Leg strength in peripheral arterial disease: Associations with disease severity and lower-extremity performance

Mary McGrae McDermott, MD,[a] Michael H. Criqui, MD, MPH,[b] Philip Greenland, MD,[a] Jack M. Guralnik, MD, PhD,[c] Kiang Liu, PhD,[a] William H. Pearce, MD,[a] Lloyd Taylor, MD,[d] Cheeling Chan, MS,[a] Lillian Celic, BS,[a] Charles Woolley, MS,[e] Michael P. O'Brien, BA,[a] and **Joseph R. Schneider, MD, PhD,[a,f]** *Chicago, Ill; San Diego, Calif; Bethesda, Md; Portland, Ore; Ann Arbor, Mich; and Evanston, Ill*

Objective: **The purpose of this study was to determine relationships between lower-extremity arterial obstruction, leg strength, and lower-extremity functioning.**

Design: **The study design was cross-sectional. A total of 514 outpatients (269 with ankle-brachial index [ABI] <0.90), aged 55 and older, were identified from three Chicago-area hospitals. Individuals with history of lower-extremity revascularization were excluded.**

Main outcome measures: **Strength in each leg, 6-minute walk, 4-meter walking velocity, accelerometer-measured physical activity, and a summary performance score were measured. The summary performance score is a composite measure of lower-extremity functioning, ranging from 0 to 12 (12 = best). The leg with the lower ABI was defined as the "index" leg, and the leg with higher ABI was defined as the "contralateral" leg.**

Results: **Index leg ABI levels were associated linearly and significantly with strength for hip extension ($P < .001$), hip flexion ($P < .001$), knee extension ($P = .066$), and knee flexion ($P = .003$), adjusting for known and potential confounders. In adjusted analyses, the index ABI was also associated linearly and significantly with strength in the contralateral leg. Adjusting for confounders, including ABI, knee extension strength, was associated independently with functional measures.**

Conclusion: **Among patients without prior leg revascularization, strength in each leg is highly correlated with the lower-leg ABI. Leg strength is associated independently with functional performance. Further study is needed to determine whether lower-extremity resistance training improves functioning in patients with peripheral arterial disease.**

(J Vasc Surg 2004;39:523-30.)

Loss of lower-extremity muscle mass and strength are increasingly recognized as causes of disability in patients with chronic disease.[1-6] In older, frail individuals, resistance training of the legs improves functioning, increases aerobic capacity, and increases treadmill-walking distance.[7-9] Reduced leg strength associated with arterial obstruction can be one mechanism by which lower-extremity peripheral arterial disease (PAD) impairs functioning. Men and women with PAD have atrophy and reduced numbers of lower-extremity skeletal muscle fibers as compared with patients without PAD.[10,11] However, to our knowledge only two prior studies have assessed the relation between PAD and leg strength.[11,12] Results of those two studies were conflicting: one study showed impaired strength in persons with PAD, and the second study did not show a reduction in leg strength among persons with PAD.

We assessed relations between lower-extremity arterial obstruction and leg strength in a large sample of men and women with and without PAD. We determined whether lower ankle-brachial index (ABI) levels are associated with greater impairments in leg strength. To determine whether lower-extremity arterial obstruction directly impairs skeletal muscle strength, we compared relations between the lower-leg ABI and both ipsilateral and contralateral leg strength. We reasoned that if lower-extremity arterial obstruction impairs strength, then the lower ABI may be highly correlated with strength in the ipsilateral but not the contralateral leg. Alternatively, because of disuse atrophy, leg strength could be similarly reduced in the index and contralateral legs. Finally, we assessed relations between leg strength and functioning among men and women with PAD, to determine whether leg strength mediates the relation between ABI and functioning in PAD.

From the Feinberg School of Medicine at Northwestern University,[a] Chicago, Illinois, University of California at San Diego,[b] Laboratory of Epidemiology, Demography, and Biometry, National Institute on Aging,[c] Bethesda, Maryland, Oregon Health and Science University,[d] Portland, University of Michigan,[e] Ann Arbor, and Evanston Hospital,[f] Evanston, Ill.

Competition of interest: none.

Reprint requests: Mary McGrae McDermott, 675 N St Clair Ste 18-200, Chicago, IL 60611 (e-mail: mdm608@northwestern.edu).

Published online Jan 30, 2004.
0741-5214/$30.00

doi:10.1016/j.jvs.2003.08.038

METHODS

Participation identification

The protocol was approved by Institutional Review Boards at Northwestern University's Feinberg School of Medicine and Catholic Health Partners Hospitals. Participants were aged 55 or older, and all gave informed consent. Of those participants with PAD, most were identified from three Chicago-area noninvasive vascular laboratories. A small number were identified from among consecutively identified patients in a large general internal medicine (GIM) practice who were screened with the ABI. Half of the participants without PAD were identified from among consecutive patients with normal lower-extremity arterial tests in the three Chicago-area noninvasive vascular laboratories, and half were identified from among consecutive patients with appointments in the GIM practice.

