-reported physical activity

At the initial study visit, participant-reported physical activity was measured with a questionnaire derived from the Harvard Alumni Activity Study that has previously been validated in participants with PAD (18). Participants were asked the following question: "During the last week, how many city blocks or their equivalent did you walk? Let 12 city blocks equal 1 mile."

Other measures

At the initial visit, height and weight were measured and body mass index (BMI) was calculated by dividing the weight in kilograms by the square of the height in meters. Cigarette smoking history was self-reported. Leg symptoms for PAD participants were characterized using the San Diego claudication questionnaire (19). Participants were classified into previously described symptom categories as follows: 1) asymptomatic PAD

(no exertional leg symptoms); 2) intermittent claudication (exertional calf pain that does not begin at rest, causes the participant to stop walking, and resolves within 10 minutes of rest), 3) pain on exertion and rest (exertional leg symptoms that sometimes begin at rest); 4) atypical exertional leg pain/carry on (exertional leg pain that does not cause the participant to stop walking); 5) atypical exertional leg pain/stop (exertional leg pain that does not begin at rest, causes the participant to stop walking, and is otherwise atypical because it does not involve the calf or does not resolve within 10 minutes of rest)(20).

Six-minute walk distance and four meter walking velocity (usual and fast paced) were measured at baseline using previously published methods.(14-16)

The principal study investigator reviewed the medication list for each participant at the initial visit, unaware of all other patient data, and identified the use of statins and ACE inhibitors for each participant.

Death

Information on deaths was obtained annually from proxies, the Social Security Administration death database, and primary care providers. Death certificate information from the state in which the death occurred, family members, or from the participants' medical records was also obtained. Deaths from cardiovascular disease (CVD) were those with ICD-10 codes in the range I00.0 through I99. This included deaths due to stroke, peripheral vascular disease, coronary heart disease and sudden cardiac death.

Statistical analyses

Age-adjusted baseline characteristics of participants across quartiles of each WIQ score (distance, speed, and climb score) were compared using linear models for continuous variables and logistic models for categorical variables.

Proportional hazards analyses were used to compare differences in all-cause and CVD mortality across WIQ score quartiles, with the highest (best) quartile for each WIQ domain used as the referent. The use of WIQ score quartiles, as opposed to continuous WIQ score values, was to facilitate assessment for a threshold effect as well as to allow findings to be more accessible to the practicing clinician. Pairwise comparisons were performed with *p* values calculated between the lowest (first or worst) and highest (fourth or best) quartile, between the second and fourth quartile, and between the third and fourth quartile. Overall *p* for trend was also calculated. Analyses were adjusted for age, sex, race, ABI, BMI, current smoking status, comorbidities (history of congestive heart failure, angina, myocardial infarction, diabetes, cancer and chronic pulmonary disease), statin and ACE inhibitor use, and physical activity. Follow-up of participants was not censored after a medical intervention.

An additional analysis was done to estimate Pearson correlation coefficients to measure the strength of association between the WIQ domain scores and baseline ABI, among PAD participants.

RESULTS

Baseline Characteristics

Figure 2 depicts reasons for exclusion among individuals identified for the study. Of the 679 participants with PAD from WALCS and WALCS II, 41 (6.0%) participants were excluded from the analyses because they did not complete the WIQ at baseline. Of the 431 participants without PAD from WALCS and WALCS II, 21 (5.1%) were excluded from the

analyses for the same reason. Baseline characteristics did not differ between those who completed the WIQ vs. those who did not (Table I).

Overall, in the entire PAD cohort, mean age was 72.7 years ± 8.4 years, ABI was 0.65 ± 0.15, and prevalence of intermittent claudication was 32%. In the non-PAD cohort, mean age was 71.5 ± 7.7 years, and ABI was 1.09 ± 0.09.

Two hundred twenty-one (34.6%) PAD participants died during a median follow-up of 4.5 years. Of these, 78 deaths (35.3%) were attributed to cardiovascular disease. 10 repeated imputations were used in competing risk analyses in cases where death certificates were unobtainable. Table II lists the age-adjusted baseline characteristics of PAD participants by WIQ stair-climbing, WIQ distance, and WIQ speed score quartiles. Lowest (worst) quartiles for the WIQ stair-climbing score were associated with fewer blocks walked in the past week, higher BMI, and higher prevalences of females, black race, angina, heart failure, prior myocardial infarction, and pulmonary disease. Lower PAD participant WIQ stair-climbing scores were also associated with a higher prevalence of pain on exertion and rest, a lower prevalence of atypical exertional leg pain/carry on, and a lower prevalence of asymptomatic PAD.

Lower (worse) quartiles for the PAD participant WIQ distance score were associated with lower ABI values and higher prevalences of females, black race, angina, heart failure, history of myocardial infarction, and pulmonary disease. Lower WIQ distance scores were associated with a higher prevalence of pain on exertion and rest, a higher prevalence of intermittent claudication, a lower prevalence of asymptomatic PAD, and a lower prevalence of atypical exertional leg pain/carry on.

