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The ankle–brachial index is associated with the magnitude of impaired walking endurance among men and women with peripheral arterial disease

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Abstract

Previous reports suggest that the severity of peripheral arterial disease (PAD), measured by the ankle–brachial index (ABI), is not associated with the magnitude of walking impairment, measured by treadmill testing. These prior studies have had small sample sizes and included only PAD participants with symptoms of intermittent claudication. We studied the association of the ABI with diverse measures of walking performance in a cross-sectional study of 156 participants with PAD with and without intermittent claudication symptoms. Outcomes included the Gardner–Skinner treadmill test, 6-minute walk, 4-meter walking velocity at usual and fastest pace, and the walking impairment questionnaire (WIQ). Adjusting for age, sex, race, comorbidities, leg symptoms, and other confounders, lower ABI values were associated with shorter distance achieved in the 6-minute walk (ABI < 0.50: 286 meters; ABI 0.50–0.70: 316 meters; ABI 0.71–0.95: 355 meters, *p* trend < 0.001), shorter maximal treadmill walking time (ABI < 0.50: 6.0 minutes; ABI 0.50–0.70: 6.9 minutes; ABI 0.71–0.95: 8.3 minutes, *p* trend = 0.009), and lower WIQ distance scores (*p* trend = 0.007) among PAD participants. The ABI was not associated significantly with walking velocity over 4 meters, treadmill time to onset of leg symptoms, or the WIQ speed or stair-climbing scores. In conclusion, among 156 participants with PAD with and without intermittent claudication, lower ABI values are associated significantly with poorer walking endurance, assessed by three distinct measures.

Keywords

ankle–brachial index; intermittent claudication; peripheral arterial disease

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Introduction

The ankle-brachial index (ABI), a ratio of Doppler-recorded systolic pressures in the lower and upper extremities, is sensitive and specific for diagnosing lower extremity peripheral arterial disease (PAD).^{1,2} In the absence of lower extremity arterial obstruction, arterial pressures increase with greater distance from the heart.³ Thus, patients without PAD have higher systolic pressures at the ankle compared with the brachial arteries.³ In the presence of lower extremity arterial obstruction, systolic pressures at the ankle are lower than the brachial arteries.^{1,3} Greater obstruction in the lower extremity arteries, or more severe PAD, is associated with greater decrements in lower-extremity systolic pressures and lower ABI values.¹

Men and women with PAD have poorer walking endurance and slower walking velocity compared to men and women without PAD.^{4,5} However, previous studies limited to participants with PAD have reported that the ABI is not associated with the degree of functional limitation.⁶⁻⁹ These prior studies included relatively small sample sizes and included only participants with classic intermittent claudication symptoms.⁶⁻⁹ Including only PAD participants with classic intermittent claudication symptoms is an important limitation because most men and women with PAD do not have symptoms of intermittent claudication.^{4,5,10} Some PAD patients without classic intermittent claudication have greater functional impairment than PAD participants with intermittent claudication.¹¹ Previous studies reporting the absence of an association of the ABI with functional impairment in PAD may not be generalizable to the large number of men and women who have PAD but do not have intermittent claudication symptoms.

This study assesses associations of the ABI with the degree of functional impairment among men and women with PAD participating in the Study to Improve Leg Circulation (SILC).^{12,13} PAD participants included those with and without intermittent claudication. Measures of functional impairment were diverse and included 6-minute walk performance, treadmill testing, walking velocity over 4 meters at usual and fastest pace, and the walking impairment questionnaire (WIQ) scores.

Methods

Study overview

Baseline data from SILC were used in the present analyses. SILC is a randomized, controlled, clinical trial of treadmill exercise and lower extremity resistance training in PAD participants with and without intermittent claudication symptoms.^{12,13} The current cross-sectional study uses baseline data from SILC. The institutional review boards of participating medical centers in Chicago approved the protocol. Participants provided written informed consent. The funding source played no role in the design, conduct, study reporting, or decision to submit the manuscript.