Exclusion criteria

PAD was defined as ABI <0.90. Absence of PAD was defined as ABI 0.90 to 1.50.[13,14] Patients with ABI values greater than 1.50 were excluded because ABI >1.50 indicates poorly compressible leg arteries and inability to gauge arterial obstruction accurately. Patients diagnosed with PAD in the vascular laboratories were excluded if they had a normal ABI at their study visit. Similarly, patients with a normal ABI from the vascular laboratories were excluded if they had ABI <0.90 at the study visit. The total number of participants excluded because of one of these ABI criteria was 151.

Patients with dementia were excluded because of concern about their ability to answer questions accurately (n = 7). Those patients with severely impaired functioning were also excluded. These exclusions included nursing home residents (n = 65), wheelchair-bound patients (n = 33), and patients with foot or leg amputations (n = 80). Non–English-speaking patients were excluded because the research staff members were not fluent in non-English languages (n = 61). Because we did not have information on graft patency, selection criteria, or postsurgical management of PAD, individuals with history of lower-extremity revascularization were excluded from analyses (n = 168).

Ankle-brachial index measurement

The ABI was measured by using previously established methods.[13,14] Lower-extremity blood pressure cuffs were placed at the ankles, 3 cm above the malleoli. Participants rested supine for 5 minutes prior to the ABI. Systolic pressures were measured in the right brachial artery, right dorsalis pedis and posterior tibial arteries, left dorsalis pedis and posterior tibial arteries, and left brachial artery by using a hand-held Doppler probe (Nicolet Vascular Pocket Dop II, Golden, Colo). Each pressure was measured twice: first in the order listed and then in reverse order. The ABI was calculated in each leg by dividing the average pressures in each leg by the average of the four brachial pressures. When one brachial artery pressure was higher than the opposite brachial artery pressure in both measurement sets, and the right and left brachial artery pressures differed by 10 mmHg or more in at least one measurement set, subclavian stenosis was suspected. The average brachial artery pressure in the arm with higher pressure was used to calculate the ABI.[14] Among participants with and without PAD, the lower-leg ABI was referred to as the "index" leg. The leg with higher ABI was referred to as the "contralateral" leg. For individuals with identical ABI values in the left and right legs, the right leg was designated as the index leg a priori. Unless otherwise indicated, the index leg ABI was used in analyses.

Leg symptom groups

Using the San Diego claudication questionnaire, we characterized leg symptoms into one of five mutually exclusive leg symptom groups. The five groups have been described previously[15] and consisted of the following: (1) intermittent claudication, (2) atypical exertional leg pain/stop, (3) atypical exertional leg pain/carry on, (4) leg pain on exertion and rest, and (5) no exertional leg pain.

Comorbidities

We documented comorbidities by using methods from the Women's Health and Aging Study and the Cardiovascular Health Study.[16-18] Disease-specific algorithms combined data from patient report, physical examination, medical record review, medications, laboratory values, and primary care physician questionnaire. Criteria developed by the American College of Rheumatology were used to diagnose knee and hip osteoarthritis.[19,20] Comorbidities assessed were angina pectoris, diabetes mellitus, myocardial infarction, stroke, heart failure, pulmonary disease, knee and hip arthritis, spinal stenosis, disk disease, and hip fracture. These comorbidities were chosen because they are associated with impaired functioning.[17,18] Angina pectoris, myocardial infarction, stroke, and heart failure were combined into one category of cardiac or cerebrovascular disease. Hip or knee arthritis, spinal stenosis, disk disease, and hip fracture were combined into one category of arthritis. A category of "other comorbid disease" was defined to include cancer and pulmonary disease.

Neuropathy

We used a monofilament to assess sensation in 11 locations on the dorsal and ventral surface of each foot, based on previous study.[21,22] Potential scores ranged from 0 to 22, where 0 indicated that the participant detected all locations tested with the monofilament and 22 indicated that none of the locations were detected.

Lower-extremity functional measures

Six-minute walk. Following a standardized protocol, participants walked up and down a 100-foot hallway for 6 minutes, covering as much distance as possible. The 6-minute walk test is highly reliable in patients with PAD (reliability coefficient = 0.94).[23]

Accelerometer-measured physical activity. The Caltrac vertical accelerometer was used to measure physical activity levels over 7 days. This device is worn at the waist. To compare activity levels between participants regardless of individual variation in age, weight, height, and sex, we programmed accelerometers with identical values for those four characteristics by using previously reported methods.[24] Thus, the accelerometers measured "activity units." Participants were telephoned at the end of the 7-day period

