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Associations of Calf Skeletal Muscle Characteristics and Peripheral Nerve Function with Self-Perceived Physical Functioning and Walking Ability in Persons with Peripheral Arterial Disease

Natalie S. Evans, MD¹, Kiang Liu, PhD², Michael H. Criqui, MD, MPH³, Luigi Ferrucci, MD, PhD⁴, Jack M. Guralnik, MD, PhD⁴, Lu Tian, ScD⁵, Yihua Liao, MS², and Mary M. McDermott, MD^{1,2}

¹Department of Medicine, Northwestern University Feinberg School of Medicine, Chicago, Ill

²Department of Preventive Medicine, Northwestern University Feinberg School of Medicine, Chicago, Ill

³University of California at San Diego School of Medicine, San Diego, Calif

⁴National Institute on Aging, Bethesda, Md

⁵Stanford University, San Francisco, Calif

Abstract

We determined whether more adverse calf muscle characteristics and poorer peripheral nerve function were associated with impairments in self-perceived physical functioning and walking ability in persons with lower extremity peripheral arterial disease (PAD). Participants included 462 persons with PAD; measures included the ankle-brachial index (ABI), medical history, electrophysiologic characteristics of nerves, and computed tomography of calf muscle. Self-perceived physical functioning and walking ability were assessed using the 36-Item Short Form Health Survey (SF-36) and the Walking Impairment Questionnaire (WIQ). Results were adjusted for age, sex, race, ABI, body-mass index, comorbidities, and other confounders. Lower calf muscle area was associated with a poorer SF-36 physical function (PF) score (overall p trend<0.001, 33.76 PF score for the lowest quartile vs. 59.74 for the highest, pair wise p <0.001) and a poorer WIQ walking distance score (p trend=0.001, 29.71 WIQ score for the lowest quartile vs. 48.43 for the highest, pair wise p <0.001). Higher calf muscle percent fat was associated with a poorer SF-36 PF score (p trend<0.001, 53.76 PF score for the lowest quartile vs. 40.28 for the highest, pair wise p =0.009). Slower peroneal nerve conduction velocity was associated with a poorer WIQ speed score (p trend=0.023, 30.49 WIQ score for the lowest quartile vs. 40.48 for the highest, pair wise p =0.031). In summary, adverse calf muscle characteristics and poorer peripheral nerve function are associated significantly and independently with impairments in self-perceived physical functioning and walking ability in PAD persons.

Keywords

peripheral arterial disease; calf muscle characteristics; peripheral nerve function; quality of life

Introduction

Lower extremity peripheral arterial disease (PAD) is widespread, affecting 8 million men and women in the United States.¹ It is associated with high rates of cardiovascular morbidity and mortality.² Individuals with PAD also are more likely than those without PAD to have depressive symptoms³ and poorer health-related quality of life by various measures.⁴

Persons with lower ankle-brachial index (ABI) values, consistent with PAD, have lower calf muscle area and higher calf muscle percent fat compared to people without PAD.⁵ Additionally, those with severe PAD have poorer peripheral nerve functioning compared to those without PAD.⁶ Although poorer peripheral nerve function has been associated with greater impairment in lower extremity performance among individuals without PAD, associations of impaired peripheral nerve function with quality of life have not been previously reported among participants with PAD.⁶ Among persons with PAD, lower calf muscle area and higher calf muscle percent fat are associated with poorer performance on the 6-minute walk and usual-paced 4-meter walking velocity tests.⁵ However, associations of calf muscle characteristics and peripheral nerve function with quality of life among people with PAD are unknown. We studied the associations of calf muscle characteristics and peripheral neuropathy with patient-perceived physical functioning and walking ability among men and women with PAD. We hypothesized that among persons with PAD, lower calf muscle area, higher calf muscle percent fat, and poorer calf muscle density would be associated with impairments in patient-perceived physical functioning and walking ability. We further hypothesized that poorer lower extremity peripheral nerve function would be associated with such impairments. Finally, we hypothesized that associations of impaired muscle and nerve function with impairments in self-perceived physical functioning and walking ability may be mediated by or related to poorer objectively measured walking performance.

