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Poorer clock draw test scores are associated with greater functional impairment in peripheral artery disease: The Walking and Leg Circulation Study II

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Abstract

We hypothesized that, in the absence of clinically recognized dementia, cognitive dysfunction measured by the clock draw test (CDT) is associated with greater functional impairment in men and women with peripheral artery disease (PAD). Participants were men and women aged 60 years and older with Mini-Mental Status Examination scores ≥ 24 with PAD ($n = 335$) and without PAD ($n = 234$). We evaluated the 6-minute walk test, 4-meter walking velocity at usual and fastest pace, the Short Physical Performance Battery (SPPB), and accelerometer-measured physical activity. CDTs were scored using the Shulman system as follows: Category 1 (worst): CDT score 0–2; Category 2: CDT score 3; Category 3 (best): CDT score 4–5. Results were adjusted for age, sex, race, education, ankle–brachial index (ABI), and comorbidities. In individuals with PAD, lower CDT scores were associated with slower 4-meter usual-paced walking velocity (Category 1: 0.78 meters/second; Category 2: 0.83 meters/second; Category 3: 0.86 meters/second; p -trend = 0.025) and lower physical activity (Category 1: 420 activity units; Category 2: 677 activity units; Category 3: 701 activity units; p -trend = 0.045). Poorer CDT scores were also associated with worse functional performance in individuals without PAD (usual and fast-paced walking velocity and SPPB, p -trend = 0.022, 0.043, and 0.031, respectively). In conclusion, cognitive impairment identified with CDT is independently associated with greater functional impairment in older, dementia-free individuals with and without PAD. Longitudinal studies are necessary to explore whether baseline CDT scores and changes in CDT scores over time can predict long-term decline in functional performance in individuals with and without PAD.

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Keywords

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Introduction

Men and women with lower-extremity peripheral artery disease (PAD) have greater functional impairment than those without PAD.^{1,2} Compared to those without PAD, individuals with PAD have slower walking speed, poorer walking endurance, and lower physical activity levels.^{1,2} Factors related to arterial obstruction and chronic limb ischemia, such as claudication symptoms, lower-extremity muscle power, nerve conduction, and altered gait biomechanics, may mediate walking performance in those with PAD.^{3–7} However, impaired walking performance in PAD is not fully explained by the degree of lower-extremity arterial obstruction.^{8,9} Understanding factors unrelated to lower-extremity arterial obstruction that are associated with functional impairment may offer new opportunities for prevention and treatment in these patients.

Cognitive impairment is a major risk factor for impaired functional performance in the aging population.^{10–13} Furthermore, individuals with PAD are at higher risk for cognitive impairment, including vascular and non-vascular types, compared to those without PAD.^{14,15} Individuals with PAD, including those with prior amputation, perform worse on multiple cognitive function tests compared to age- and education-matched controls without PAD,^{16,17} and perform similarly to individuals who have suffered mild cerebrovascular accidents.¹⁶ Studies are needed to assess whether subtle aberrations in cognitive function are associated with functional impairment in individuals with PAD.¹⁸

To our knowledge, this cross-sectional study is the first to determine whether subclinical cognitive impairment, assessed by the clock draw test (CDT), is associated with poorer functional performance among older, non-demented individuals with and without PAD. The PAD participants were similar to those in other PAD cohorts recruited from a clinical setting. For example, PAD participants included a large proportion of individuals without classic symptoms of intermittent claudication.^{19,20} This study also evaluated whether the association between CDT and functional performance was independent of severity of arterial obstruction, measured by the ankle–brachial index (ABI), other atherosclerotic disease (angina, coronary disease, stroke, congestive heart failure), and atherosclerotic risk factors such as hypertension, cholesterol levels, smoking, and diabetes.

Methods

Subjects

PAD participants were recruited consecutively from participants diagnosed with PAD in three Chicago-area non-invasive vascular laboratories.^{2,6} Non-PAD participants were identified consecutively during appointments in a large general internal medicine practice at Northwestern University and consecutively from participants with normal lower-extremity

arterial studies in the three non-invasive vascular laboratories.^{2,6} All participants gave written, informed consent.