Participant identification

Recruitment for SILC has been described.¹³ Potential PAD participants were recruited from non-invasive vascular laboratories and from relevant clinics that included large proportions

of patients with PAD at Chicago-area hospitals. Newspaper and radio advertisements, mailings to Chicago residents aged 60 years and older, fliers, and other community outreach methods were also used for recruitment.

Inclusion and exclusion criteria

The inclusion criterion was an ABI ≥ 0.95 . Exclusion criteria for SILC have been described^{12,13} and are summarized here briefly. Potential participants who were nursing home residents or had dementia, an above or below-knee amputation and critical limb ischemia were excluded. Potential participants unable to walk on a treadmill, unwilling to attend three-times weekly exercise sessions, unable to speak English, or who failed to complete run-in exercise sessions were excluded.^{12,13} Potential participants with recent major surgery, scheduled major surgery, unstable angina, or uncontrolled blood pressure were excluded. Participants whose baseline exercise stress test suggested possible coronary ischemia were excluded, unless they had a recent exercise stress test with imaging that demonstrated absence of coronary ischemia. Potential participants who were already exercising at a level comparable to that offered by the intervention, those participating in another clinical trial, those whose walking was primarily limited by a condition other than PAD, and those with a baseline Short Physical Performance Battery (SPPB) score of ≤ 12 were excluded.¹⁴ The SPPB is a battery of functional performance measures, including assessments of walking velocity, leg strength and balance, that predicts mobility loss and mortality in older men and women.¹⁴

Ankle-brachial index measurement

A hand-held Doppler probe (Nicolet Vascular Pocket Dop II; Nicolet Biomedical Inc, Golden, CO, USA) was used to obtain systolic pressures in the right and left brachial, dorsalis pedis, and posterior tibial arteries.^{12,13,15} Each pressure was measured twice. The ABI was calculated by dividing the mean of the dorsalis pedis and posterior tibial pressures in each leg by the average of the four brachial pressures.¹⁵ Average brachial pressures in the arm with the 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 mmHg or more in at least one measurement set. In these participants, subclavian stenosis was possible.¹⁶ The lowest leg ABI was used in analyses.

Medical history

Medical history was obtained by certified health interviewers using standardized techniques.^{12,13} Participants were asked whether a physician had ever told them that they had angina, heart failure, diabetes, myocardial infarction, cancer, or pulmonary disease. Participants were asked whether they had a history of lower extremity revascularization.

Functional performance measures

Six-minute walk—The 6-minute walk test is a measure of walking endurance that has excellent test/re-test reliability in individuals with PAD.^{12,17–19} Following an established protocol,^{17–19} participants walk up and down a 100-foot hallway for 6 minutes after standardized instructions to cover as much distance as possible. The distance completed at

the end of 6 minutes is recorded. The intra-class correlation coefficient for test/re-test reliability of the 6-minute walk was 0.90 ($p < 0.001$) in our laboratory among 155 PAD participants who completed the tests approximately 1–2 weeks apart¹²

Four-meter walking velocity—Walking velocity over 4 meters was measured with a 4-meter walk performed at ‘usual’ and ‘fastest’ pace.^{14,19} A research assistant gave standardized instructions and demonstrated the usual and fastest paced walks prior to measurement. For the usual paced walk, participants were instructed to walk at their usual pace, ‘as if going down the street to the store’. For the fastest paced walk, participants were instructed to walk at their fastest pace. The stop-watch was started with the command ‘go’. Each walk was performed twice. The faster walk in each pair was used in analyses.^{14,19} The intra-class correlation coefficients for test/re-test reliability were 0.83 ($p < 0.0001$) for the usual paced and 0.88 ($p < 0.0001$) for the fast paced 4-meter walk in our laboratory among the 155 PAD participants who completed the tests approximately 1–2 weeks apart.¹²

Treadmill walking performance

Maximal treadmill walking distance and distance to onset of ischemic leg symptoms were measured with the Gardner–Skinner protocol.²⁰ Participants able to walk at least 2.0 miles per hour (mph) (3.33 km/h) began exercising at 2.0 mph and zero grade. Grade was increased by 2% every 2 minutes. Participants unable to walk at least 2.0 mph began at 0.5 mph (modified Gardner protocol). Speed was increased by 0.50 mph every 2 minutes until the participant reached 2.0 mph, after which, speed was maintained at 2.0 mph and grade was increased by 2% every 2 minutes until the participant could not continue. This protocol has a coefficient of variation of 12% in people with PAD.²⁰