Lower (worse) quartiles for the PAD participant WIQ speed score were associated with lower ABI and higher prevalences of females, black race, angina, heart failure, history of myocardial infarction, pulmonary disease, and diabetes. Furthermore, participants in the lowest (worst) quartiles for WIQ speed score had a higher prevalence of pain on exertion and rest, a higher prevalence of intermittent claudication, a lower prevalence of asymptomatic PAD and a lower prevalence of atypical exertional leg pain/carry on.

Table III lists the age-adjusted baseline characteristics of non-PAD participants by WIQ stair-climbing, WIQ distance, and WIQ speed score quartiles. Lower (worse) quartiles for the non-PAD participant WIQ stair-climbing score were associated with a lower prevalence of males, higher BMI, fewer blocks walked in the past week, higher prevalences of black race, angina, CHF, MI, pulmonary disease, and diabetes. Lower quartiles were also associated with shorter six minute walk distance and slower four meter walking velocity, at both usual and fast speeds.

Given a very large number of non-PAD participants with a WIQ distance score of 100, the software used in this analysis grouped both 3rd and 4th quartile scoring participants into the 3rd quartile. Lower (worse) quartiles for the non-PAD participant WIQ distance score were associated with higher BMI, fewer blocks walked in the past week, higher prevalence of black race, angina, CHF, pulmonary disease, and diabetes. Lower quartiles were also associated with shorter six minute walk distance and slower four meter walking velocity at both usual and fast speeds.

Lower (worse) quartiles for the non-PAD participant WIQ speed score were associated with a lower prevalence of males, higher BMI, fewer blocks walked in the past week, higher prevalences of black race, angina, CHF, MI, pulmonary disease, and diabetes. Lower quartiles were also associated with shorter six minute walk distance and slower four meter walking velocity at both usual and fast speeds.

WIQ stair-climbing score and mortality

Table IVa and Table IVb show the associations of WIQ stair-climbing score quartiles with all-cause and CVD mortality among PAD and non-PAD participants, respectively. These data are adjusted for age, sex, race, ABI, BMI, smoking status, comorbidities, statin and ACE inhibitor use, and physical activity.

Poorer WIQ stair-climbing scores at baseline were associated with higher all-cause mortality (p for trend = 0.02) among PAD participants. PAD participants in the first and second WIQ stair climbing quartiles had adjusted hazard ratios of 1.70 (95% CI 1.08 – 2.66, p=0.02) and 1.75 (95% CI 1.13 – 2.70, p=0.01), respectively, for all-cause mortality when compared to those in the highest (best) WIQ stair climbing quartile. Poorer WIQ stair-climbing scores were also significantly associated with higher CVD mortality (p for trend = 0.04) among PAD participants. When compared to those in the highest (best) quartile, PAD participants in the first and second WIQ stair climbing quartiles had adjusted hazard ratios of 3.11 (95% CI 1.30 – 7.47, p = 0.01) and 3.32 (95% CI 1.43 – 7.72, p = 0.01) for CVD mortality, respectively (Table IVa). No significant associations were observed between WIQ stair-climbing score and all-cause mortality (p for trend = 0.94) or CVD mortality (p for trend = 0.29) among non-PAD participants (Table IVb).

WIQ distance score

After adjusting for age, sex, race, ABI, BMI, smoking status, comorbidities, statin and ACE inhibitor use, and physical activity, no significant associations were observed between the WIQ distance score and all-cause mortality (p for trend = 0. 20) or CVD mortality (p for trend = 0.51) among PAD participants. (Table Va). No significant associations were observed between WIQ distance score and all-cause mortality (p for trend = 0.69) or CVD mortality (p for trend = 0.69) among non-PAD participants. (Table Vb).

WIQ speed score

After adjusting for age, gender, race, ABI, BMI, smoking status, comorbidities, statin and ACE inhibitor use, and physical activity, no significant associations were observed between the WIQ speed score and all-cause mortality (p for trend = 0.07) or CVD mortality (p for trend = 0.33) among PAD participants. In pairwise comparisons, PAD participants with WIQ speed scores in the second quartile had an adjusted hazard ratio of 1.71 (95% CI 1.12 – 2.60) for all-cause mortality compared to those with WIQ speed scores in the fourth (best) quartile (Table VIa). There were no other significant associations of WIQ speed quartiles with mortality among PAD participants. No significant associations were observed between WIQ speed score and all-cause mortality (p for trend = 0.26) or CVD mortality (p for trend = 0.78) among non-PAD participants. (Table VIb).

Correlation of WIQ domain scores and ABI among PAD participants

Statistically significant but weak correlations were observed between ABI and WIQ distance and WIQ speed scores (0.270, $p < 0.0001$ and 0.178, $p < 0.0001$; respectively). No correlation was observed between WIQ stair climbing score and ABI with a Pearson coefficient of 0.074, p = 0.06 (Table VII).