Methods

Participant identification

The protocol was Institutional Review Board-approved by Northwestern University Feinberg School of Medicine and Catholic Health Partners Hospitals. Participants gave informed consent. Participants included 223 persons attending their fourth annual follow-up visit in the Walking and Leg Circulation Study (WALCS) and 239 individuals newly identified for the present study (WALCS II). WALCS is a prospective, observational study designed to identify predictors of functional decline in PAD. Participants were age 59 and older and identified consecutively from among patients diagnosed with PAD in three Chicago-area non-invasive vascular laboratories. Recruitment methods have been reported previously.⁵

Exclusion criteria

PAD was defined as $ABI < 0.90$.⁷⁻⁹ Absence of PAD was defined as $ABI \geq 0.90$ and $ABI \leq 1.30$.¹⁰ Individuals with $ABI > 1.30$ were excluded because this indicates poorly compressible leg arteries and inability to gauge arterial perfusion accurately.

At study entry, patients with dementia were excluded because of their inability to answer questions accurately. Nursing home residents, wheelchair-bound patients, and patients with foot or leg amputations were excluded because they have severely impaired functioning. Non-English-speaking patients were excluded because investigators were not fluent in non-English languages. Patients with recent major surgery were excluded. Persons with a normal ABI and a history of lower extremity revascularization were excluded because they could not be clearly classified with vs. without PAD.

Ankle brachial index measurement

The ABI was measured using established methods.^{7, 8, 10, 11} After participants rested supine for five minutes, a hand-held Doppler probe (Nicolet Vascular Pocket Dop II, Golden, CO) was used to measure systolic pressures in the right brachial, dorsalis pedis, and posterior tibial arteries and the left dorsalis pedis, posterior tibial, and brachial arteries. Each pressure was measured twice. The ABI was calculated in each leg by dividing average pressures in each leg by the average of the four brachial pressures. 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 mm Hg in at least one measurement set, since in such cases subclavian stenosis was possible.¹² Lowest leg ABI was used in analyses.

Leg symptoms

We used the San Diego claudication questionnaire to measure the presence and type of leg symptoms based on previous study.¹³ This interview-administered questionnaire is derived from the original Rose Claudication questionnaire.¹⁶ The San Diego Claudication Questionnaire measures leg symptoms in both the right and left legs and allows categorization of leg symptoms into one of the following groups: no exertional pain (asymptomatic), pain on exertion and rest, non-calf claudication, non-Rose calf claudication, and Rose claudication.⁷

Calf skeletal muscle characteristics

Calf muscles are supplied by the superficial femoral artery, which is commonly affected by atherosclerosis.^{14, 15} Hence we chose these muscles for study. Additionally, persons with PAD frequently have symptoms in the calf muscles with exercise.¹⁶ We used a computed tomography (CT) scanner (LightSpeed, General Electric Medical Systems, Waukesha, WI) to obtain 2.5 mm cross-sectional images of the calf muscle at 66.7% of the distance from distal to proximal tibia. We analyzed the images with BonAlyse (BonAlyse Oy, Jyväskylä, Finland) imaging software that identifies muscle, fat, and bone and uses validated methods to measure density and geometry.¹⁷ We traced the calf muscle manually, excluding subcutaneous fat and bone. When quantifying muscle area, the software quantifies voxels within a range corresponding to muscle density (9 to 271 mg/cm³), excluding voxels that

correspond to fat density (-270 to 8 mg/cm^3). Intramuscular fat is quantified by summing voxels corresponding to fat within muscle tissue. Previous cadaver studies demonstrate that these methods provide an estimate of muscle cross-sectional area that is highly correlated with direct anatomic measures.¹⁸ Because larger individuals require greater muscle mass to support their larger frame, muscle area was adjusted for the square of individual tibia length.

