Asymptomatic Peripheral Arterial Disease Is Independently Associated With Impaired Lower Extremity Functioning
The Women’s Health and Aging Study
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Background—We report the implications of asymptomatic lower extremity peripheral arterial disease (PAD) for lower extremity functioning among participants in the Women’s Health and Aging Study, an observational study of disabled women ≥65 years of age living in and around Baltimore.

Methods and Results—The ankle brachial index (ABI) and measures of upper and lower extremity functioning were measured among study participants. Of 933 women with ABI ≥1.50, 328 (35%) had an ABI <0.90, consistent with PAD. Sixty-three percent of PAD participants had no exertional leg pain. Among participants without exertional leg pain, lower ABI levels were associated with slower walking velocity, poorer standing balance score, slower time to arise 5 times consecutively from a seated position, and fewer blocks walked per week, adjusting for age, sex, race, cigarette smoking, and comorbidities. ABI was not associated independently with measures of upper extremity functioning.

Conclusions—Asymptomatic PAD is common and is independently associated with impaired lower extremity functioning. In addition to preventing cardiovascular morbidity and death, further study is warranted to identify effective interventions to improve functioning among the growing number of men and women with asymptomatic PAD.

Key Words: arteries • aging • peripheral vascular disease

Lower extremity peripheral arterial disease (PAD) affects 18% of men and women ≥55 years of age in general medical practices.1 PAD is associated with a 5- to 6-fold increased risk of cardiovascular morbidity and death.2 Although intermittent claudication has been considered the most classic manifestation of PAD, recent data show that most men and women with PAD do not have classic intermittent claudication symptoms.3,4 It is unclear whether men and women in a community-dwelling setting with PAD unaccompanied by intermittent claudication have any manifestations of PAD.

We studied the prevalence of asymptomatic PAD and its implications for lower extremity functioning among older, community-dwelling, disabled women participating in the Women’s Health and Aging Study (WHAS). The WHAS is an observational study including the one-third most disabled women ≥65 years of age living in and around Baltimore, Maryland. Our study aims were (1) to describe the prevalence of asymptomatic PAD among WHAS participants; (2) to determine whether the number of blocks walked per week influenced the prevalence of exertional leg pain in PAD participants; and (3) to determine whether asymptomatic PAD was associated with poorer lower extremity functioning.

PAD is associated with an increased burden of comorbidities that might impair all aspects of functioning. To determine whether PAD has a specific predilection for impairing lower extremity functioning, we also analyzed relations between the ankle-brachial index (ABI) and measures of upper extremity functioning.

Methods

The WHAS is a prospective observational study of disabled women sponsored by the Epidemiology, Demography, and Biometry Program of the National Institute on Aging and conducted by Johns Hopkins Medical Institutions. The study was approved by the Institutional Review Board. All participants gave informed consent. Complete data on study methods have been published.3 The sampling frame consisted of 32 538 women ≥65 years of age residing in 12 adjacent zip code regions in Baltimore City and Baltimore County. A stratified random sample of 6521 women was selected by the use of Medicare enrollment files. Strata were defined by age groups: 65 to 74 years, 75 to 84 years, and ≥85 years. Eligibility required a Mini-Mental Status Examination score of ≥18 and functional difficulty in ≥2 of these 4 areas: upper extremity, mobility, higher functioning, and basic self-care. The response rate to the screening interview was 78%. Of 1409 eligible women, 71% agreed to participate.

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Data Collection
Baseline data were collected between November 1992 and January 1995. Participants underwent a baseline interview, with assessment of health habits, medications, presence and duration of chronic diseases, and causes and extent of difficulty with daily functioning and activities. Within 2 weeks of the baseline visit, a study nurse performed a 3-hour examination in each participant’s home.

Participants who reported pain in either leg while walking were categorized as having exertional leg pain. The term “asymptomatic” refers to participants without exertional leg pain. Women unable to walk were excluded from analyses.

Subjective Measures of Lower Extremity Function
Participants were asked (a) “by yourself, that is, without help from another person or special equipment, do you have any difficulty walking up 10 steps without resting?” and (b) “by yourself, that is, without help from another person or special equipment, do you have difficulty walking one-quarter mile?” Participants were asked to report the number of times they left their home and neighborhood in the past week. They were asked to report the number of city blocks walked and the number of stairs climbed in the past week. Because results for these latter data were skewed, responses were categorized on a 0 to 3 scale. Participants who walked <1 block per week were categorized as 0, participants who walked 1 to 6 city blocks were categorized as 1, participants who walked 7 to 12 blocks were categorized as 2, and participants who walked >12 blocks were categorized as 3. Participants who climbed <1 flight of stairs were categorized as 0, participants who climbed 1 to 2 were categorized as 1, participants who climbed 3 to 4 were categorized as 2, and participants who climbed >4 were categorized as 3.