DISCUSSION

Among 638 men and women with PAD, lower baseline WIQ stair-climbing scores were associated with higher all-cause and cardiovascular disease mortality, respectively, over a median follow-up of 4.5 years. After adjustment for baseline ABI, comorbidities, age, and other confounders, those in the lowest WIQ stair-climbing score quartile were 1.70 times

more likely to die from any cause and 3.11 times more likely to die from cardiovascular disease compared to those in the highest (best) WIQ stair-climbing score quartile at baseline. In contrast, we found no statistically significant associations between baseline WIQ speed or WIQ distance scores with all-cause or cardiovascular disease mortality, among the PAD participants. Furthermore, no independent association was observed between baseline WIQ stair-climbing, WIQ distance, and WIQ speed scores with all-cause and CVD mortality among non-PAD participants.

Previous studies have also assessed associations of subjective measures of walking performance or global health-related quality of life with mortality in patients with PAD. In the Peripheral Arteriopathy and Cardiovascular Events (PACE) study(21), the Walking Impairment Questionnaire was administered to 60 Italian participants with PAD and intermittent claudication. Over a median follow-up of 24 months, WIQ speed and WIQ stair-climbing scores below the median were associated with an increased risk of cardiovascular events as compared to scores above the median after adjusting for ABI and other confounders(21). As compared to this prior work, the current study includes PAD participants both with and without intermittent claudication symptoms. Since most people with PAD do not have classic symptoms of intermittent claudication(20), the current data are more generalizable to the typical individual with PAD. More recently, Issa et al.(5) reported that among 503 Dutch PAD patients undergoing non-cardiac vascular surgery, those with a poor subjective health-related quality of life, measured with the EuroQol Questionnaire one year after surgery, were at highest risk for all-cause mortality over three year follow-up when compared to those who reported the highest subjective health-related quality of life. Participants who reported severe mobility impairment at baseline were at greatest risk for three-year mortality. As compared to the data reported here, the study by Issa et al. did not adjust for ABI and included a higher proportion of participants with claudication. It is possible that baseline ABI is a confounder of the association of patient reported walking ability and quality of life with mortality. In addition, the EuroQol Questionnaire focuses more on global health-related quality of life and incorporates a non-specific and generalized mobility measure. In contrast, the WIQ, a PAD-specific questionnaire, is a more precise measure of patient-perceived mobility across specific dimensions such as stair-climbing ability, walking distance, and walking speed.

In contrast to the WIQ stair-climbing score, data presented here show that the WIQ distance and speed scores were not associated independently with all-cause or cardiovascular disease mortality. This association may represent greater precision of the WIQ stair-climbing score as a measure of overall cardiovascular fitness, as compared to the WIQ walking distance and walking speed. Similarly, objectively measured stair-climbing ability is generally considered a reliable surrogate of peak oxygen consumption and has been used as a preoperative screening tool in patients undergoing lung resection to predict risk for perioperative death (22). While to our knowledge no published literature is available that provides data on the predictive ability of the WIQ stair-climbing score and peak oxygen consumption in PAD patients, earlier studies by Brunelli et al. found that patients who performed poorly in a stair-climbing test were at higher risk for postoperative death after lung resection (23, 24). Thus, poor WIQ stair-climbing scores, as compared to WIQ walking distance or walking speed abilities, may better identify a subset of patients with poorer overall cardiovascular status and greater mortality risk when used in men and women with PAD.

Limitations

Study participants were identified from medical centers within Chicago. Although data may not be generalizable to PAD participants outside of Chicago, there is no reason to believe that the relationships reported here would not be maintained in other settings. Also, 6% of eligible participants were excluded from analysis as they did not complete the WIQ at

baseline. However, the baseline characteristics of those who did not complete the WIQ did not differ significantly from those who completed it.

Finally, while we adjusted for confounders including comorbidities, we cannot rule out the possibility that residual confounding or unidentified characteristics among participants with poorer WIQ scores contributed to the observed association with mortality risk.

Conclusion

Men and women with PAD who have poorer WIQ stair-climbing scores are at higher all-cause and cardiovascular disease mortality risk compared to those with higher WIQ stair-climbing scores. Data reported here demonstrate that the WIQ stair-climbing score provides additional data about all-cause and CVD mortality risk, beyond that provided by baseline ABI. These findings may potentially be helpful for clinicians who use the WIQ scores to assess patient perceived walking performance and risk. These results also help to place into better perspective the potential significance of interventions that improve WIQ stair climbing scores. Future study is necessary to confirm findings reported here and determine whether interventions that improve WIQ stair-climbing score are associated with a survival benefit.