Participants were aged 60 years and older at the time of data collection. A total of 800 men and women with and without PAD attended their fifth annual follow-up visit for the Walking and Leg Circulation Study (WALCS)^{2,6} or their first annual follow-up visit in the WALCS II cohort^{4,5} between December 12, 2003, and February 17, 2006. Investigators collected clock draw data and functional performance measures at these visits.

Participation rates and exclusion criteria at baseline for both the WALCS and WALCS II cohorts have been described and are summarized briefly here.^{2,4-6} Potential participants who were legally blind, had recently undergone major surgery, resided in nursing homes, were wheelchair-bound, and/or had lower-extremity amputations were excluded because of their severely impaired functioning. Non-English-speaking participants were excluded because investigators were not fluent in non-English languages.

Participants with prior lower-extremity revascularization or previously documented ABI < 0.90 who had a normal ABI at the study visit were excluded because they could not be clearly classified as PAD or non-PAD ($n = 52$). After application of these exclusion criteria, 635 participants remained who had completed the CDT or functional performance measures. Participants with an ABI greater than 1.30 ($n = 17$) and those with a Mini-Mental Status Examination (MMSE) score of less than 24 ($n = 45$) were excluded. Four participants missing all functional performance measures were also excluded. A total of 569 participants (335 with PAD) were eligible for analysis. All eligible patients were deemed dementia-free based on the following: (1) MMSE ≥ 24 at the time of CDT measurement (sensitivity 84%, specificity 99%),²¹ (2) no self-reported dementia at enrollment into WALCS or WALCS II, and (3) no report of dementia by the subject's doctor or family at enrollment into WALCS or WALCS II. The MMSE has a sensitivity of 84% and specificity of 99% for the diagnosis of dementia.²¹

Ankle-brachial index measurement

PAD was defined as an ABI < 0.90. Absence of PAD was defined as an ABI 0.90–1.30. Participants rested supine for 5 minutes, and then a hand-held Doppler probe (Nicolet Vascular Pocket Dop II; VIASYS, Golden, CO, USA) was used to measure systolic pressures in this order: right brachial, dorsalis pedis, and posterior tibial arteries and left dorsalis pedis, posterior tibial, and brachial arteries. Pressures were repeated in reverse to minimize measurement error. The ABI was calculated in each leg by dividing average pressures in each leg by the average of the four brachial pressures.^{2,4-6} 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, since in such cases subclavian stenosis was possible.²² Zero values for the dorsalis pedis and posterior tibial vessels were excluded from the ABI calculation. The lowest leg ABI was used in analyses.²

Comorbidities

In the current analysis, comorbidities and characteristics were included in analyses if they were known or were likely to affect CDT scores and/or functional performance, based on published literature.^{18,23–26} These included cancer, pulmonary disease, severity of arterial obstruction measured by ABI, and cardiovascular disease (myocardial infarction, angina pectoris, stroke, congestive heart failure).^{14,17,25,27} Algorithms developed for the Women's Health and Aging Study and the Cardiovascular Health Study were used to document comorbidities.^{20,28} These algorithms combine data from participant report, physical examination, medical record review, medications, laboratory values, and a primary care physician questionnaire. Hypertension was defined as patient report of physician-diagnosed hypertension or as indicated on the primary care physician questionnaire. Total cholesterol levels were measured using enzymatic reaction with peroxidase/phenol-4-aminophenazone indicator reaction.²⁹ High-density lipoprotein (HDL) cholesterol was measured using a direct enzymatic colorimetric assay.³⁰ Because only 69% of participants had total and HDL cholesterol values measured at the follow-up visit, our analyses were performed in the entire cohort and then separately in the subset of participants with total and HDL cholesterol data.

Other participant characteristic measurements

Body mass index (BMI) was calculated as weight (kg)/height (m)² using measures obtained at the study visit. Lower-extremity revascularization was based on participant report and required confirmation with either medical record review or the primary care physician questionnaire. Smoking status, alcohol use, and education level were measured by self-report.