Peripheral nerve function

Electroneurography is considered the gold standard for measurement of peripheral nerve function and has been validated for measuring both sensory and motor peripheral nerve function.^{19–21} Nerve function was measured in both legs by the electrodiagnostic supervisor at Northwestern Memorial Hospital, who is certified by the American Association of Electrodiagnostic Technologists and has 30 years of experience in electrodiagnostic testing. The technician was blinded to participants' history, including presence of diabetes or PAD. Results for the leg with lowest ABI were used in analyses comparing nerve function between individuals. We selected the peroneal nerve for study because its length increases its susceptibility to arterial obstruction at multiple locations in the lower extremities. Ulnar motor nerve conduction velocity (NCV) in one randomly selected upper extremity was also measured. The testing room was maintained at > 25 degrees Celsius.

Peroneal NCV (lower extremity motor nerve testing): Surface recording electrodes were placed on the dorsum of the foot. Two stimulating bipolar electrodes were placed over the peroneal nerve, one on the anterior ankle and the other behind the knee, and a ground electrode was placed between the recording and stimulating electrodes. A mild electrical impulse was applied that progressively increased until the maximum amplitude was obtained. The time required for electrical impulses to travel from the ankle to the recording electrode (t_1) and from the knee to the recording electrode (t_2) were recorded along with the distance between the two pairs of electrodes (distance) and the amplitude of the sinusoids (a_1 and a_2). The NCV was calculated as: $(\text{distance})/(\text{t}_2 - \text{t}_1)$. Peroneal amplitude was measured from baseline to the negative peak.

Ulnar NCV (upper extremity motor nerve): The active electrode was placed over the abductor digiti minimi muscle. The reference electrode was placed at the base of the fifth digit. A ground electrode was placed over the dorsum of the hand. The ulnar nerve was stimulated at the wrist and above the elbow. The distance between the two stimulation points and the time required for travel of electrical stimulation between these two points were used to calculate ulnar motor NCV.

Comorbidities

Algorithms developed for the Women's Health and Aging Study were used to document comorbidities,²² including diabetes mellitus, angina, myocardial infarction, stroke, heart failure, spinal stenosis, and disk disease.

Functional measures

Six-minute walk—Patients with PAD are particularly impaired in walking endurance. Thus, the 6-minute walk is sensitive to the functional limitations experienced by persons

with PAD. Following a standardized protocol,^{7, 8, 23} participants walk up and down a 100-foot hallway for 6 minutes after instructions to cover as much distance as possible.

Four-meter walking velocity—Walking velocity was measured using a 4-meter walk performed at usual pace, for which participants were instructed to walk “as if going down the street to the store.” The walk was performed twice and the faster walk used in analyses.^{24, 25}

Subjective measures of physical function and patient-perceived walking ability measures

The Medical Outcomes Study Short-Form 36 (SF-36) includes scales for pain, general health perceptions, mental health, physical functioning, physical and emotional roles, and vitality, each scored on a scale of 0 to 100 (100 = best), along with summary scores of the mental health and physical domains. The SF-36 has been standardized, validated, and used successfully in a variety of patient populations. The Walking Impairment Questionnaire (WIQ) measures impairments in walking distance, walking speed, and stair climbing as reported by participants. We focused our analyses on the SF-36 physical functioning domain and WIQ scores, since these measures are most relevant to the functional limitations persons with PAD typically experience.

Other measures

Height and weight were measured at the study visit. Body mass index (BMI) was calculated as weight (kg)/(height (meters))². Cigarette smoking history and alcohol consumption were based on self-report. History of lower extremity revascularization was determined based on participant report and confirmed by medical record review or the primary care physician questionnaire. The primary care physician questionnaire is a questionnaire sent to participants' primary care physicians that asks about the patient's medical history, hospitalizations, and revascularization procedures.