Walking impairment questionnaire

The walking impairment questionnaire (WIQ) is a PAD-specific measure of self-reported walking limitations with three domains: walking distance, walking speed, and stair climbing.²¹ Each domain is scored on a 0–100 scale, where 0 represents the most extreme limitation and 100 represents no difficulty walking long distances (distance score), walking rapidly (speed score), or climbing three stair flights (stair-climbing score).²¹

Other measures

Height and weight were measured and body mass index (BMI) was calculated as weight/(square of height in meters). Smoking history was obtained with a standardized questionnaire. Leg symptoms were measured with the San Diego claudication questionnaire.²²

Statistical analyses

The following ABI categories were defined in an a priori fashion: ABI < 0.50, ABI 0.50–0.70, ABI 0.71–0.95. Differences in baseline participant characteristics across baseline ABI categories were assessed using chi-square tests and analyses of variance. Differences in functional performance measures (maximal treadmill walking time, treadmill time to onset of leg symptoms, 6-minute walk, 4-meter walking velocity at usual and fastest pace, and

WIQ scores) across ABI categories were assessed using analysis of covariance, adjusting for age, sex, and race (Model 1). These analyses were repeated with additional adjustment for comorbidities (angina, myocardial infarction, heart failure, stroke, diabetes), BMI, leg symptoms, and cigarette smoking (Model 2). We also tested for the presence of an interaction between presence versus absence of intermittent claudication and the association of the ABI with functional performance measures. Pearson correlation coefficients were calculated for associations of the ABI with each functional performance measure. Partial correlation coefficients were calculated with adjustment for age, sex, race, comorbidities, BMI, leg symptoms, and smoking.

Analyses were performed using SAS Statistical Software version 9.2 (SAS Inc, Cary, NC, USA).

Results

Of 485 persons who attended a baseline visit, 329 met one or more exclusion criteria, leaving 156 participants. The five most common reasons for exclusion and the corresponding proportion of potential participants meeting each criterion follow: SPPB score of 12 (37.4%), unwillingness to attend exercise sessions three times weekly (11.8%), abnormal baseline exercise stress test (6.6%), walking limited by a condition other than PAD (4.9%), and failure to complete the study's run-in period (4.7%).

Baseline characteristics of the 156 eligible participants according to ABI categories are shown in Table 1. There were no differences in age, sex, or race across ABI categories. Most participants did not have classic symptoms of intermittent claudication. Higher ABI values were associated with a greater prevalence of participants without exertional leg symptoms. In unadjusted analyses, the distance achieved in the 6-minute walk test, maximal treadmill walking time, and the WIQ distance score were significantly lower among participants with lower ABI values (Table 1).

Table 2 shows correlation coefficients of the ABI with functional performance measures. Adjusting for age, sex, race, comorbidities, smoking, BMI, and leg symptoms, there were significant associations of the ABI with maximal treadmill walking time, 6-minute walk, walking velocity at fastest pace, and the WIQ distance score. The partial correlation for the association of the ABI with the WIQ speed score was of borderline significance ($p = 0.075$).

Table 3 shows age, sex, and race-adjusted associations of the ABI with functional performance measures (Model 1). Lower ABI values were associated with shorter maximal treadmill walking time (p trend = 0.001), shorter distance achieved in the 6-minute walk (p trend < 0.001), and lower WIQ distance scores (p trend = 0.007). Participants with ABI < 0.50 achieved shorter maximal treadmill walking time ($p = 0.0011$), shorter 6-minute walk distance ($p < 0.001$), and had a lower WIQ distance score ($p = 0.007$) compared to participants with ABI 0.71–0.95. Participants with ABI 0.50–0.70 achieved shorter maximal treadmill walking time ($p = 0.038$) and shorter 6-minute walk distance ($p = 0.036$) compared to participants with ABI 0.71–0.95. There were no significant associations of ABI with

treadmill time to onset of leg symptoms, 4-meter walking velocity, or the WIQ distance and speed scores, adjusting for age, sex, and race (Table 3).