Cognitive function data

Clock draw testing—Clock draw testing correlates well with the Folstein MMSE and has a sensitivity and specificity of 86% and 72% to detect cognitive dysfunction in elderly patients.³¹ Subjects were given a piece of paper with a circle on it and given verbatim instructions as follows: “This circle represents a clock face. Please put in the numbers so it looks like a clock and then set the time to 10 minutes past 11.” Three reviewers independently scored each clock-draw, using the scoring system developed by Shulman et al.^{31–33} Scores range from 0 to 5, with 5 as the best possible score. Table 1 shows scoring criteria. Clock draw test results that differed among the three reviewers were discussed and resolved through consensus. To assess test–re-test reliability of the clock draw test measurements, 10% of clock draws were randomly selected for an additional independent rescoring. The coefficient of variability was 1.99%, indicating excellent test–re-test reliability. Participants were categorized as follows: Category 1: CDT score 0–2; Category 2: CDT score 3; Category 3: CDT score 4–5. These categories represented clinically meaningful differences in cognitive function and were associated with appropriate distributions of the number of participants in each category.

Mini-Mental Status Examination—The Folstein MMSE was administered to all subjects. The MMSE is a widely used screen for dementia that awards a given subject up to 30 points, and a score of < 24 has a sensitivity of 84% and a specificity of 99% for the

diagnosis of clinical dementia.²¹ The MMSE tests multiple domains, including orientation, repetition, naming, attention, calculation, visual-spatial ability, and complex motor commands.

Functional performance measures

Six-minute walk test—Participants walked up and down a 100-foot (30.5-meter) hallway for 6 minutes after instructions to cover as much distance as possible, and investigators recorded the distance covered in feet.^{2,34}

Four-meter walking velocity—Walking velocity was measured with a 4-meter walk performed at ‘usual’ and ‘fastest’ pace, based on previous study.^{8,35} Each walk was performed twice, and the faster walk in each pair was used in analyses.^{36,37}

Short physical performance battery (SPPB)—The short physical performance battery (SPPB) combines data from the usual-paced 4-meter walking velocity, time to rise from a seated position five times, and standing balance. Participants sat in a straight-backed chair with arms folded across the chest. The time to stand five times consecutively and as quickly as possible was recorded.^{36,37} To measure standing balance, investigators asked participants to hold three increasingly difficult standing positions for 10 seconds each: standing with feet together side-by-side and parallel (side-by-side stand), standing with feet parallel with the toes of one foot adjacent to and touching the heel of the opposite foot (semi-tandem stand), and standing with one foot directly in front of the other (tandem stand).^{36,37}

Individuals receive a zero score for each task they are unable to complete. Scores of 1–4 are assigned to tasks, based upon quartiles of performance for over 5000 participants in the Established Populations for the Epidemiologic Study of the Elderly.^{36,37} Scores are summed to obtain the SPPB, ranging from 0 to 12.^{36,37}

Accelerometer-measured physical activity—Physical activity levels were measured objectively and continuously for 7 days using a vertical accelerometer (Caltrac; Muscle Dynamics Fitness Network Inc., Torrance, CA, USA).³⁸ The Caltrac accelerometer is worn at the hip and primarily measures walking activity. Caltrac data were available for 251 PAD participants and 195 non-PAD participants. By study design, only one-half of WALCS I participants were asked to wear the accelerometer to measure physical activity. Participants reported the number of activity units displayed on the accelerometer by telephone to investigators and returned their accelerometer by mail. Accelerometers were identically programmed for all participants, allowing comparison of physical activity levels in ‘activity units’ between participants, irrespective of individual variation in age, weight, height, and sex.³⁹

Statistical analyses and approval

Clinical characteristics were compared between PAD and non-PAD participants using general linear models for continuous variables and chi-square tests for categorical variables. Similarly, associations of CDT scores with clinical characteristics were evaluated among

participants with and without PAD, respectively. Analysis of covariance was employed to analyze the relationship between CDT and functional performance measures after adjustment for age, sex, education, race, ABI, cardiovascular disease (angina, myocardial infarction, stroke, congestive heart failure), cancer, pulmonary disease, and study cohort in those with and without PAD. This model was repeated in the subgroup with available cholesterol data (PAD: $n = 307$, non-PAD: $n = 216$) with additional adjustment for cardiovascular disease risk factors (hypertension, cholesterol, smoking, alcohol use, and diabetes). Because previous study showed that the CDT and MMSE scores are highly correlated ($r = 0.65$), our analyses did not adjust for MMSE.³² Analyses were performed with SAS Statistical Software Version 9.0 (SAS Inc., Cary, NC, USA). Statistical significance was defined as $\alpha < 0.05$.