Statistical analyses

The SF-36 and WIQ scores were calculated across quartiles of measures of calf muscle characteristics and peripheral nerve function using analyses of covariance, adjusting for age and sex (Model 1). Analyses were repeated with additional adjustment for race, ABI, BMI, leg symptoms, cigarette smoking, height, prior lower extremity revascularization, recruitment cohort (WALCS vs. WALCS II), and comorbidities including diabetes, cardiac or cerebrovascular disease, arthritis, spinal stenosis, disk disease, pulmonary disease, and cancer (Model 2). In model 2, analyses of muscle area were additionally adjusted for tibial length, and peroneal and ulnar nerve conduction velocity and amplitude were adjusted for alcohol use (Model 2). Analyses that remained statistically significant in fully adjusted models were repeated with additional adjustment for a corresponding objective measure of functional performance (Model 3). Associations with the SF-36 physical functioning score, WIQ distance score, and WIQ stair climbing score were adjusted additionally for six-minute walk performance. The WIQ walking speed score was additionally adjusted for usual-paced four-meter walking speed.

Analyses were performed using SAS Statistical Software version 9.0 (SAS Inc., Cary, NC).

Results

The 462 participants with PAD had a mean age of 75.0 ± 8.3 years and included 53.3% men. Seventeen percent were African-American. Mean ABI was 0.63 ± 0.16 . The mean BMI was 27.8 ± 5.1 kg/m². Prevalences of current smoking and diabetes were 15.6% and 32.3%, respectively. Fifty-eight percent had cardiac or cerebrovascular disease, and 51.7% had arthritis of the knee or hip or vertebral disk disease.

Figure 1 shows associations between calf muscle area and the SF-36 PF score and WIQ scores. Lower calf muscle area was associated significantly with a poorer SF-36 physical functioning (PF) score (p trend < 0.001), a poorer WIQ walking distance score (p trend=0.005), a poorer WIQ walking speed score (p trend=0.015), and a poorer WIQ stair-climbing score (p trend=0.004), in Model 1 analyses. These associations remained statistically significant in Model 2 after additional adjustment for ABI, BMI, leg symptoms, smoking, height, comorbidities, and study cohort (Figure 1). In Model 3, which additionally adjusted for objective measures of walking performance, the relationships between calf muscle area and SF-36 PF were statistically significant but associations with all WIQ measures were no longer statistically significant (Figure 1).

Figure 2 shows associations between calf muscle density and the SF-36 PF score and WIQ scores. Lower calf muscle density was significantly associated with poorer SF-36 PF score (p trend < 0.001), poorer WIQ walking distance score (p trend < 0.001), poorer WIQ walking speed score (p trend < 0.001), and poorer WIQ stair-climbing score (p trend=0.001), in Model 1. Lower muscle density remained associated with poorer SF-36 PF score (p trend < 0.001), poorer WIQ walking distance score (p trend=0.018), and poorer WIQ walking speed score (p trend=0.004) in Model 2. These associations were no longer statistically significant in Model 3 (Figure 2).

Figure 3 shows associations between calf muscle percent fat and quality of life and walking ability measures. Higher calf muscle percent fat was significantly associated with poorer SF-36 PF score (p trend < 0.001), WIQ walking distance score (p trend < 0.001), WIQ walking speed score (p trend < 0.001), and WIQ stair-climbing score (p trend < 0.001) in Model 1. In Model 2, lower calf muscle percent fat was significantly associated only with poorer SF-36 PF (p trend < 0.001). In Model 3, this association was no longer statistically significant (Figure 3).

Table 1 shows associations of quartiles of peroneal nerve function and SF-36 PF score and WIQ measures. In Model 1, lower peroneal NCV was significantly associated with poorer SF-36 PF score (p trend < 0.001), WIQ speed score (p trend=0.003), and WIQ stair-climbing score (p trend=0.001). These relationships remained statistically significant in Model 2 (Table 1). There were no significant associations in Model 3 (Table 1).

Similar significant associations were observed between lower peroneal nerve amplitude and poorer SF-36 PF score (p trend < 0.001), WIQ walking distance score (p trend=0.036), and WIQ stair-climbing score (p trend=0.007), in Model 1. In Model 2, only the association of peroneal nerve amplitude and the SF-36 PF score remained significant (p trend=0.037).