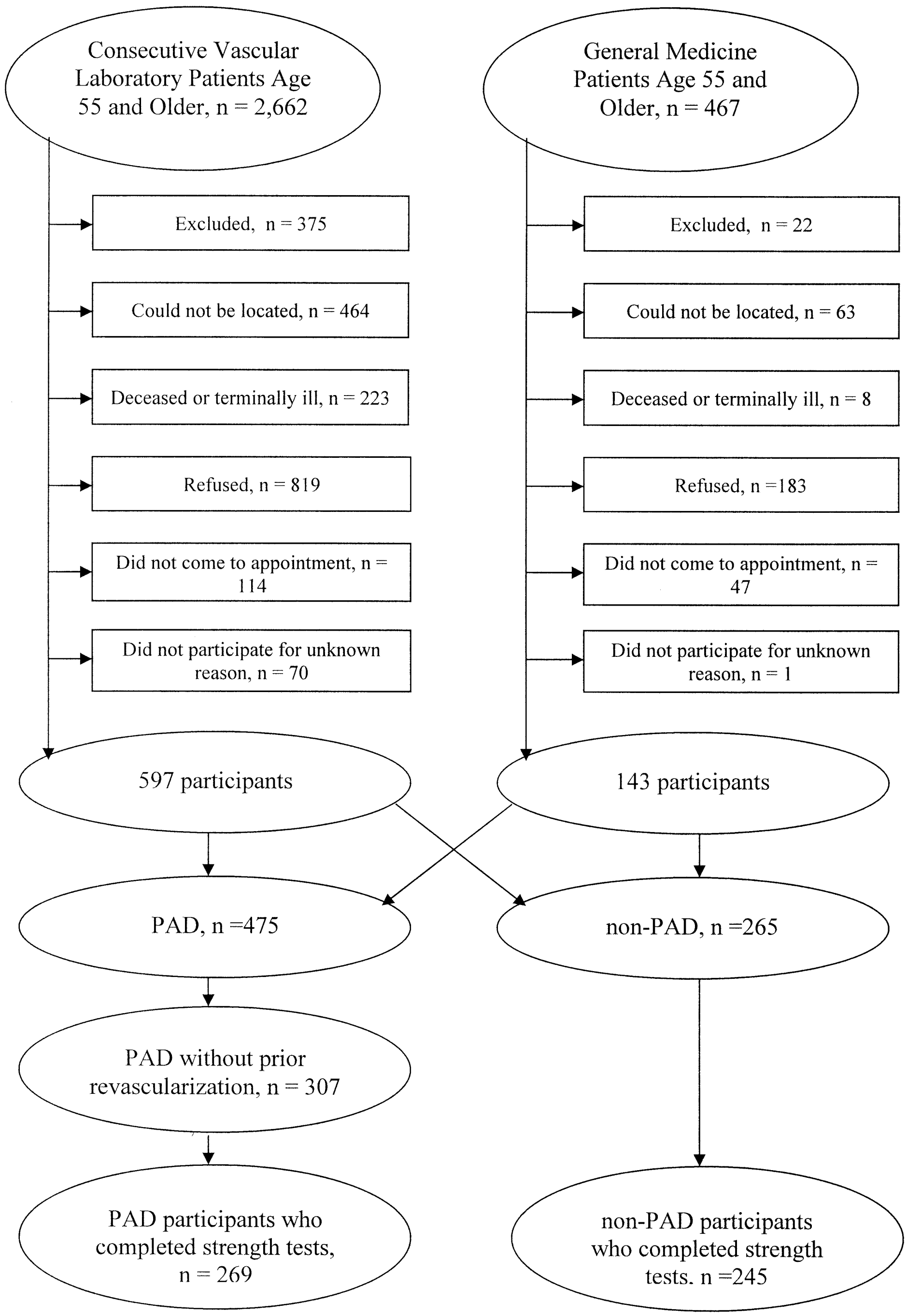

Fig 1. Reasons for nonparticipation among potentially eligible identified patients. *PAD*, Peripheral artery disease.

to obtain the final number of activity units displayed on the accelerometer. Because of a shortage of accelerometers, they were distributed only to 49% of the participants. There were no significant differences in age, race, sex, or average ABI of participants between those participants who did or did not wear the accelerometer.

Summary performance score

Repeated chair rises. The repeated chair rise test measures leg strength and balance.[25-27] Participants sit in a straight-backed chair with arms folded across their chest and stand up five consecutive times as quickly as possible. Time required for the five chair rises was measured.

Table I. Age and sex-adjusted characteristics of participants (N = 514)

	PAD (*n* = *269*)	*Non-PAD* (*n* = *245*)
African American race, %	17	16
Ankle-brachial index*	0.662	1.09
Currently smoke, %*	18	5
Comorbidities		
Arthritis, %*	41	58
Diabetes, %†	30	19
Cardiac or cerebrovascular disease, %*	55	40
Lower extremity functional measures		
Six-minute walk distance, ft*	1173	1402
Four-meter normal pace velocity, m/sec‡	0.891	0.930
Seven-day caltrac physical activity, activity units§	864 (n = 125)	1040 (n = 107)
Summary performance score, 0-12 score (12 = best)	9.57	9.93
Strength in index leg, Newton-meters		
Hip extension*	61.4	71.6
Hip flexion*	54.0	61.7
Knee extension	46.3	49.5
Knee flexion*	29.1	35.4
Strength in contralateral leg, Newton-meters		
Hip extension*	60.7	74.6
Hip flexion*	54.6	62.9
Knee extension§	47.1	51.4
Knee flexion*	29.4	36.4

Values are expressed as means (SD) and adjusted means unless otherwise indicated. Cardiac or cerebrovascular disease is defined as one or more of the following: history of myocardial infarction, heart failure, angina, stroke. Arthritis is defined as one or more of the following: spinal disc disease, hip and knee arthritis, hip fracture, and spinal stenosis. Index leg refers to leg with lower ABI. Contralateral leg refers to leg with higher ABI.
P values for comparisons between the PAD and non-PAD groups: $*P \leq .001$, $^{\dagger}P \leq .003$, $^{\ddagger}P \leq .03$, $^{\S}P \leq .01$.