Subjective Measures of Upper Extremity Function
Participants were asked (a) “by yourself, that is, without help from another person or special equipment, do you have any difficulty using your fingers to grasp or handle?” and (b) “by yourself, that is, without help from another person or special equipment, do you have any difficulty raising your arms up over your head?”

Objective Measures of Leg Functioning
4-Meter Walk
A 4-m distance was marked out in the participant’s home, and the participant was timed performing 2 walks at her usual pace and 1 walk at her most rapid pace. Participants lined up with both feet at the starting line. Timing began with a verbal command. Correlation between the 2 usual paced walks was high ($r=0.96$). The faster of the 2 usual paced walks was used in analyses.

Chair Stands
The chair stands measure leg strength and balance. Participants were seated in a straight-backed chair with arms folded across their chest and asked to stand 5 times consecutively as quickly as possible. Time in seconds to complete 5 chair stands was recorded.

Balance Tests
Static balance was assessed with 3 increasingly difficult standing positions: (a) feet together side by side; (b) standing with the heel of one foot adjacent to the toes of the other foot; (c) one foot directly in front of the other. An ordinal 0 to 4 scoring system derived from a previous study was assigned on the basis of the participant’s ability to hold each stand for up to 10 seconds.

Summary Performance Score
The summary performance score, measured by a 0 to 12 ordinal scale, represents the participant’s performance for (a) usual paced walking velocity, (b) time for 5 chair rises, and (c) standing balance score. Participants unable to perform a task receive a zero. A 1 to 4 score is assigned to participants who complete each measure. The summary performance score represents the sum of the three 0 to 4 scores. This combined score predicts mortality, nursing home admission, and disability among older men and women.

Objective Measures of Upper Extremity Function
Grip strength was measured with the use of a JAMAR hand dynamometer (model BK-7498, Fred Sammons, Inc). Three grip strengths in each hand were recorded. The highest strength measured in the strongest hand was used in analyses.

Ankle Brachial Index
An ABI $<0.90$ is 95% sensitive and 99% specific for angiographically significant PAD. Participants with ABI 0.90 to 1.50 were classified as not having PAD. Women with ABI $>1.50$ were excluded because these participants generally have artificially elevated lower extremity arterial pressures from calcified lower extremity arterial vessels. The ABI was measured with the use of a Doppler stethoscope (Parks model 841-A). Two systolic pressures in the right brachial artery and each posterior tibial artery were measured, respectively. The highest pressure in each artery was used to calculate the ABI. The ABI was obtained by dividing the lower of the right and left posterior tibial pressures by the brachial artery pressure.

Comorbidity Measurements
Disease ascertainment algorithms were developed for 17 comorbidities by the Disease Ascertainment Working Group of the WHAS.
These algorithms combine data from the interview, medications, physical examination, medical record review, blood test results, and a primary care physician questionnaire.

Statistical Analyses
χ² tests and t tests were used to compare characteristics between women with ABI <0.90 and women with ABI ≥0.90 and ABI ≤1.50, adjusting for the age-stratified sampling described above. χ² tests for trend and ANOVA were used to compare performance on each functional measure between participants with ABI <0.50, participants with ABI 0.50 to <0.90, and participants with ABI 0.90 to ≤1.50. Multiple logistic regression and multiple linear regression analyses were performed to determine the independent relation between ABI and each functional measure, controlling for age, race, current cigarette smoking, and comorbidities. Comorbidities assessed were angina, myocardial infarction, congestive heart failure, stroke, hip osteoarthritis, knee osteoarthritis, disk disease, spinal stenosis, rheumatoid arthritis, hip fracture, diabetes mellitus, pulmonary disease, Parkinson’s disease, and cancer. These comorbidities have been shown to influence lower extremity functioning.

Results
Of 1002 WHAS participants, 933 had an ABI ≤1.50. Of these, 35% had an ABI <0.90, consistent with PAD. Table 1 shows characteristics of study participants. The prevalence of exertional leg pain was comparable between participants with and those without PAD.

Figure 1 shows the prevalence of back disease and lower extremity arthritis according to ABI and presence of exertional leg pain. Many PAD participants had arthritis or back disease, which also might cause exertional leg pain. Thus exertional leg pain may or may not have been a consequence of PAD. However, among participants without exertional leg pain, a large proportion of PAD and non-PAD participants had knee arthritis and/or hip arthritis.