Table 2 shows associations of ulnar nerve function and physical functioning and walking ability measures. In Model 1, slower ulnar NCV was significantly associated with poorer SF-36 PF score (p trend=0.001), WIQ walking speed score (p trend=0.010), and WIQ stair-climbing score (p trend=0.013). In Model 2, slower ulnar NCV remained significantly associated with poorer SF-36 PF score (p trend=0.040). In Model 3, there were no significant associations. Lower ulnar nerve amplitude was significantly associated with poorer SF-36 PF score (p trend <0.001), WIQ walking distance score (p trend=0.001), WIQ walking speed score (p trend <0.001), and WIQ stair-climbing score (p trend <0.001), in Model 1. In Model 2, all of these associations remained statistically significant. In Model 3, there were no significant associations.

Discussion

Our results show that pathophysiologic findings in calf muscle and impaired peripheral nerve function were associated with lower SF-36 PF scores and lower WIQ scores in persons with PAD. After adjustment for age and sex, lower calf muscle area, lower calf muscle density, and higher calf percent fat were associated with poorer SF-36 PF scores and poorer WIQ walking speed, distance, and stair-climbing scores. After additional adjustment for race, smoking, BMI, and comorbidities, lower calf muscle area and density were significantly associated with poorer SF-36 PF scores and WIQ walking distance, speed, and stair-climbing scores. Higher calf muscle percent fat was significantly associated only with SF-36 PF scores. But after additional adjustment for objective measures of functioning, calf muscle area and muscle density were significantly associated only with SF-36 PF scores. These latter findings suggest that associations of pathophysiologic findings with impaired performance on objective measures of functioning may explain associations of pathophysiologic findings with impairments in self-perceived physical functioning and walking ability among men and women with PAD. Slower peroneal nerve conduction velocity was significantly associated only with SF-36 PF scores and WIQ walking speed and stair-climbing scores. However, these associations were not statistically significant after adjustment for objective measures of functioning, suggesting that the association of pathophysiologic findings in lower extremity nerve function with impaired objective measures of performance may explain the associations of pathophysiologic changes in nerve function with impaired subjective physical functioning and walking impairment.

To our knowledge, this is the first study to examine calf muscle characteristics and peripheral nerve function and their associations with patient-perceived physical functioning and walking ability in persons with PAD. Previous studies demonstrate that people with PAD have poorer quality of life than persons without PAD,²⁶ and persons with PAD have quality of life that is as poor as if not worse than that of persons with other cardiovascular diseases.²⁷ Prior studies show that people with PAD have worse calf muscle characteristics and peripheral nerve function compared to those without PAD, but other studies have not reported patient-reported physical functioning or patient-perceived walking ability in patients with PAD.¹⁷ Additionally, there are few therapies that improve quality of life in patients with PAD. A better understanding of clinical characteristics associated with impaired quality of life in persons with PAD should improve our understanding of the mechanisms underlying such impairments.

Previous work also shows that leg ischemia may lead directly to muscle denervation,²⁸ and that persons with PAD have progressive worsening of neuropathy over time.²⁹ Findings reported here suggest that more adverse pathophysiologic findings in calf muscle and peripheral nerve function among persons with PAD may contribute to poorer self-perceived physical functioning and walking ability, although definitive conclusions cannot be drawn given the cross-sectional design of this study.