Standing balance. Participants attempt to hold three increasingly difficult standing positions for 10 seconds each: standing with feet together side by side, standing with the toes of one foot adjacent to the heel of the second foot while feet were parallel, and standing with one foot directly in front of and in contact with the other.[25-27]

Four-meter walking velocity. The walking velocity of each participant was measured over a marked 4-meter distance in a hallway.[25-27] Participants walked this distance twice at their "usual" pace. The faster walk was used in analyses.

Calculating the summary performance score. The summary performance score predicts risk of future nursing home placement, mobility loss, and mortality among community-dwelling older men and women.[25-27] The score is calculated by assigning a value of 0 to 4 for performance on 4-meter walking velocity, five chair rises, and standing balance, respectively, based on cut points derived from normative data of representative community populations. The sum of these three scores is the summary performance score, ranging from 0 to 12 (12 = best).[27]

Leg strength

Leg strength for each participant was measured by using a musculoskeletal fitness evaluation (MFE) chair. The MFE chair measures isometric strength in Newton-meters for knee flexion, knee extension, hip flexion, and hip extension by using strain gauges connected to a computerized data-collecting unit. Participants sat in the MFE chair and pushed against leg attachments for 5 seconds. They were instructed to build to their maximum strength. The highest recorded strength during the last 3 seconds of effort was used in analyses. Strength measurements were performed twice, and the higher value was used in analyses.

Body mass index

Height and weight were measured at the study visit. Body mass index (BMI) was calculated as kg/m^2.

Statistical analyses

Differences in characteristics of the study population were assessed by using age- and sex-adjusted general linear models for continuous variables and binary variables. For binary variables, the test of significance was based on logistic regression models.

Among persons with and without PAD, mean strength in the index and contralateral legs were compared across the index leg ABI categories (ABI <0.50, ABI 0.50-<0.70, ABI 0.70-<0.90, ABI 0.90-<1.10, and ABI 1.10-1.50) by using general linear models. The test for linear trend across the ABI categories was based on multiple linear regression analyses, using ABI as an independent variable. These analyses were repeated, adjusting for known and potential confounders: age, sex, race (African American versus non–African American), education, BMI, comorbid diseases, neuropathy score, and leg symptoms.

To account for the interdependence of the leg data on the same patient, the relations between ABI and strength in the index and contralateral legs among PAD participants whose ABI differed by at least 0.20 were compared by using linear mixed models, adjusting for age, sex, and race. These analyses were repeated among participants with ABI 1.10-1.50 in both legs.

The independent relation between ABI and each functional measure was determined by using multiple linear regression analyses, adjusting for age, sex, race, education, BMI, number of comorbid diseases, neuropathy score, and leg symptoms. These analyses were repeated with the additional adjustment for the four leg strength variables in the index leg, to determine whether associations between ABI and functioning were attenuated after additional adjustment for leg strength. All analyses were performed by using SAS statistical software version 8.2 (SAS Institute Inc, Cary, NC). *P* values were two-tailed, and $P < .05$ was considered to indicate statistical significance, except as noted earlier.