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Figure 1: Description of inclusion and exclusion criteria
Inclusion criteria for PAD participants: WALCS participants were age 55 or older, diagnosed with PAD at three Chicago-area non-invasive vascular diagnostic laboratories WALCS II participants were age 59 or older, diagnosed with PAD at three Chicago-area non-invasive vascular diagnostic laboratories **Inclusion criteria for non-PAD participants:** age 55 or older with approximately half identified as having normal ABI values at three Chicago-area non-invasive vascular diagnostic laboratories and the remainder identified from consecutive patients in a general medicine practice at Northwestern University. **Exclusion criteria for PAD and non-PAD participants:** Did not complete WIQ at baseline Nursing home residents Wheelchair-bound Lower extremity amputation Non-English-speaking ABI of 1.40 or higher (non-compressible arteries) Recent major surgery Dementia Unable to return for 12-month follow-up
PAD= peripheral arterial disease WALCS= Walking and Leg Circulation Study WIQ= Walking Impairment Questionnaire ABI= ankle-brachial index

Figure 1.
Description of inclusion and exclusion criteria

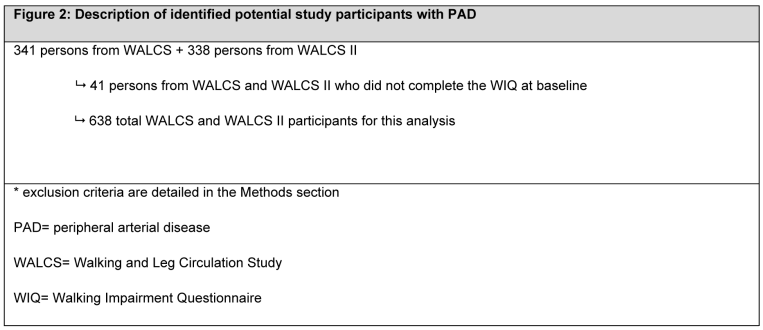

Figure 2.
Description of identified potential study participants with PAD

Table I

Baseline Clinical Characteristics of Peripheral Arterial Disease Participants With and Without Walking Impairment Questionnaire

	Without WIQ (N=41)	With WIQ (N=638)	*p* value
Age, y	72.4 (10.2)	72.7 (8.3)	0.82
Male, %	56.1	56.6	0.95
Black race, %	24.4	16.8	0.21
ABI	0.64 (0.1)	0.65 (0.2)	0.79
BMI, kg/m^2	26.5 (4.9)	27.7 (5.1)	0.15
Current Smoker, %	22.0	18.1	0.62
Angina, %	26.8	33.5	0.38
CHF, %	29.3	22.7	0.34
MI, %	22.0	24.6	0.70
Pulmonary Disease, %	41.3	35.7	0.46
Cancer, %	19.5	17.6	0.75
Diabetes, %	39.0	31.8	0.34
Blocks walked in the past week, n	32.1 (70.1)	32.5 (56.1)	0.96

Values shown are mean (Standard deviation) unless otherwise indicated. WIQ = Walking Impairment Questionnaire; PAD = peripheral arterial disease; ABI = ankle brachial index; BMI = body mass index; CHF = congestive heart failure; MI = myocardial infarction.

Table II

Age-adjusted Clinical Characteristics of Peripheral Arterial Disease Participants Across WIQ Score Quartiles (n=638)

	WIQ Stair Climbing Score Quartiles				
	1st Quartile [≤ 25.0]	2nd Quartile [25.0 – 41.7]	3rd Quartile [41.7 – 66.7]	4th Quartile [> 66.7]	*p* for trend
Male, %	40.3*	52.2*	63.2	73.9*	< 0.001
Black race, %	23.3	11.3	13.9	16.4	0.06
ABI	0.64 (0.01)	0.63 (0.01)	0.66 (0.01)	0.66 (0.01)	0.10
BMI, kg/m^2	29.0* (0.4)	27.2 (0.4)	27.5 (0.4)	26.6 (0.4)	< 0.001
Current Smoker, %	15.6	18.8	16.1	19.0	0.37
Angina, %	36.0*	41.8	30.8	25.8	0.01
CHF, %	32.7*	29.2	13.7	15.6*	< 0.001
MI, %	31.0*	28.4	23.4	14.9*	0.002
Pulmonary Disease, %	49.9*	37.1	31.6	22.2*	< 0.001
Cancer, %	12.0	20.1	21.1	16.7	0.31
Diabetes,%	40.0	26.2	25.3	31.1	0.05
Blocks walked in the past week, n	14.3* (4.1)	26.5* (4.6)	43.4 (4.1)	48.9 (4.6)	< 0.001
Pain on exertion and rest	35.1	22.1	11.3	7.68	< 0.0001
Atypical exertional leg pain/stop	18.0	14.9	30.3	21.5	0.088
Atypical exertional leg pain/carry on	1.67	9.86	7.45	20.2	< 0.0001
Asymptomatic PAD	19.2	12.7	20.4	28.4	0.015
Intermittent claudication	25.5	40.0	29.8	22.1	0.263
Six minute walk, ft	846.6 (24.5)	1091.4 (27.0)	1271.2 (24.1)	1311.6 (27.1)	<.0001
Four meter velocity at usual speed, m/sec	0.74 (0.01)	0.87 (0.02)	0.94 (0.01)	0.96 (0.02)	<.0001
Four meter velocity at fast speed, m/sec	1.00 (0.02)	1.17 (0.02)	1.27 (0.02)	1.31 (0.02)	<.0001
Statin use,%	40.2	44.2	46.6	41.6	0.63
Inhibitor use, %	29.4	27.1	27.3	27.6	0.73