One potential mechanism of the association of more adverse calf muscle characteristics and worse peripheral nerve function with greater impairment in quality of life is that these adverse calf muscle characteristics and peripheral nerve function may be associated with poorer overall health compared to the absence of these pathophysiologic findings. However, we found that many associations of more adverse calf muscle characteristics and worse peripheral nerve function with impairments in self-perceived physical functioning and walking ability remained statistically significant even after additional adjustment for confounders. On the other hand, our finding that poorer ulnar nerve function also is associated with decreased quality of life suggests that the peripheral nerve measures may in part be markers of overall health. There is evidence that persons with prolonged hospitalizations and at the extremes of weight are more likely to develop prolonged ulnar neuropathies associated with surgery, but data about whether ulnar nerve function is a marker of global health are sparse.³⁰

A limitation of this study is that we did not include other subscales of the SF-36, which includes items on general health, bodily pain, and vitality, which may have broadened the understanding of whether relationships between physiological characteristics and self-perception of functioning extend beyond physical functioning and walking.

In conclusion, persons with PAD who have smaller calf muscle area, lower calf muscle density, and higher calf muscle percent fat have impaired quality of life. Similarly, PAD persons with decreased peroneal and ulnar nerve conduction velocity have impaired self-perceived physical functioning and walking ability. Several studies have shown improvements in PAD patients' quality of life with supervised treadmill walking exercise,^{31–33} and a recent study has shown improvement in quality of life with resistance training.³³ However, it is unknown whether these improvements in quality of life associated with exercise interventions are mediated by improvements in calf skeletal muscle pathophysiologic findings or peripheral nerve abnormalities.

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Figure 1.

Associations of mean calf muscle area (cm^2) and quality of life and walking ability scores Model 1 adjusted for age and sex; Model 2 adjusted for age, sex, race, ankle-brachial index, body-mass index, leg symptoms, smoking, prior lower extremity revascularization, height, tibia length, comorbidities including diabetes, cardiac or cerebrovascular disease, arthritic diseases, pulmonary disease, and cancer, and recruitment cohort. Model 3 adjusted for Model 2 variables plus 6-minute walk and 4-meter usual pace. Quartile 1 <4565; quartile 2 4570–5281; quartile 3 5294–6347; quartile 4 >6364 cm^2 SE: standard error; SF-36: Medical Outcomes Short Form; WIQ: Walking Impairment Questionnaire

Figure 2.

Associations of mean calf muscle density (mg/cm^3) and quality of life and walking ability scores

Model 1 adjusted for age and sex; Model 2 adjusted for age, sex, race, ankle-brachial index, body-mass index, leg symptoms, smoking, prior lower extremity revascularization, height, comorbidities including diabetes, cardiac or cerebrovascular disease, arthritic diseases, pulmonary disease, and cancer, and recruitment cohort. Model 3 adjusted for Model 2 variables plus 6-minute walk and 4-meter usual pace.

Quartile 1 <29.6; quartile 2 29.6–32.8; quartile 3 32.9–35.9; quartile 4 >35.9 mg/cm^3

SE: standard error; SF-36: Medical Outcomes Short Form; WIQ: Walking Impairment Questionnaire

Figure 3.

Associations of mean calf percent fat and quality of life and walking ability scores. Model 1 adjusted for age and sex; Model 2 adjusted for age, sex, race, ankle-brachial index, body-mass index, leg symptoms, smoking, height, tibia length, alcohol use, comorbidities including diabetes, cardiac or cerebrovascular disease, arthritic diseases, pulmonary disease, and cancer; and study cohort. Model 3 adjusted for Model 2 variables plus 6-minute walk and 4-meter usual pace.

Quartile 1 <4.44; quartile 2 4.44–6.96; quartile 3 6.98–12.66; quartile 4 >12.66%

SE: standard error; SF-36: Medical Outcomes Short Form; WIQ: Walking Impairment Questionnaire

Table 1

Adjusted associations between baseline quartiles of peroneal nerve functioning and mean self-perceived physical functioning and walking ability measures (standard error) among participants with peripheral arterial disease