In analyses adjusting for age, sex, race, smoking, BMI, comorbidities, and leg symptoms (Model 2, Table 2), lower ABI values were associated with shorter maximal treadmill walking time (p trend = 0.009), shorter distance achieved in the 6-minute walk test (p trend < 0.001), and lower WIQ distance scores (p trend = 0.007). In pair-wise comparisons for Model 2, participants with ABI < 0.50 achieved shorter maximal treadmill walking time (p = 0.009), had shorter 6-minute walk distances (p < 0.001) and lower WIQ distance scores (p = 0.006) compared to participants with ABI 0.71–0.95. Participants with ABI 0.50–0.70 had shorter 6-minute walk distance (p = 0.02) compared to participants with ABI 0.71–0.95. In Model 2, there were no significant associations of ABI with treadmill time to onset of leg symptoms, velocity over 4 meters, or the WIQ speed or stair-climbing scores (Table 2).

There was no significant interaction between presence versus absence of intermittent claudication and the association of ABI with functional performance (data not shown).

Discussion

Among 156 PAD participants, including those with and without symptoms of intermittent claudication, we found that lower ABI values were associated significantly with poorer walking endurance compared to higher ABI values. Significant associations of lower ABI values with impaired walking endurance were observed for distinct outcomes including maximal treadmill walking time, the 6-minute walk, and the WIQ distance score. In fully adjusted analyses, participants with an ABI < 0.50 and those with an ABI of 0.50–0.70 each had a significantly poorer 6-minute walk performance compared to participants with an ABI of 0.71–0.95. Participants with an ABI < 0.50 had a significantly lower maximal treadmill walking time and WIQ distance scores compared to those with an ABI of 0.71–0.95. Together, these findings suggest that among PAD participants with and without claudication symptoms, lower ABI values are associated with greater limitations in walking endurance. However, the ABI was not associated with usual or fastest paced walking velocity over 4 meters, treadmill time to onset of ischemic leg symptoms, or the WIQ speed or stair-climbing scores.

Several prior studies of participants with PAD and intermittent claudication reported no association of the ABI with treadmill walking performance (6–9). These prior studies had relatively small sample sizes, included only PAD participants with intermittent claudication symptoms, and measured walking performance with treadmill testing only. In contrast, the current study consists of a larger sample size, included PAD participants with and without intermittent claudication symptoms, and measured walking performance with multiple diverse measures. Our inclusion of PAD participants without intermittent claudication is an important distinction because some PAD patients without intermittent claudication have greater functional impairment than those with intermittent claudication.^{4,11}

Among 740 men and women in the Walking and Leg Circulation Study (WALCS), we previously reported that lower ABI values were associated with a poorer 6-minute walk

performance, slower walking velocity, lower physical activity, and poorer balance.²³ However, this prior study included 460 participants with PAD and 280 without PAD. Significant associations of lower ABI values with greater functional impairment may have been driven by differences in functional performance between participants with versus without PAD. Associations of the ABI with functional performance were not analyzed separately in the entire cohort of PAD participants in this prior report.²³ In addition, this prior study did not include treadmill walking data or WIQ scores.²³ In a separate study of 127 PAD participants, including participants with and without intermittent claudication, we previously reported independent associations of lower ABI values with poorer 6-minute walk performance and slower walking velocity at usual and fastest pace adjusting for age and sex.¹⁵ In contrast to this prior study, the current study includes measures of treadmill walking performance and three WIQ score measures. In addition, this prior study did not adjust for multiple potential confounders. These latter characteristics along with differences in inclusion criteria may explain the distinction between the prior study's finding that lower ABI values were associated with slower walking velocity¹⁵ and the current data that did not document an association of the ABI with walking velocity.