	WIQ Distance Score Quartiles				
	1st Quartile [≤ 14.5]	**2nd Quartile [14.5 – 37.1]**	**3rd Quartile [37.1 – 67.9]**	**4th Quartile [> 67.9]**	***p* for trend**
Male, %	49.0*	53.5*	56.6	67.9*	< 0.001
Black race, %	24.1	20.2	9.0	12.6*	0.001
ABI	0.59* (0.01)	0.64* (0.01)	0.66* (0.01)	0.70 (0.01)	< 0.001
BMI, kg/m^2	28.9* (0.4)	27.8 (0.4)	27.2 (0.4)	26.7 (0.4)	< 0.001
Current Smoker, %	14.0	19.8	18.2	16.8	0.90
Angina, %	40.5	32.8*	35.5	25.0*	0.01
CHF, %	31.0	22.0	17.4	19.2*	0.002
MI, %	31.6*	27.7	20.6	17.3*	0.001
Pulmonary Disease, %	46.4	32.8	35.7	28.6*	0.001
Cancer, %	16.7	19.7	17.0	16.6	0.92
Diabetes,%	40.0	26.5	26.1	31.7	0.18
Blocks walked in the past week, n	10.9* (4.2)	23.9* (4.1)	31.4* (4.2)	64.4 (4.2)	< 0.001
Pain on exertion and rest	32.4	19.9	18.1	7.65	< 0.0001
Atypical exertional leg pain/stop	17.1	22.0	27.1	20.5	0.48
Atypical exertional leg pain/carry on	1.27	5.65	7.75	21.8	< 0.0001
Asymptomatic PAD	11.3	15.1	15.7	38.5	< 0.0001
Intermittent claudication	37.5	36.4	30.4	11.3	< 0.0001
Six minute walk, ft	783.8 (24.6)	1107.1 (24.0)	1230.8 (24.2)	1375.9 (24.2)	< 0.0001
Four meter velocity at usual speed, m/sec	0.76 (0.02)	0.87 (0.02)	0.91 (0.02)	0.96 (0.02)	< 0.0001
Four meter velocity at fast speed, m/sec	1.03 (0.02)	1.18 (0.02)	1.24 (0.02)	1.29 (0.02)	<.0.0001
Statin use,%	43.2	39.8	46.0	42.8	0.99
Inhibitor use, %	29.2	24.9	28.5	28.1	0.75

	WIQ Speed Score Quartiles				
	1st Quartile [≤ 17.4]	**2nd Quartile [17.4 – 32.6]**	**3rd Quartile [32.6 – 54.3]**	**4th Quartile [> 54.3]**	***p* for trend**
Male, %	47.5*	50.4*	58.2	71.4*	< 0.001

	WIQ Speed Score Quartiles				
	1st Quartile [≤ 17.4]	**2nd Quartile [17.4 – 32.6]**	**3rd Quartile [32.6 – 54.3]**	**4th Quartile [> 54.3]**	***p* for trend**
Black race, %	24.0	16.8	12.0	14.0*	0.04
ABI	0.62* (0.01)	0.62* (0.01)	0.67 (0.01)	0.68 (0.01)	< 0.001
BMI, kg/m^2	29.4* (0.4)	27.6* (0.4)	27.1 (0.4)	26.5 (0.4)	< 0.001
Current Smoker, %	12.4	19.1	18.3	19.0	0.62
Angina, %	40.0	30.8*	38.0	25.4*	0.02
CHF, %	31.4*	28.3*	20.0	11.2*	< 0.001
MI, %	32.6	23.3	24.1	18.0*	0.01
Pulmonary Disease, %	41.0*	40.2	33.2	27.2*	< 0.001
Cancer, %	11.4	20.5	20.1	17.0	0.05
Diabetes,%	37.5	35.8	27.4	23.9	0.01
Blocks walked in the past week, n	11.5* (4.2)	22.6* (4.2)	37.3* (4.1)	59.8 (4.3)	< 0.001
Pain on exertion and rest	32.7	23.9	15.7	6.50	< 0.0001
Atypical exertional leg pain/stop	16.9	22.6	22.9	21.9	0.4924
Atypical exertional leg pain/carry on	3.10	3.77	11.4	18.2	< 0.0001
Asymptomatic PAD	16.3	15.7	18.5	31.0	0.001
Intermittent claudication	30.3	33.2	30.8	22.4	0.035
Six minute walk, ft	815.0 (24.2)	1037.2 (23.7)	1248.0 (23.2	1397.5 (24.6)	<.0001
Four meter velocity at usual speed, m/sec	0.74 (0.01)	0.84 (0.01)	0.92 (0.01)	0.99 (0.01)	<.0001
Four meter velocity at fast speed, m/sec	1.00 (0.02)	1.13 (0.02)	1.27 (0.02)	1.34 (0.02)	<.0001
Statin use,%	43.5	42.7	47.2	39.2	0.78
Inhibitor use, %	27.7	36.5	28.4	20.4	0.08

Values shown are mean (Standard Error) unless otherwise indicated. WIQ = Walking Impairment Questionnaire; PAD = peripheral arterial disease; ABI = ankle brachial index; BMI = body mass index; CHF = congestive heart failure; MI = myocardial infarction.