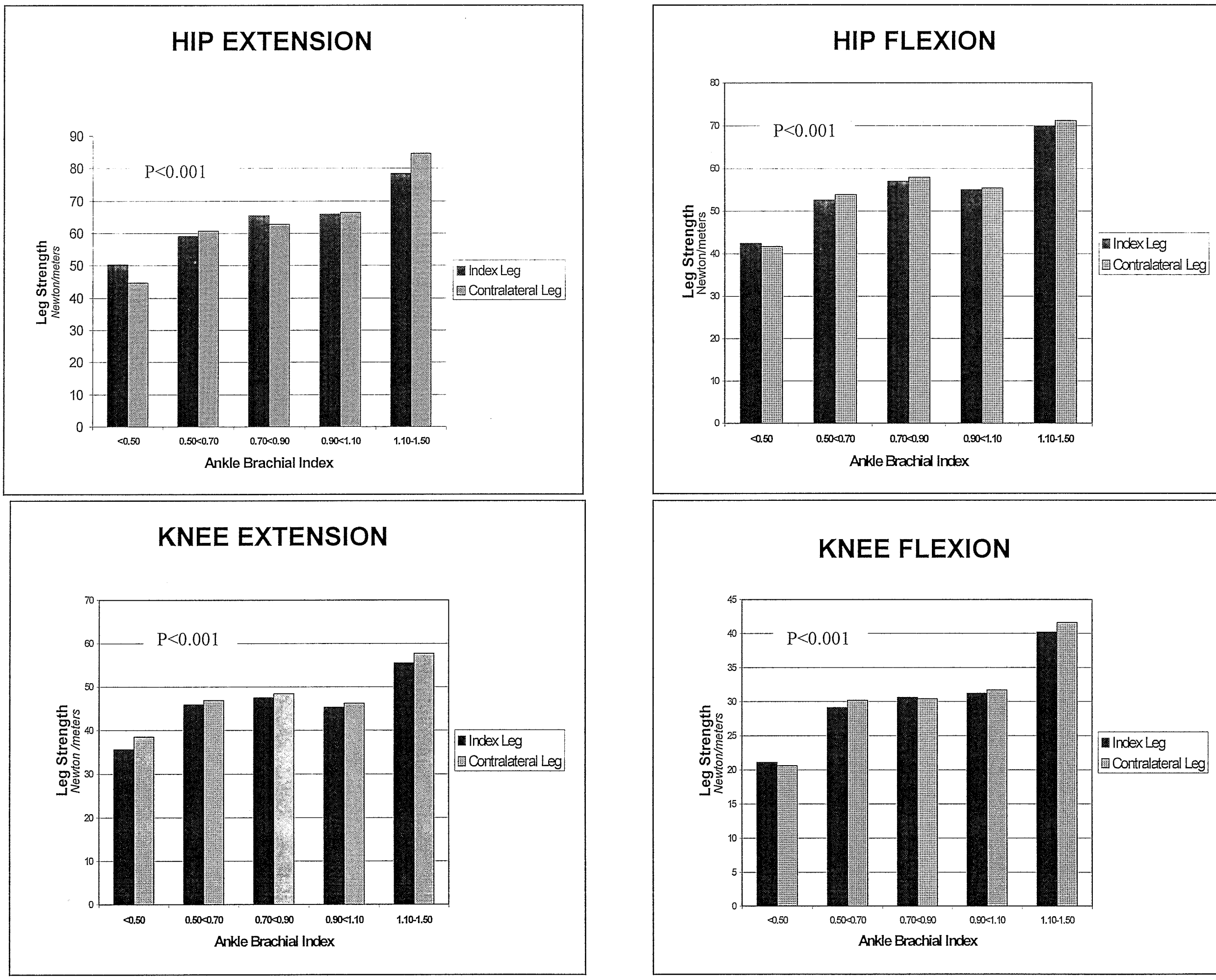

Fig 2. Association between lowest leg ankle-brachial index and strength in ipsilateral and contralateral legs among men and women without prior lower-extremity revascularization (n = 514).

RESULTS

Fig 1 shows the number of study participants among those identified.

The average age of participants with PAD was 73.2 years ± 8.0 versus 69.5 years ± 8.1 for participants without PAD ($P < .001$). Among individuals with PAD, 56.9% were men versus 48.6% among those without PAD. Among participants with ABI <0.90, we found that 30.5% had intermittent claudication and 19.7% had no exertional leg pain. Table I shows characteristics of the study population. Leg strength was higher in participants without PAD than in participants with PAD.

Fig 2 and Fig 3 show relations between ABI and leg strength. In unadjusted and fully adjusted analyses, we observed significant linear relations between ABI and strength in the index leg and between ABI and strength in the contralateral leg. For each ABI category, average strengths were similar between the index and contralateral legs (Fig 2-3). Leg strength in patients with ABI 0.90 to <1.10 was consistently lower than strength in patients with ABI 1.10 to 1.50.

Table II shows relations between ABI and strength in the index and contralateral legs among PAD participants whose ABI differed by at least 0.20 between their index and contralateral legs. After adjusting for age, sex, and race, there were no significant differences in strength between the index and contralateral legs (Table II).

Table III shows regression coefficients relating ABI to each functional measure before and after adjusting for leg strength. Prior to adjusting for leg strength, ABI was related significantly to each functional measure, adjusting for known and potential confounders. These relations between ABI and functioning were attenuated slightly after additional adjustment for strength as demonstrated by relatively small reductions in the regression coefficients and increases in the P value for ABI after adding the leg strength variables to the model. Thus, leg strength appears to be a modest contributor to the relation between ABI and leg