This study has limitations. First, although this study is larger than previous reports of PAD participants,⁶⁻⁹ the sample size is relatively small, limiting statistical power to detect associations of the ABI with some outcomes. Some associations reported here, such as associations of the ABI with walking velocity and treadmill time to onset of ischemic leg symptoms, may be statistically significant in larger sample sizes. Second, the SILC had multiple exclusion criteria, including regular exercise and higher levels of functional performance, measured by the short physical performance battery, at baseline.¹³ These exclusion criteria limit the generalizability of the findings to relatively frail PAD participants who do not engage in regular exercise. However, including PAD participants without exertional leg symptoms and those with leg symptoms other than intermittent claudication enhances the generalizability of the data, since most men and women with PAD do not have classic intermittent claudication symptoms.

Although data presented here demonstrate independent associations of the ABI with walking endurance, other characteristics are also associated with walking impairment in PAD.²⁴⁻²⁸ Ischemia-related calf muscle pathology, increased inflammatory biomarker levels, and PAD-related gait abnormalities are associated with greater functional impairment in patients with PAD.²⁴⁻²⁸ Furthermore, the ABI may be an imprecise measure of blood flow to the lower extremities, since medial calcinosis can elevate lower extremity arterial pressures, independent of arterial perfusion.²⁹ Thus, the ABI has limitations as a measure of lower extremity oxygen delivery and functional performance in PAD.

Among PAD participants with and without intermittent claudication, lower ABI values were associated significantly with poorer walking endurance, measured by three distinct outcomes. Our data demonstrate that clinicians can use the ABI to gauge walking endurance-related functional limitations among patients with PAD. However, available data indicate that other characteristics, such as calf muscle characteristics and inflammation, are also related to walking impairment in PAD.²⁴⁻²⁸

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Table 1

Associations of ankle–brachial index categories with characteristics of men and women with peripheral arterial disease ($n = 156$)^a

	ABI < 0.50 ($n = 49$)	ABI 0.50–0.70 ($n = 66$)	ABI 0.71–0.95 ($n = 41$)	<i>p</i> trend
Age, years	68.9 (9.3)	72.4 (11.3)	69.7 (9.4)	0.639
Male sex, %	42.9	50.0	51.2	0.417
African American, %	44.9	39.4	34.2	0.299
Intermittent claudication, %	32.7	47.0	22.0	0.364
No exertional leg symptoms, %	2.0	6.0	14.6	0.030
Atypical exertional leg symptoms, %	65.3	47.0	63.4	0.759
Ankle–brachial index	0.42 (0.06)	0.60 (0.06)	0.85 (0.07)	< 0.001
Body mass index, kg/m ²	30.6 (7.7)	30.0 (6.0)	30.4 (6.8)	0.867
Diabetes, %	51.0	47.0	31.7	0.074
Current smoker, %	30.6	22.7	17.1	0.132
Former smoker, %	55.1	60.6	56.1	0.895
Hypertension, %	85.4	83.1	78.1	0.369
Angina, %	8.3	10.9	17.1	0.212
Myocardial infarction, %	10.4	28.8	25.0	0.084
Heart failure, %	8.2	18.5	12.5	0.491
Stroke, %	10.4	27.3	22.5	0.139
Pulmonary disease, %	19.2	7.6	14.6	0.482
Prior lower extremity revascularization, %	46.9	34.9	22.0	0.015
Functional performance measures				
Six-minute walk, meters	290 (83)	312 (81)	355 (92)	< 0.001
Four-meter usual pace, meters/second	0.82 (0.14)	0.80 (0.15)	0.83 (0.16)	0.772
Four-meter fast pace, meters/second	1.08 (0.22)	1.07 (0.22)	1.12 (0.27)	0.470
Maximal treadmill walking time, minutes	5.81 (3.59)	6.99 (3.34)	8.63 (4.79)	< 0.001
Treadmill time to onset of leg symptoms, minutes	2.59 (1.46)	3.28 (2.42)	3.02 (2.53)	0.297
WIQ distance score, 0–100 scale	22.0 (21.0)	27.9 (25.1)	36.5 (23.9)	0.007
WIQ speed score, 0–100 scale	26.9 (20.6)	26.3 (21.5)	31.4 (23.8)	0.340
WIQ stair climbing score, 0–100 scale	42.2 (26.8)	35.3 (24.0)	43.8 (23.8)	0.873

^aData for continuous variables are means (standard deviations).