*for pairwise comparison with 4th quartile (best) as referent, *p* value < 0.05

Table III

Age-adjusted Clinical Characteristics of Non-PAD Participants Across WIQ Score Quartiles (n=410)

WIQ Stair Climbing Score Quartiles

	1st Quartile [≤ 41.7]	2nd Quartile [41.7 –66.7]	3rd Quartile [66.7 – 87.5]	4th Quartile [> 87.5]	*p* for trend
Male, %	32.21%	54.14%	47.04%	62.72%	0.0001
Black race, %	26.27%	17.86%	14.29%	10.24%	0.003
ABI	1.08(0.01)	1.09(0.01)	1.09(0.01)	1.11(0.01)	0.018
BMI, kg/m^2	31.83(0.49)	29.02(0.50)	26.36(0.59)	26.47(0.70)	<0.0001
Current Smoker, %	7.50%	9.52%	7.10%	2.56%	0.11
Angina, %	35.67%	22.48%	12.42%	7.81%	<0.0001
CHF, %	23.65%	14.14%	10.21%	4.85%	<0.0001
MI, %	22.04%	12.90%	10.11%	8.25%	0.01
Pulmonary Disease, %	42.53%	34.94%	25.36%	11.67%	<0.0001
Cancer, %	14.60%	18.30%	16.93%	16.53%	0.97
Diabetes,%	30.18%	21.93%	17.54%	8.69%	0.001
Blocks walked in the past week, n	32.24(5.12)	39.18(5.25)	66.05(6.20)	59.33(7.30)	<0.0001
Six minute walk, ft	1085.6(46.77)	1460.8(45.62)	1601.0(60.60)	1632.6(71.12)	<.0001
Four meter velocity at usual speed, m/sec	0.82(0.02)	0.97(0.02)	1.02(0.03)	1.01(0.04)	<.0001
Four meter velocity at fast speed, m/sec	1.09(0.03)	1.29(0.03)	1.41(0.05)	1.36(0.05)	<.0001
Statin use,%	26.80%	33.12%	23.53%	24.44%	0.74
Inhibitor use, %	23.72%	24.23%	21.30%	18.35%	0.42

WIQ Distance Score Quartiles

	1st Quartile [≤ 44.6]	2nd Quartile [44.6 – 83.0]	3rd Quartile [83.0 – 100]	*p* for trend
Male, %	38.45%	55.38%	46.87%	0.13
Black race, %	31.17%	20.01%	11.43%	<.0001
ABI	1.07(0.01)	1.08(0.01)	1.10(0.01)	0.01
BMI, kg/m^2	32.01(0.56)	29.65(0.55)	26.90(0.40)	<.0001
Current Smoker, %	9.07%	11.97%	3.89%	0.02
Angina, %	37.64%	24.72%	13.00%	<.0001

WIQ Distance Score Quartiles

	1st Quartile [≤ 44.6]	2nd Quartile [44.6 – 83.0]	3rd Quartile [83.0 – 100]	*p* for trend
CHF, %	26.03%	14.97%	9.12%	<.0001
MI, %	18.99%	15.34%	11.64%	0.07
Pulmonary Disease, %	47.74%	31.54%	23.76%	<.0001
Cancer, %	17.16%	16.26%	15.75%	0.95
Diabetes,%	36.22%	23.84%	12.35%	<.0001
Blocks walked in the past week, n	20.27(5.65)	35.34(5.54)	64.89(4.03)	<.0001
Six minute walk, ft	1067.6(49.95)	1371.9(54.52)	1591.8(37.76)	<.0001
Four meter velocity at usual speed, m/sec	0.81(0.03)	0.92(0.03)	1.01(0.02)	<.0001
Four meter velocity at fast speed, m/sec	1.08(0.04)	1.22(0.04)	1.38(0.03)	<.0001
Statin use,%	30.25%	26.69%	26.77%	0.54
Inhibitor use, %	26.40%	22.89%	20.30%	0.14