All authors had full access to these data and take responsibility for their integrity. The Institutional Review Boards of Northwestern University Feinberg School of Medicine and Catholic Health Partners Hospitals approved this study protocol.

Results

Table 2 shows baseline characteristics of PAD and non-PAD participants. Compared to those without PAD, PAD participants were older, included a higher prevalence of males, had lower levels of education, scored lower on the MMSE, and had higher prevalences of smoking, hypertension, diabetes, and cardiovascular disease (angina, myocardial infarction, stroke, and congestive heart failure). PAD participants also had higher average cholesterol levels, lower average high-density lipoprotein levels, and higher rates of statin use compared to those without PAD. PAD participants had significantly greater impairment on all functional performance measures before adjustment. A total of 28% of PAD participants reported symptoms of intermittent claudication.

In unadjusted analyses of PAD participants, lower CDT scores were associated with older age, female sex, lower MMSE scores, and a lower prevalence of pulmonary disease (Table 3). In unadjusted analyses of PAD participants, lower CDT scores were also associated with slower usual- and fast-paced walking velocity, lower SPPB scores, and lower levels of physical activity (Table 3). After adjustment for age, sex, race, education level, ABI, cardiovascular disease, cancer, pulmonary disease and study cohort, lower CDT scores were associated with slower usual-paced walking velocity (p -trend = 0.025) and lower physical activity (p -trend = 0.045) among PAD subjects (Table 4).

In unadjusted analyses of participants without PAD, lower CDT scores were associated with older age, cardiovascular disease, lower levels of education, lower MMSE scores, slower usual and fast-paced walking velocity, and poorer SPPB scores (Table 3). After adjustment for age, sex, race, education level, ABI, cardiovascular disease, cancer, pulmonary disease, and study cohort, lower CDT scores continued to be associated with slower usual-paced walking velocity (p -trend = 0.022), slower fast-paced walking velocity (p -trend = 0.043), and poorer SPPB scores (p -trend = 0.031) among participants without PAD (Table 4).

The test for interaction for ABI and the association of CDT with functional performance measures was not significant for any of the functional performance measures (6-minute walk, $p = 0.076$; 4-meter usual-paced walking velocity, $p = 0.145$; 4-meter fast-paced walking velocity, $p = 0.170$; short physical performance battery, $p = 0.673$; accelerometer-measured physical activity, $p = 0.247$). The test for interaction for presence or absence of PAD and the association of CDT with functional performance measures was also not significant for any measure (6-minute walk, $p = 0.5321$; 4-meter usual-paced walking velocity, $p = 0.406$; 4-meter fast-paced walking velocity, $p = 0.4845$; short physical performance battery, $p = 0.932$; accelerometer-measured physical activity, $p = 0.309$).

Because PAD and cerebrovascular disease often coexist, reflecting the systemic nature of atherosclerotic disease, we adjusted for atherosclerotic risk factors to determine whether these atherosclerotic disease risk factors were potential mediators of the association between CDT and functional performance measures. A total of 307 PAD participants and 216 non-PAD participants had cholesterol data available. This smaller sample size had less statistical power and only the association between CDT and 4-meter usual-paced walking velocity remained statistically significant when analyses described above were repeated in this smaller cohort (PAD: p -trend = 0.019, non-PAD: p -trend = 0.049). After additional adjustment for cardiovascular disease risk factors (hypertension, total cholesterol, HDL cholesterol, smoking, diabetes, alcohol use), the association between CDT score and 4-meter usual-paced walking velocity remained significant in both PAD and non-PAD participants (p -trends = 0.019 and 0.038, respectively). These findings suggest that atherosclerotic disease risk factors may not mediate associations of poorer CDT scores with greater functional impairment.