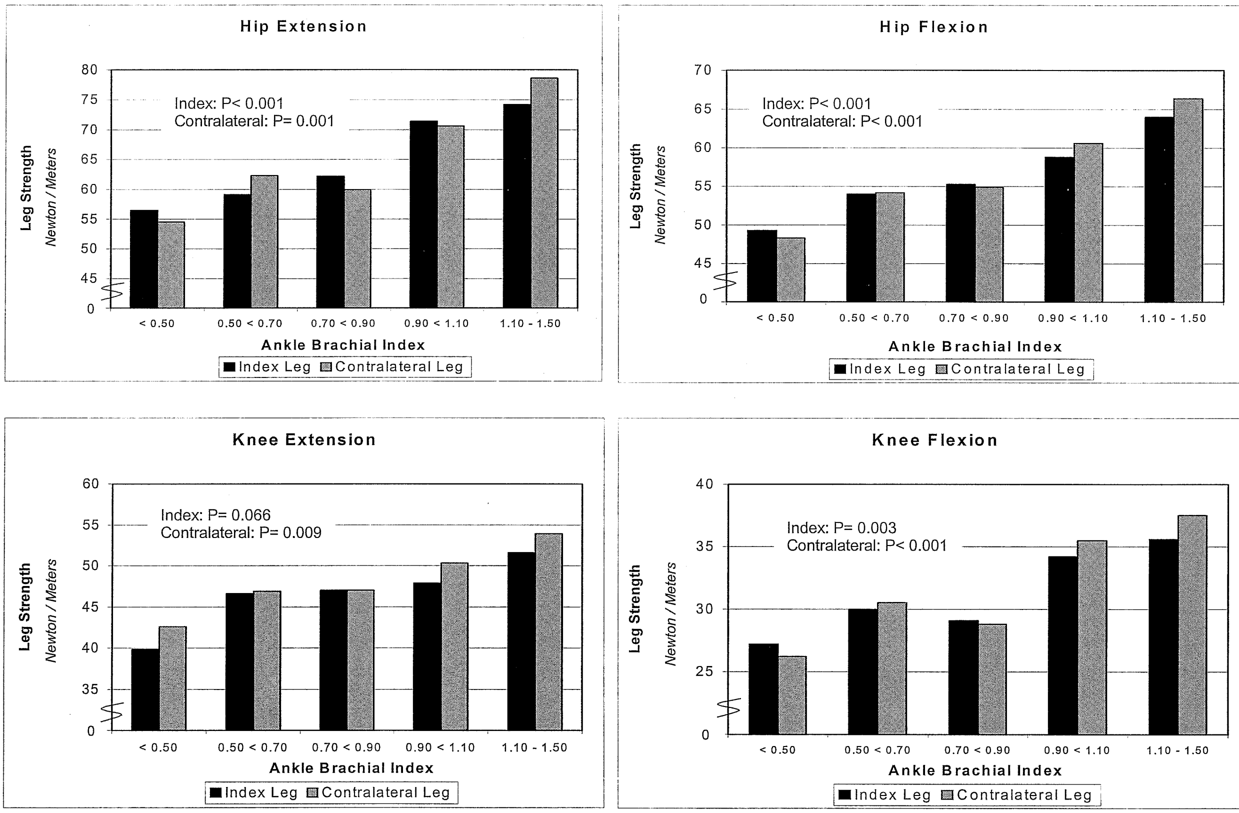

Fig 3. Adjusted associations between lowest leg ankle-brachial index and strength in ipsilateral and contralateral legs among men and women without prior lower-extremity revascularization (n = 514).

functioning. However, knee extension was associated significantly with each functional measure after adjusting for ABI and other known and potential confounders.

DISCUSSION

Among persons with and without PAD who have not had prior lower-extremity revascularization, strength in both legs is highly associated with the lower-leg ABI. Even among patients with PAD with substantial differences in ABI between their left and right legs, strength in each leg was highly associated with the lower-leg ABI. There are two potential explanations for this finding. First, a high correlation between left- and right-leg ABI values may explain why the lower-leg ABI is strongly associated with leg strength in both legs. However, we found that the lower-leg ABI was highly correlated with bilateral leg strength even in patients with a difference in ABI of $\geq$0.20 between the right and left legs. Alternatively, lower-extremity arterial obstruction may not directly influence leg strength. Instead, PAD-related disuse atrophy may result in reduced strength in both legs. Consistent with this hypothesis, previous data show that the lower-leg ABI is highly correlated with physical activity levels in patients with and without PAD.[13,24]

Data reported here also show that knee extension strength is associated with each functional outcome measure and that leg strength appears to contribute to the associations between ABI and leg functioning. Although our data were cross-sectional, findings are consistent with previous study showing that progressive resistance training in patients with PAD with intermittent claudication significantly increases treadmill walking performance, although to a lesser degree than treadmill training.[29] Thus, leg strengthening programs may play a role in improving functioning in persons with PAD. In addition, further study is needed to determine whether increasing physical activity levels in persons with PAD delay or prevent disuse atrophy in lower-extremity skeletal muscles.

Our findings show that participants with low normal ABI values of 0.90 to 1.10 have poorer leg strength than participants with ABI values of 1.10 to 1.50. Individuals with ABI values of 0.90 to 1.10 are likely to have mild or subclinical PAD which may negatively affect leg strength. Findings reported here are consistent with a previous study showing that lower-extremity functioning is poorer in persons with ABI values of 0.90 to 1.10 as compared with persons with ABI values of 1.10 to 1.50.[13] Finally, we found that knee extension strength was associated independently with lower-extremity functioning and physical activity level, adjusting for confounders, including ABI. This finding is consistent with previous study.[28]

Table II. Adjusted comparisons in leg strength between the index (lower ABI) and contralateral legs in patients whose right- and left-leg ankle-brachial index differ by ≥0.20

		Leg strength in leg with lower ABI ankle-brachial index							
		<0.50 n = 13		*0.50 < 0.70 n = 45*		*0.70 < 0.90 n = 25*		*1.10-1.50 n = 116**	
Hip extension, Newton-meters	*Index leg*	46.1	*P* = .107	58.4	*P* = .955	55.9	*P* = .265	77.0	*P* = .067
	Contralateral leg	36.6		58.2		60.3		83.6	
Hip flexion, Newton-meters	*Index leg*	47.5	*P* = .587	54.6	*P* = .411	52.6	*P* = .549	67.7	*P* = .553
	Contralateral leg	46.6		56.2		51.5		68.6	
Knee extension, Newton-meters	*Index leg*	41.9	*P* = .220	44.4	*P* = .323	44.3	*P* = .158	53.6	*P* = .179
	Contralateral leg	45.1		46.5		48.3		55.7	
Knee flexion, Newton-meters	*Index leg*	19.5	*P* = .700	30.1	*P* = .866	27.1	*P* = .487	38.7	*P* = .201
	Contralateral leg	18.5		30.3		28.4		40.0	

Analyses excluded patients with ABI level 0.90 to 1.10 and patients with prior lower-extremity revascularization. Comparisons were adjusted for age, sex, and race. *P* values were derived from linear mixed models.
*Participants with ABI 1.10-1.50 in both legs.