WIQ Speed Score Quartiles

	1st Quartile [≤ 32.6]	2nd Quartile [32.6 – 50.0]	3rd Quartile [50.0 – 71.7]	4th Quartile [> 71.7]	*p* for trend
Male, %	41.06%	37.08%	55.47%	56.99%	0.001
Black race, %	27.31%	20.47%	10.72%	14.48%	0.003
ABI	1.07(0.01)	1.06(0.01)	1.11(0.01)	1.12(0.01)	<.0001
BMI, kg/m^2	32.15(0.54)	29.28(0.54)	27.72(0.59)	25.99(0.57)	<.0001
Current Smoker, %	13.43%	3.49%	5.74%	4.98%	0.02
Angina, %	39.07%	22.22%	16.67%	9.19%	<.0001
CHF, %	27.40%	18.30%	7.89%	4.21%	<.0001
MI, %	18.76%	16.65%	11.33%	9.83%	0.047
Pulmonary Disease, %	48.96%	29.82%	25.76%	18.16%	<.0001
Cancer, %	16.93%	19.29%	14.75%	15.31%	0.80
Diabetes,%	34.31%	28.86%	9.40%	10.23%	<.0001
Blocks walked in the past week, n	20.74(5.60)	46.41(5.57)	60.07(6.12)	62.22(5.92)	<.0001
Six minute walk, ft	1106.1(48.24)	1347.5(49.28)	1525.1(60.67)	1736.1(58.48)	<.0001
Four meter velocity at usual speed, m/sec	0.84(0.03)	0.91(0.03)	0.98(0.03)	1.08(0.03)	<.0001
Four meter velocity at fast speed,	1.11(0.03)	1.21(0.04)	1.30(0.04)	1.49(0.04)	<.0001

	WIQ Speed Score Quartiles				
	1st Quartile [≤ 32.6]	**2nd Quartile [32.6 – 50.0]**	**3rd Quartile [50.0 – 71.7]**	**4th Quartile [> 71.7]**	***p* for trend**
m/sec					
Statin use,%	30.23%	29.69%	24.33%	25.29%	0.75
Inhibitor use, %	26.73%	29.73%	13.20%	19.07%	0.07

Values shown are mean (Standard Error) unless otherwise indicated. WIQ = Walking Impairment Questionnaire; PAD = peripheral arterial disease; ABI = ankle brachial index; BMI = body mass index; CHF = congestive heart failure; MI = myocardial infarction.

* for pairwise comparison with 4th quartile (best) as referent, *p* value < 0.05

Table IVa

Adjusted Associations of WIQ stair climbing score quartiles with total and cardiovascular disease mortality among PAD Participants. (n = 638)

	HR (95% Confidence Interval)	pairwise *p* value	*p* for trend
All-cause mortality			
1st quartile [≤ 25.0]	1.70 (1.08 – 2.66)	0.02	0.02
2nd quartile [25.0 – 41.7]	1.75 (1.13 – 2.70)	0.01	
3rd quartile [41.7 – 66.7]	1.26 (0.82 – 1.91)	0.29	
4th quartile [> 66.7]	1.0 (referent)	NA	
Cardiovascular disease mortality			
1st quartile [≤ 25.0]	3.11 (1.30 – 7.47)	0.01	0.04
2nd quartile [25.0 – 41.7]	3.32 (1.43 – 7.72)	0.01	
3rd quartile [41.7 – 66.7]	2.03 (0.88 – 4.71)	0.10	
4th quartile [> 66.7]	1.0 (referent)	NA	

Adjusted for age, sex, race, body mass index, smoking status, ankle brachial index, comorbidities, physical activity, statin use and ACE inhibitor use. WIQ = Walking Impairment Questionnaire; CVD = cardiovascular disease; PAD = peripheral arterial disease; HR = hazard ratio. Pairwise *p* value shows statistical significance relative to the 4th quartile.

Table IVb

Adjusted Associations of WIQ stair climbing score quartiles with total and cardiovascular disease mortality among non-PAD Participants

	HR (95% Confidence Interval)	pairwise *p* value	*p* for trend
All-cause mortality			
1st quartile [≤ 41.7]	0.70(0.29 - 1.67)	0.42	0.94
2nd quartile [41.7 – 66.7]	0.71(0.31 - 1.60)	0.41	
3rd quartile [66.7 – 87.5]	0.43(0.18 - 1.04)	0.06	
4th quartile [> 87.5]	1.0 (referent)	NA	
Cardiovascular disease mortality			
1st quartile [≤ 41.7]	2.62(0.45 - 15.21)	0.28	0.29
2nd quartile [41.7 – 66.7]	2.55(0.49 - 13.41)	0.27	
3rd quartile [66.7 – 87.5]	0.48(0.07 - 3.36)	0.46	
4th quartile [> 87.5]	1.0 (referent)	NA	

Adjusted for age, sex, race, body mass index, smoking status, ankle brachial index, comorbidities, physical activity, statin use and ACE inhibitor use. WIQ = Walking Impairment Questionnaire; CVD = cardiovascular disease; PAD = peripheral arterial disease; HR = hazard ratio. Pairwise *p* value shows statistical significance relative to the 4^{th} quartile.