Discussion

Our findings demonstrate an independent association between greater cognitive impairment, identified by CDT score, and greater functional impairment among PAD participants with MMSE scores > 23 and without a diagnosis of dementia. Among PAD participants, lower CDT scores were associated with slower usual-paced walking velocity and lower levels of physical activity. This association was also present among participants without PAD; lower CDT scores were associated with slower usual- and fast-paced walking velocity and lower SPPB scores. These associations were independent of age, sex, race, education, ABI, comorbidities, and other confounders. Adjustment for cardiovascular risk factors (hypertension, diabetes, total and HDL cholesterol) did not attenuate the association between CDT and usual-paced walking velocity in PAD or non-PAD participants.

This study is unique for multiple reasons. This study is the first, to our knowledge, to establish an association between cognitive impairment and objective measures of functional performance that have been associated with mobility loss and all-cause mortality in individuals with PAD.^{8,35} Multiple studies have examined the association between PAD and cognitive dysfunction^{1,6,17,40} as well as the association of ABI or PAD with cognitive decline and/or incidence of dementia.^{14,15,25,27} Coppin et al. found that poor executive function is associated with slower gait speed and worse performance on complex walk tasks

in older individuals.¹³ However, no studies have assessed the association between cognitive impairment and functional performance in older individuals with PAD.

Second, no other study of cognitive function in PAD subjects has utilized CDT, which tests various neurocognitive domains such as visual-spatial ability, executive function, attention, comprehension, planning, visual memory, motor programming and execution, numeracy, abstract thinking, and inhibition of the tendency to be pulled by perceptual features of the stimulus.^{32,41} Analyses by Phillips et al. and Waldstein et al. have demonstrated deficiencies in visual-spatial ability, psychomotor speed, and executive function in participants with lower ABIs or lower-extremity amputation compared to age- and education-matched controls.^{7,16,42} However, both studies used a series of more sophisticated research tools to measure these neurocognitive domains. While not exhaustive, the CDT is an efficient screen for cognitive dysfunction because it calls upon participants to use multiple cognitive domains and has the advantages of being easily and rapidly administered and scored. If linked to functional performance decline in longitudinal analysis, the CDT may have important prognostic significance in the clinical care of PAD patients and can be easily adopted in a busy clinical environment. Furthermore, the CDT may be a more appropriate tool for screening for cognitive impairment in elderly, relatively high-functioning individuals with PAD. False negatives on the MMSE are more common in people with early cognitive impairment than more advanced impairment.⁴³ Also, the MMSE may insufficiently assess visual-spatial or visual-constructive abilities compared to the CDT.⁴⁴

We are not able to discern from available data the mechanisms of the association between CDT and functional performance. However, there are at least two possible mechanisms for our findings. First, atherosclerotic disease is a systemic phenomenon. It is conceivable that atherosclerosis in the cerebral vasculature may mediate the association of lower CDT with greater impairment of functional performance. However, additional adjustment for atherosclerotic risk factors did not substantially attenuate the association between CDT and functional performance in those with or without PAD. Second, cognitive dysfunction can lead to maladaptive behavior, which may mediate the process by which subtle cognitive impairment contributes to impaired functional performance. For example, individuals with cognitive impairment are more likely to engage in suboptimal health behaviors such as medication non-adherence,^{45,46} unhealthy eating habits, or sporadic healthcare follow-up. Poorer health behaviors may result in global health deterioration, which in turn may impair functional performance. Future investigation should determine whether and to what degree these behaviors are a source of functional impairment in PAD participants compared to those without PAD.