	SF-36 physical functioning score			WIQ walking distance score		
	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
1Q (<39)	38.81 (2.30)	41.11 (2.22)	47.87 (2.00)	33.86 (3.09)	35.23 (2.97)	44.07 (2.77)
2Q (39-42)	50.23 (2.35)	50.39 (2.19)	51.27 (1.87)	40.42 (3.14)	40.78 (2.91)	41.23 (2.58)
3Q (43-46)	53.89 (2.19)	52.37 (2.06)	50.29 (1.80)	40.61 (2.90)	39.84 (2.71)	36.79 (2.45)
4Q (>46)	52.17 (2.51)	50.76 (2.47)	48.66 (2.10)	42.76 (3.30)	42.15 (3.22)	38.76 (2.86)
p value	<0.001	0.002	0.578	0.227	0.432	0.293
p trend	<0.001	0.003	0.882	0.062	0.173	0.128
Peroneal nerve conduction velocity (m/s)	WIQ walking speed score			WIQ stair climbing score		
	29.00 (2.35)	30.49 (2.20)	36.47 (1.98)	36.40 (2.85)	38.86 (2.73)	45.02 (2.65)
	37.44 (2.37)	37.93 (2.16)	38.09 (1.85)	43.60 (2.89)	45.06 (2.68)	45.71 (2.48)
	35.40 (2.22)	33.73 (2.04)	30.93 (1.78)	47.34 (2.71)	45.82 (2.54)	43.24 (2.40)
	40.96 (2.52)	40.48 (2.42)	38.38 (2.07)	50.57 (3.09)	48.46 (3.03)	46.57 (2.80)
	0.006	0.012	0.012	0.006	0.130	0.804
	0.003	0.023	0.790	0.001	0.028	0.894
	SF-36 physical functioning score			WIQ walking distance score		
	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
	41.08 (2.41)	43.16 (2.31)	50.28 (2.07)	33.35 (3.16)	35.11 (3.05)	43.74 (2.84)
Peroneal nerve amplitude (mm)	48.38 (2.32)	49.77 (2.17)	51.18 (1.89)	38.39 (3.05)	39.66 (2.86)	40.36 (2.61)
	52.45 (2.35)	50.82 (2.23)	48.42 (1.88)	43.82 (3.06)	41.38 (2.91)	38.26 (2.58)
	52.57 (2.35)	50.44 (2.24)	48.40 (1.89)	41.48 (3.06)	41.25 (2.91)	38.51 (2.57)
	0.002	0.029	0.677	0.104	0.450	0.518
	<0.001	0.037	0.342	0.036	0.157	0.180
	WIQ walking speed score			WIQ stair climbing score		
	29.92 (2.43)	31.25 (2.30)	37.61 (2.05)	35.17 (2.93)	36.93 (2.81)	43.02 (2.72)
	36.66 (2.33)	37.73 (2.14)	38.26 (1.88)	46.48 (2.86)	48.18 (2.65)	49.55 (2.52)
	39.62 (2.34)	37.80 (2.18)	34.86 (1.86)	48.82 (2.84)	47.26 (2.68)	44.93 (2.48)
	29.92 (2.43)	31.25 (2.30)	37.61 (2.05)	35.17 (2.93)	36.93 (2.81)	43.02 (2.72)

	4Q >4.20)	35.44 (2.37)	34.53 (2.21)	32.58 (1.88)	46.40 (2.86)	44.95 (2.71)	42.85 (2.50)
	p value	0.040	0.131	0.150	0.005	0.021	0.210
	p trend	0.081	0.408	0.036	0.007	0.098	0.550

SF: Medical Outcomes Short Form; WtQ: Walking Impairment Questionnaire.

1Q: first quartile; 2Q: second quartile; 3Q: third quartile; 4Q: fourth quartile.

Model 1: Adjusted for age and sex.

Model 2: Adjusted for age, sex, race, ankle-brachial index, body-mass index, leg symptoms, smoking, height, alcohol use, comorbidities (diabetes mellitus, angina, myocardial infarction, heart failure, stroke, disk disease, and spinal stenosis), and study cohort.

P trend: based on a general linear model with quartile group as an ordinal variable with values from 1 to 4.