Table Va

Adjusted Associations of WIQ distance score quartiles with total and cardiovascular disease mortality among PAD Participants. (n = 638)

	HR (95% CI)	*p* value	*p* for trend
All-cause mortality			
1st quartile [≤ 14.5]	1.22 (0.79 - 1.88)	0.38	0.20
2nd quartile [14.5 – 37.1]	1.49 (0.98 - 2.25)	0.06	
3rd quartile [37.1 – 67.9]	1.26 (0.84 - 1.89)	0.27	
4th quartile [> 67.9]	1.0 (referent)	NA	
Cardiovascular disease mortality			
1st quartile [≤ 14.5]	1.30 (0.60 - 2.81)	0.51	0.51
2nd quartile [14.5 – 37.1]	1.13 (0.51 - 2.50)	0.77	
3rd quartile [37.1 – 67.9]	1.30 (0.63 - 2.69)	0.48	
4th quartile [> 67.9]	1.0 (referent)	NA	

Adjusted for age, sex, race, body mass index, smoking status, ankle brachial index, comorbidities, physical activity, statin use and ACE inhibitor use. WIQ = Walking Impairment Questionnaire; CVD = cardiovascular disease; PAD = peripheral arterial disease; HR = hazard ratio. Pairwise *p* value shows statistical significance relative to the 4^{th} quartile.

Table Vb

Adjusted Associations of WIQ distance score quartiles with total and cardiovascular disease mortality among non-PAD Participants

	HR (95% CI)	*p* value	*p* for trend
All-cause mortality			
1st quartile [≤ 44.6]	1.36(0.69 - 2.69)	0.37	0.69
2nd quartile [44.6 – 83.0]	1.05(0.56 - 1.95)	0.88	
3rd quartile [83.0 –100]	1.0 (referent)	NA	
Cardiovascular disease mortality			
1st quartile [≤ 44.6]	1.09(0.35 - 3.37)	0.88	0.68
2nd quartile [44.6 – 83.0]	1.55(0.58 - 4.13)	0.38	
3rd quartile [83.0 –100]	1.0 (referent)	NA	

Adjusted for age, sex, race, body mass index, smoking status, ankle brachial index, comorbidities, physical activity, statin use and ACE inhibitor use. WIQ = Walking Impairment Questionnaire; CVD = cardiovascular disease; PAD = peripheral arterial disease; HR = hazard ratio. Pairwise *p* value shows statistical significance relative to the 4^{th} quartile.

Table VIa

Adjusted Associations of WIQ speed score quartiles with total and cardiovascular disease mortality among PAD Participants. (n = 638)

	HR (95% CI)	*p* value	*p* for trend
All-cause mortality			
1st quartile [≤ 17.4]	1.57 (1.00 - 2.44)	0.05	0.07
2nd quartile [17.4 – 32.6]	1.71 (1.12 - 2.60)	0.01	
3rd quartile [32.6 – 54.3]	1.34 (0.88 - 2.05)	0.17	
4th quartile [> 54.3]	1.0 (referent)	NA	
Cardiovascular disease mortality			
1st quartile [≤ 17.4]	1.61 (0.75 - 3.49)	0.23	0.33
2nd quartile [17.4 – 32.6]	1.80 (0.84 - 3.82)	0.13	
3rd quartile [32.6 – 54.3]	1.50 (0.71 - 3.16)	0.30	
4th quartile [> 54.3]	1.0 (referent)	NA	

Adjusted for age, sex, race, body mass index, smoking status, ankle brachial index, comorbidities, physical activity, statin use and ACE inhibitor use. WIQ = Walking Impairment Questionnaire; CVD = cardiovascular disease; PAD = peripheral arterial disease; HR = hazard ratio. Pairwise *p* value shows statistical significance relative to the 4^{th} quartile.

Table VIb

Adjusted Associations of WIQ speed score quartiles with total and cardiovascular disease mortality among non-PAD Participants

	HR (95% CI)	*p* value	*p* for trend
All-cause mortality			
1st quartile [≤ 32.6]	1.43(0.64 - 3.19)	0.38	0.26
2nd quartile [32.6 – 50.0]	1.06(0.47 - 2.39)	0.89	
3rd quartile [50.0 – 71.7]	0.89(0.39 - 2.05)	0.79	
4th quartile [> 71.7]	1.0 (referent)	NA	
Cardiovascular disease mortality			
1st quartile [≤ 32.6]	1.38(0.35 - 5.50)	0.65	0.78
2nd quartile [32.6 – 50.0]	2.25(0.59 - 8.61)	0.24	
3rd quartile [50.0 – 71.7]	0.94(0.21 - 4.27)	0.94	
4th quartile [> 71.7]	1.0 (referent)	NA	

Adjusted for age, sex, race, body mass index, smoking status, ankle brachial index, comorbidities, physical activity, statin use and ACE inhibitor use. WIQ = Walking Impairment Questionnaire; CVD = cardiovascular disease; PAD = peripheral arterial disease; HR = hazard ratio. Pairwise *p* value shows statistical significance relative to the 4^{th} quartile.

Table VII

Correlation between baseline ABI and WIQ domain score in PAD participants

	Pearson coefficient	*p* value
WIQ stair climbing score	0.074	0.06
WIQ distance score	0.270	< 0.0001
WIQ speed score	0.178	< 0.0001

ABI = ankle brachial index

WIQ = Walking Impairment Questionnaire

PAD = peripheral arterial disease

$P < 0.05$ is statistically significant