We are also not able to discern why lower CDT scores were associated significantly and independently with poorer performance on a greater number of functional measures among participants without PAD compared to those with PAD. However, it is possible that characteristics such as adverse calf muscle characteristics,⁵ impaired peripheral nerve function,⁴ or elevated levels of inflammation^{47,48} are more important determinants of functional impairment than mild cognitive dysfunction in those with PAD. Interestingly, in the adjusted analysis, the type of functional performance measure associated with lower CDT scores differed between PAD and non-PAD participants; PAD participants with low

CDT scores had significantly slower usual-paced walking velocity and lower physical activity levels, which are measures of baseline function. However, non-PAD participants with low CDT scores had slower usual- and fast-paced walking velocities and worse SPPB scores, which are activities that require higher levels of effort and more discrete tasks. This suggests a difference in the mechanisms of association between the two groups, perhaps related to a difference in specific neurocognitive deficits between the two groups which the CDT cannot discriminate. Interestingly, low CDT scores in both groups were not associated with less distance covered on a 6-minute walk, which is essentially a test of endurance and may require the least amount of cognitive effort.

This study has limitations. First, the data are cross-sectional. Results should not be construed to indicate causal associations. Second, the CDT does not capture all domains of cognitive impairment. However, the CDT has been shown to have high sensitivity and specificity for cognitive dysfunction in the elderly population.^{31,49} Third, our sample size was relatively small, limiting statistical power to detect the presence of an interaction between PAD status and the association of cognitive impairment with functional impairment. Fourth, we are not able to determine the mechanisms of the association between CDT and functional performance. Fifth, some participants in the WALCS II cohort were missing functional performance data. However, the proportion of individuals missing data was small, and there were no significant differences in characteristics between those with versus without functional performance data. Finally, the participants who were recruited from the WALCS cohort completed the CDT at their fifth annual follow-up for the WALCS cohort. Of the original 741 WALCS subjects, only 345 were able to return for follow-up testing, mostly due to death or severe impairment. Therefore, our findings may not be generalizable to the WALCS participants who did not return for the fifth annual follow-up visit at which the CDT was measured. However, it is important to point out that 79% of participants identified from our WALCS II cohort completed the CDT and functional performance measures.

In conclusion, our findings demonstrate that cognitive impairment assessed by CDT is associated with functional impairment independent of ABI in older, non-demented individuals with and without PAD. Further prospective study is needed to determine the mechanisms of the association between CDT scores and functional performance in PAD participants and whether the mechanisms of association are unique to PAD participants compared to the general population. Longitudinal data are necessary to determine whether baseline CDT score or decline in CDT score predicts decline in functional performance, institutionalization, or mortality in PAD participants.

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Table 1Criteria for clock draw test scoring^a

Score	Criteria
5	'Perfect clock' <ul style="list-style-type: none"> • Appropriate hand length • Appropriate number position • Enough numbers present to indicate understanding of the full orientation of numbers on the clock
4	<ul style="list-style-type: none"> • '10 minutes past 11' correctly represented • Minor visual-spatial errors such as numbers are located on or outside the circle, additional lines, inconsistent numbers, or criteria for appropriate number position not met
3	<ul style="list-style-type: none"> • Inaccurate representation of '10 minutes past 11' when the visual-spatial organization is well done
2	<ul style="list-style-type: none"> • Moderate visual-spatial disorganization of numbers such that accurate denotation of '10 minutes past 11' is impossible
1	<ul style="list-style-type: none"> • Numbers appear in an unrecognizable sequence
0	<ul style="list-style-type: none"> • Inability to make any reasonable representation of a clock <ul style="list-style-type: none"> – No numbers – Hands do not indicate '10 minutes past 11'

^aParticipants are handed a piece of paper with a circle drawn on it and are read the following script: "This circle represents a clock face. Please put in the numbers so it looks like a clock and then set the time to 10 minutes past 11."