Table 2

Adjusted associations between baseline quartiles of ulnar nerve functioning and mean self-perceived physical functioning and walking ability measures (standard error) among participants with peripheral arterial disease

	SF-36 physical functioning score			WIQ walking distance score		
	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
Ulnar nerve conduction velocity (m/s)	1Q (<48)	42.34 (2.28)	45.54 (2.19)	49.15 (1.90)	36.59 (3.01)	39.33 (2.87)
	2Q (48–51)	47.28 (2.34)	46.83 (2.16)	49.22 (1.83)	36.96 (3.05)	35.87 (2.79)
	3Q (52–54)	52.69 (2.49)	50.32 (2.33)	48.81 (1.98)	40.30 (3.24)	38.64 (3.02)
	4Q (>54)	52.72 (2.33)	51.59 (2.23)	50.48 (1.89)	43.07 (3.06)	43.07 (2.91)
	p value	0.005	0.220	0.938	0.418	0.367
	p trend	0.001	0.040	0.680	0.106	0.298
	WIQ walking speed score			WIQ stair climbing score		
	1Q (<48)	30.18 (2.30)	32.54 (2.18)	35.85 (1.91)	36.09 (2.80)	39.30 (2.68)
	2Q (48–51)	35.91 (2.35)	35.28 (2.13)	36.80 (1.83)	47.60 (2.86)	47.36 (2.63)
	3Q (52–54)	37.01 (2.49)	35.22 (2.30)	33.36 (1.99)	46.92 (3.02)	44.85 (2.83)
Ulnar nerve amplitude (mm)	4Q (>54)	38.87 (2.32)	38.28 (2.19)	36.54 (1.89)	46.91 (2.82)	45.96 (2.69)
	p value	0.057	0.369	0.5743	0.010	0.167
	p trend	0.010	0.095	0.9225	0.013	0.172
	SF-36 physical functioning score			WIQ walking distance score		
	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
	1Q (<8.0)	37.59 (2.46)	39.92 (2.31)	45.51 (2.04)	32.36 (3.27)	34.33 (3.06)
	2Q (8.0–13.8)	49.73 (2.30)	50.86 (2.16)	52.16 (1.86)	36.65 (3.02)	39.17 (2.83)
	3Q (14.0–22.0)	50.11 (2.25)	49.12 (2.10)	49.15 (1.80)	38.76 (2.99)	36.11 (2.78)
	4Q (>22.0)	55.51 (2.44)	53.09 (2.32)	50.40 (2.00)	48.19 (3.20)	47.01 (3.03)
	p value	<0.001	0.001	0.113	0.009	0.025
	p trend	<0.001	0.001	0.262	0.001	0.022
	WIQ walking speed score			WIQ stair climbing score		
	1Q (<8.0)	26.09 (2.48)	28.23 (2.31)	33.31 (2.07)	31.91 (3.03)	34.76 (2.86)
	2Q (8.0–13.8)	35.08 (2.30)	36.65 (2.13)	37.49 (1.87)	44.40 (2.79)	46.09 (2.62)
	3Q (14.0–22.0)	36.93 (2.25)	35.41 (2.07)	34.52 (1.80)	46.90 (2.76)	46.49 (2.57)

4Q (>22.0)	42.39 (2.45)	40.23 (2.31)	37.22 (2.02)	52.17 (2.99)	48.82(2.85)	46.75 (2.67)
p value	<0.001	0.005	0.3714	<0.001	0.003	0.117
p trend	<0.001	0.002	0.4271	<0.001	0.002	0.097

SF: Medical Outcomes Short Form; WtQ: Walking Impairment Questionnaire.

1Q: first quartile; 2Q: second quartile; 3Q: third quartile; 4Q: fourth quartile.

Model 1: Adjusted for age and sex.

Model 2: Adjusted for age, sex, race, ankle-brachial index, body-mass index, leg symptoms, smoking, height, alcohol use, comorbidities (diabetes mellitus, angina, myocardial infarction, heart failure, stroke, disk disease, and spinal stenosis), and study cohort.

P trend: based on a general linear model with quartile group as an ordinal variable with values from 1 to 4.