Table III. Relationships between ankle-brachial index, leg strength, and functional performance (N = 514)

	Model 1		*Model 2*					
Dependent variables	*Ankle-brachial index,* β	R^2	*Ankle brachial index,* β	*Hip extension,* β	*Hip flexion,* β	*Knee extension,* β	*Knee flexion,* β	R^2
Six-minute walk distance, ft	507*	0.464	428*	0.526	1.05	3.78*	0.853	0.518
Four-meter normal pace velocity, m/sec	0.099†	0.374	0.079‡	0.0004	−0.0005	0.002*	0.0002	0.406
Seven-day physical activity (N = 231)	338‡	0.296	188	−0.438	3.49	5.35†	−1.76	0.339
Summary performance score, 0-12 score, (12 = best)	1.43§	0.379	1.10†	0.006	−0.006	0.026*	−0.002	0.436

Model 1 was adjusted for age, sex, race, BMI, education, comorbidities (cardiac or cerebrovascular disease, arthritis, pulmonary disease, cancer, diabetes), neuropathy score, and leg symptoms. Additional adjustments were made in Model 2 for leg strength (hip extension, hip flexion, knee extension, and knee flexion) in leg with lower ABI. Values shown are regression coefficients (β) unless otherwise indicated. In each model, the functional outcome was the dependent variable. Regression coefficients represent the change in each functional outcome for each unit change in the independent variables (ankle-brachial index, hip extension, hip flexion, knee extension, knee flexion), controlling for other variables in the model. Leg strength was measured in Newton-meters.
*$P \leq .001$; †$P \leq .01$; ‡$P \leq .05$; §$P \leq .002$.

Previous studies have shown inconsistent results regarding PAD and leg strength. Regensteiner et al[11] studied 26 men with PAD and intermittent claudication and 6 age-matched control subjects without PAD. Gastrocnemius muscle strength in the leg with lower ABI among participants with PAD was 43% less than control subjects, and anterior tibial muscle strength was 31% less than that of control subjects. However, another study found no reduction in hip and knee extensor muscle strength in 31 patients with PAD and intermittent claudication as compared with 15 control subjects without PAD.[12] In contrast to these studies, our population included more participants and included participants with PAD with and without intermittent claudication.

Our study is limited by its cross-sectional design. Our data do not allow us to determine whether reduced leg strength in patients with PAD is a direct effect of lower-extremity ischemia, whether it is secondary to PAD-related inactivity and muscle atrophy, or whether it is due to an unidentified confounder. However, to our knowledge, no prior studies have described the relation between leg strength and ABI level in a large cohort of patients with and without PAD. Participants in this study were identified from noninvasive vascular laboratories and a large general medicine practice. Findings may not be generalizable to individuals in other settings. However, our recruitment methods allowed us to identify participants with a wide range of PAD severity who are regularly encountered by practicing clinicians.

In frail, older patients with heart failure and chronic obstructive pulmonary disease, resistance training of the legs improves functioning, increases aerobic capacity, and increases treadmill-walking time.[7-9] Our data suggest that further study is justified to determine whether lower-extremity resistance training improves performance on measures of lower-extremity functioning in patients with PAD. Prospective study is also needed to determine the effects of lower-extremity revascularization on leg strength.