Table 2

Characteristics of participants with and without peripheral artery disease

	PAD participants	Non-PAD participants	<i>p</i> -value
<i>n</i>	335	234	
Age, years	74.46 (7.71)	70.90 (7.34)	< 0.001
Male, %	53.4	41.9	0.007
African American, %	15.2	19.2	0.209
Ankle-brachial index	0.61 (0.15)	1.09 (0.09)	< 0.001
Body mass index, kg/m ²	28.10 (5.24)	28.98 (5.89)	0.066
Cardiovascular disease, %	61.4	32.5	< 0.001
Angina, %	33.4	18.8	< 0.001
Myocardial infarction, %	26.9	12.8	< 0.001
Stroke, %	21.5	7.69	< 0.001
Congestive heart failure, %	29.0	12.4	< 0.001
Pulmonary disease, %	42.4	38.5	0.348
Statin use, %	57.3	30.3	< 0.001
Current smoker, %	15.5	4.3	< 0.001
Alcohol use	3.67 (6.56)	3.35 (5.12)	0.533
Cancer, %	21.8	23.5	0.630
Diabetes, %	32.5	23.1	0.014
Hypertension, %	71.6	56.2	< 0.001
Total cholesterol, mg/dl	176 (43) ^a	189 (50) ^b	0.001
High-density lipoprotein, mg/dl	53 (19) ^a	59 (24) ^b	0.003
Education			0.007
Less than high school education, %	7.2	6.4	
High school and college graduates, %	74.3	63.7	
Professional/graduate training, %	18.5	29.9	
Mini-Mental Status Exam, range 0–30, 30 = best	28.19 (1.72)	28.67 (1.56)	< 0.001
Six-minute walk test, feet	1107.62 (394.16)	1478.95 (401.84)	< 0.001
Four-meter usual-pace, m/s	0.85 (0.19)	0.96 (0.20)	< 0.001
Four-meter fast-pace, m/s	1.16 (0.28)	1.31 (0.26)	< 0.001
SPPB, range 0–12, 12 = best	9.23 (2.82)	10.35 (2.40)	< 0.001
Accelerometer-measured physical activity, activity units	676 (420)	967 (563)	< 0.001

Data shown are means (standard deviation).

^aBased on 235 subjects;^bbased on 161 subjects.

PAD, peripheral artery disease; SPPB, short physical performance battery.

Table 3

Characteristics of participants with and without peripheral artery disease according to clock draw score categories

	Participants with PAD				<i>p</i> -trend	Participants without PAD				<i>p</i> -trend
	Clock draw score:					Clock draw score:				
	0–2	3	4–5			0–2	3	4–5		
<i>n</i>	25	93	217			8	65	161		
Age	79.88 (8.70)	74.41 (7.39)	73.86 (7.51)		0.003	73.88 (10.29)	72.95 (6.80)	69.93 (7.22)		0.003
Male, %	28.0	51.6	57.1		0.013	37.5	38.5	43.5		0.476
African American, %	28.0	16.1	13.4		0.083	37.5	21.5	17.4		0.180
Ankle–brachial index	0.55 (0.14)	0.61 (0.15)	0.62 (0.15)		0.091	1.09 (0.09)	1.10 (0.09)	1.08 (0.09)		0.393
Body mass index, kg/m ²	26.59 (4.85)	27.89 (4.94)	28.35 (5.40)		0.124	30.75 (4.03)	28.99 (5.30)	28.88 (6.20)		0.547
Cardiovascular disease, %	64.0	56.3	63.2		0.506	75.0	38.5	28.0		0.010
Angina, %	32.0	35.5	32.7		0.825	50.0	20.0	16.8		0.079
Myocardial infarction, %	24.0	23.7	28.6		0.386	50.0	13.8	10.6		0.020
Stroke, %	36.0	21.5	19.8		0.126	12.5	13.8	5.0		0.037
Congestive heart failure, %	28.0	26.9	30.0		0.644	37.5	13.8	10.6		0.075
Pulmonary disease, %	8.0	41.9	46.5		0.002	37.5	35.4	39.8		0.594
Statin use, %	56.00	64.5	54.4		0.289	37.5	32.3	29.2		0.526
Current smoker, %	16.0	17.2	14.7		0.665	0.0	6.2	3.7		0.749
Alcohol use, drinks/week	3.44 (6.21)	3.77 (7.22)	3.66 (6.33)		0.974	1.06 (1.59)	3.15 (5.33)	3.55 (5.14)		0.239
Cancer, %	20.0	23.7	21.2		0.860	12.5	32.3	20.5		0.263
Diabetes, %	28.0	39.8	30.0		0.407	25.0	21.5	23.6		0.843
Hypertension, %	76.0	64.5	74.2		0.391	87.5	50.8	56.9		0.723
Total cholesterol, mg/dl	180 (51)	167 (39)	179 (44)		0.223	180 (26)	191 (60)	189 (47)		0.977
HDL, mg/dl	52 (17)	56 (21)	53 (18)		0.477	60 (22)	60 (27)	58 (23)		0.661
Education					0.145					0.003
Less than high school, %	8.0	8.6	6.5			0	12.3	4.4		
High school and college graduates, %	80.0	76.3	72.8			100.0	67.7	60.3		
Professional/graduate training, %	12.0	15.1	20.7			0.0	20.0	35.4		
MMSE score	27.12 (1.88)	27.75 (1.79)	28.51 (1.58)		<0.001	27.50 (1.69)	28.08 (1.76)	28.96 (1.38)		<0.001
Six-minute walk test, feet	916 (375)	1118 (380)	1124 (399)		0.076	1278 (332)	1406 (438)	1517 (385)		0.023