Table 2

Correlations between the ankle–brachial index and walking performance measures.

	Unadjusted		Adjusted ^a	
	Correlation coefficient	<i>p</i> -value	Correlation coefficient	<i>p</i> -value
Maximal treadmill walking time	0.303	< 0.001	0.264	< 0.001
Treadmill time to onset of leg symptoms	0.072	0.411	0.108	0.251
Six-minute walk	0.355	< 0.001	0.369	< 0.001
Four-meter usual pace	0.104	0.196	0.132	0.126
Four-meter fast pace	0.126	0.116	0.170	0.048
WIQ distance score	0.273	0.001	0.306	< 0.001
WIQ speed score	0.095	0.255	0.160	0.075
WIQ climb score	0.022	0.787	0.031	0.735

^a Partial correlation with adjustment for age, sex, race, smoking, angina, myocardial infarction, heart failure, stroke, diabetes, body mass index, and leg symptoms.

Adjusted associations of ankle-brachial index categories with functional performance measures among men and women with peripheral arterial disease ($n = 156$)

Table 3

	ABI	n	Model 1			Model 2		
			Mean value (standard error)	p trend	Mean value (standard error)	p trend	Mean value (standard error)	p trend
Maximal treadmill walking time, minutes	< 0.50	49	5.87 (0.55) **	0.001	6.00 (0.58) **	0.009		
	0.50–0.70	66	6.97 (0.47) *		6.92 (0.49)			
	0.71–0.95	41	8.58 (0.60)		8.32 (0.64)			
Treadmill time to onset of leg symptoms, minutes	< 0.50	47	2.62 (0.31)	0.259	2.59 (0.34)	0.222		
	0.50–0.70	58	3.20 (0.28)		3.14 (0.31)			
	0.71–0.95	29	3.12 (0.40)		3.22 (0.46)			
Six-minute walk, meters	< 0.50	49	286 (11) **	< 0.001	286 (11) **	< 0.001		
	0.50–0.70	66	317 (9.8) *		316 (10) *			
	0.71–0.95	41	351 (12.4)		355 (12)			
Four-meter usual pace, meters/second	< 0.50	49	0.81 (0.02)	0.827	0.80 (0.02)	0.313		
	0.50–0.70	66	0.81 (0.02)		0.80 (0.02)			
	0.71–0.95	41	0.82 (0.02)		0.83 (0.02)			
Four-meter fast pace, meters/second	< 0.50	49	1.07 (0.03)	0.507	1.06 (0.03)	0.118		
	0.50–0.70	66	1.08 (0.03)		1.08 (0.03)			
	0.71–0.95	41	1.10 (0.03)		1.13 (0.03)			
WIQ distance score	< 0.50	47	22.1 (3.5)	0.007	21.7 (3.5)	0.007		
	0.50–0.70	59	27.8 (3.1)		26.8 (3.1)			
	0.71–0.95	36	36.6 (4.0)		36.7 (4.1)			
WIQ speed score	< 0.50	48	27.4 (3.0)	0.379	25.1 (3.1)	0.1740		
	0.50–0.70	58	25.6 (2.8)		25.7 (2.8)			
	0.71–0.95	39	31.7 (3.3)		31.7 (3.5)			
WIQ stair-climbing score	< 0.50	47	43.2 (3.6)	0.956	42.5 (3.7)	0.970		
	0.50–0.70	60	34.2 (3.2)		33.8 (3.2)			
	0.71–0.95	38	44.3 (4.0)		43.6 (4.1)			

Model I adjusts for age, sex, and race. Model II adjusts for age, sex, race, current smoking status, angina, myocardial infarction, heart failure, stroke, diabetes, body mass index, and leg symptoms.

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$p < 0.05$ for the pairwise comparison with the reference group (ABI 0.71–0.95);
 $p < 0.01$ for the pairwise comparison with the reference group (ABI 0.71–0.95);

*

ABI, ankle–brachial index.