REFERENCES

1. Casaburi R. Skeletal muscle dysfunction in chronic obstructive pulmonary disease. Med Sci Sports Exerc 2001;S662-70.
2. Bernard S, Leblanc P, Whittom F, Carrier G, Jobin J, Belleau R, et al. Peripheral muscle weakness in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med 1998;158:629-34.
3. Wuyum B, Payen JF, Levy P. Metabolism and aerobic capacity of skeletal muscle in chronic respiratory failure related to chronic obstructive pulmonary disease. Eur Respir J 1992;5:157-62.
4. Sullivan M, Green H, Cobb F. Skeletal muscle biochemistry and histology in ambulatory patients with long-term heart failure. Circulation 1990;81:518-27.
5. Massie BM, Simonini A, Sahgal P, Wells L, Dudley GA. Relation of systemic and local muscle exercise capacity to skeletal muscle characteristics in men with congestive heart failure. J Am Coll Cardiol 1996;27:140-5.
6. Mancini DM, Walter G, Reichek N, Lenkinski R, McCully KK, Mullen JL, et al. Contribution of skeletal muscle atrophy to exercise intolerance and altered muscle metabolism in heart failure. Circulation 1992;85:1364-73.
7. Frontera WR, Meredith CN, O'Reilly KP, Evans WJ. Strength conditioning in older men: Skeletal muscle hypertrophy and improved function. J Appl Physiol 1988;64:1038-44.
8. Vincent KR, Braith RW, Feldman RA, Kallas HE, Lowenthal DT. Improved cardiorespiratory endurance following 6 months of resistance exercise in elderly men and women. Arch Intern Med 2002;162:673-8.
9. Brochu M, Savage P, Lee M, Dee J, Cress ME, Poehlman ET, et al. Effects of resistance training on physical function in older disabled women with coronary heart disease. J Appl Physiol 2002;92:672-6.
10. Farinon AM, Marbini A, Gemignani F, Govoni E, Bragaglia MM, Sianesi M, et al. Skeletal muscle and peripheral nerve changes caused by chronic arterial insufficiency–significance and clinical correlations–histological, histochemical and ultrastructural study. Clin Neuropathol 1984;3:240-52.
11. Regensteiner JG, Wolfel EE, Brass EP, Carry MR, Ringel SP, Hargarten ME, et al. Chronic changes in skeletal muscle histology and function in peripheral arterial disease. Circulation 1993;87:413-21.
12. Scott-Okafor H, Silver KKC, Parker J, Almy-Albert T, Gardner AW. Lower extremity strength deficits in peripheral arterial occlusive disease patients with intermittent claudication. Angiology 2001;52:7-14.
13. McDermott MM, Greenland P, Liu K, Guralnik JM, Celic L, Criqui MH, et al. The ankle brachial index as a measure of leg functioning and physical activity in peripheral arterial disease: The Walking and Leg Circulation Study. Ann Intern Med 2002;136:873-83.
14. Olin JW. The clinical evaluation and office based detection of peripheral arterial disease. In: Hirsch AT, Olin FW, eds. An office-based approach to the diagnosis and treatment of peripheral arterial disease, I: the epidemiology and practical detection of peripheral arterial disease. Am J Med Continuing Education Series, 1998:10-17.
15. McDermott MM, Greenland P, Liu K, Guralnik JM, Criqui MH, Dolan NC, et al. Leg symptoms in peripheral arterial disease: Associated clinical characteristics and functional impairment. JAMA 2001;286:1599-606.
16. Guralnik JM, Fried LP, Simonsick EM, Kasper JD, Lafferty ME. The Women's Health and Aging Study: Health and social characteristics of older women with disability. Bethesda, MD. National Institute on Aging, 1995. NIH publication No. 95-4009, Appendix E.
17. Ettinger WH, Fried LP, Harris T, Shemanski L, Schulz R, Robbins J, et al. Self-reported causes of physical disability in older people: The Cardiovascular Health Study. J Am Geriatr Soc 1994;42:1035-44.
18. Boult C, Kane RL, Louis TA, Boult L, McCaffrey D. Chronic conditions that lead to functional limitation in the elderly. J Gerontol Med Sci 1994;49:M28-36.
19. Altman R, Alarcon G, Appelrouth D, Bloch D, Borenstein D, Brandt K, et al. The American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hip. Arthritis Rheum 1991;34:505-14.
20. Altman R, Asch E, Bloch D, Bole G, Borenstein D, Brandt K, et al. Development of criteria for the classification and reporting of osteoarthritis. Arthritis Rheum 1986;29:1039-49.
21. Birke JA, Sims DS. Plantar sensory threshold in the ulcerative foot. Lepr Rev 1986;57:261-7.
22. Olmos PR, Cataland S, O'Dorision TM, Casey CA, Smead WL, Simon SR. The Semmes-Weinstein Monofilament as a potential predictor of foot ulceration in patients with noninsulin-dependent diabetes. Am J Med Sci 1995;309:76-82.
23. Montgomery PS, Gardner AW. The clinical utility of a six-minute walk test in peripheral arterial occlusive disease patients. J Am Geriatr Soc 1998;46:706-11.
24. McDermott MM, Ohlmiller SA, Liu K, Guralnik JM, Martin GJ, Pearce WH, et al. Gait alterations associated with walking impairment in peripheral arterial disease. J Am Geriatr Soc 2001;49:747-54.
25. Guralnik JM, Ferrucci L, Simonsick E, Salive ME, Wallace RB. Lower extremity function in persons over 70 years as a predictor of subsequent disability. N Engl J Med 1995;332:556-61.
26. Guralnik JM, Simonsick EM, Ferrucci L, Glynn RJ, Berkman LF, Blazer DG, et al. A short physical performance battery assessing lower extremity function: Association with self-reported disability and prediction of mortality and nursing home admission. J Gerontol Med Sci 1994;49:M85-M94.
27. Guralnik JM, Ferrucci L, Pieper CF, Leveille SG, Markides KS, Ostir GV, et al. Lower extremity function and subsequent disability: Consistency across studies, predictive models, and value of gait speed alone compared with the short physical performance battery. J Gerontol A Biol Sci Med Sci 2000;55:M221-31.
28. Ferrucci L, Guralnik JM, Buchner D, Kasper J, Lamb SE, Simonsick EM, et al. Departures from linearity in the relationship between measures of muscular strength and physical performance: The Women's Health and Aging Study. J Gerontol A Biol Sci Med Sci 1997;52:M275-85.
29. Hiatt WR, Wolfel EE, Meier RH, Regensteiner JG. Superiority of treadmill walking exercise versus strength training for patients with peripheral arterial disease. Circulation 1994;90:1866-74.

Submitted May 12, 2003; accepted Aug 21, 2003.