	Participants with PAD				Participants without PAD			
	Clock draw score:				Clock draw score:			
	0-2	3	4-5	p-trend	0-2	3	4-5	p-trend
Four-meter usual-pace, m/s	0.74 (0.18)	0.83 (0.17)	0.87 (0.20)	0.002	0.73 (0.26)	0.92 (0.20)	0.99 (0.19)	< 0.001
Four-meter fast-pace, m/s	0.99 (0.27)	1.15 (0.26)	1.19 (0.28)	0.002	1.11 (0.26)	1.25 (0.25)	1.35 (0.25)	< 0.001
SPPB, range 0-12, 12 = best	7.59 (3.84)	9.10 (2.53)	9.46 (2.76)	0.007	7.63 (3.07)	10.06 (2.48)	10.61 (2.24)	0.002
Accelerometer-measured physical activity, activity units	359 (233)	660 (445)	714 (411)	0.005	714 (490)	960 (655)	983 (527)	0.362

Data shown are means (standard deviation).

MMSE, Mini-Mental Status Examination; SPPB, short physical performance battery.

Table 4

Adjusted associations between clock draw test scores and functional performance measures in participants with ($n = 335$) and without ($n = 234$) peripheral artery disease

Functional performance measure	Clock draw score category	Participants with PAD		Participants without PAD	
		<i>n</i>	Mean (SE)	<i>n</i>	Mean (SE)
Six-minute walk, feet	Score 0–2	23	1001 (75)	7	1414 (133)
	Score 3	92	1124 (36)	62	1460 (46)
	Score 4–5	209	1112 (24)	158	1490 (28)
			P -trend = 0.427		P -trend = 0.450
Four-meter usual-paced walking velocity, m/s	Score 0–2	23	0.78 (0.04)	8	0.80 (0.06)
	Score 3	93	0.83 (0.02)	65	0.95 (0.02)
	Score 4–5	214	0.86 (0.01)	159	0.98 (0.01)
			P -trend = 0.025		P -trend = 0.022
Four-meter fast-paced walking velocity, m/s	Score 0–2	23	1.07 (0.05)	7	1.17 (0.09)
	Score 3	93	1.15 (0.03)	65	1.28 (0.03)
	Score 4–5	213	1.18 (0.02)	159	1.33 (0.02)
			P -trend = 0.066		P -trend = 0.043
Short physical performance battery, score 0–12, 12 = best	Score 0–2	22	8.55 (0.58)	8	8.08 (0.80)
	Score 3	88	9.10 (0.27)	63	10.27 (0.29)
	Score 4–5	206	9.36 (0.18)	152	10.50 (0.18)
			P -trend = 0.160		P -trend = 0.031
Accelerometer-measured physical activity, activity units ^a	Score 0–2	16	420 (101)	7	838 (209)
	Score 3	72	677 (46)	53	991 (77)
	Score 4–5	163	701 (30)	135	964 (47)
			P -trend = 0.045		P -trend = 0.890

All analyses adjusted for age, sex, race, education level, cardiovascular disease, cancer, pulmonary disease, ankle-brachial index, and study cohort. PAD, peripheral artery disease; SE, standard error.

^aOnly one-half of WALCS participants underwent physical activity measurement.