Among women who walked <4 blocks per week, we did not find linear relations between ABI and the prevalence of exertional leg pain (data not shown). Among women who walked ≥4 blocks per week, those with poorest arterial perfusion (ABI ≤0.50) had the highest prevalence of exertional leg pain, whereas women with normal ABI had the lowest prevalence of exertional leg pain (Figure 2).

Of 933 participants with ABI ≤1.50, 359 (38.4%) either had exertional leg pain or did not walk. Of 574 participants without exertional leg pain, 198 (34.5%) had ABI <0.90 consistent with PAD and 48 (8.4%) had ABI <0.50 consistent with severe PAD.

Table 2 shows relations between ABI category and functioning among women without exertional leg pain. Lower ABI values were significantly associated with poorer lower extremity functioning. The ABI was not significantly associated with upper extremity functioning.

Table 3 shows regression coefficients and odds ratios relating ABI level to lower and upper extremity functioning. Adjusting for age, race, cigarette smoking, and comorbidities, lower ABI levels were associated significantly with poorer performance in all objective measures of leg functioning except usual paced walking speed. Lower ABI levels were also associated independently with walking fewer blocks per week and difficulty walking one-quarter mile. In contrast, we found no significant associations between ABI level and upper extremity functioning. Congestive heart failure was associated independently with poorer functioning on all measures except the subjective measures of upper extremity functioning and 2 of the subjective measures of lower extremity functioning (difficulty walking one-quarter mile and difficulty climbing 1 flight of stairs).
Discussion

Although only 6.7% of WHAS participants had been told by a doctor that they had PAD or intermittent claudication, 35% had an ABI \( < 0.90 \), consistent with significant PAD. This prevalence of PAD was higher than that previously reported among less-selected community-dwelling populations. In the Cardiovascular Health Study, 12% of participants \( \geq 65 \) years of age had ABI \( \leq 0.90 \), and in the Systolic Hypertension in the Elderly Program, 25.5% had PAD.\(^{15,16}\) PAD prevalence in the WHAS was less than the 88% prevalence reported in a study of 60 nursing home residents, however.\(^{17}\) Together these data suggest that disabled persons may have a higher prevalence of PAD than nondisabled persons.

Most women with PAD did not have exertional leg pain. We observed an inverse relation between ABI level and exertional leg pain prevalence among participants who walked \( \geq 4 \) blocks per week but not among participants who walked \(< 4 \) blocks. Thus exertional leg pain correlates with lower extremity arterial perfusion among participants who walk even short distances outside the home. In contrast, PAD participants who walk fewer than 4 blocks per week may include women who experience exertional leg symptoms with any walking activity and women who have restricted their walking activity to avoid exertional leg symptoms. This heterogeneity may account for the lack of association between ABI level and exertional leg pain among women who walk \(< 4 \) blocks per week.

### Table 2. Relations Between ABI and Measures of Lower and Upper Extremity Functioning Among Women \( \geq 65 \) Years of Age Without Exertional Leg Pain

<table>
<thead>
<tr>
<th>Objective measures of lower extremity function</th>
<th>ABI &lt;0.50 (n=48)</th>
<th>ABI 0.50 to &lt;0.90 (n=150)</th>
<th>ABI 0.90 to 1.50 (n=376)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Usual paced 4-m walking velocity, m/s</td>
<td>0.76 (0.33)</td>
<td>0.84 (0.40)</td>
<td>0.98 (0.42)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fastest paced 4-m walking velocity, m/s</td>
<td>0.50 (0.24)</td>
<td>0.55 (0.27)</td>
<td>0.64 (0.26)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Time for 5 chair stands, s</td>
<td>16.60 (4.73)</td>
<td>16.02 (5.33)</td>
<td>14.44 (4.09)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Standing balance score, 0–4 scale</td>
<td>1.77 (1.22)</td>
<td>1.76 (1.31)</td>
<td>2.23 (1.34)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Summary performance score, 0–12 scale</td>
<td>5.15 (2.77)</td>
<td>5.54 (2.96)</td>
<td>6.80 (3.12)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Subjective measures of upper extremity function</th>
<th>ABI &lt;0.50 (n=48)</th>
<th>ABI 0.50 to &lt;0.90 (n=150)</th>
<th>ABI 0.90 to 1.50 (n=376)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any difficulty using fingers to grasp or handle</td>
<td>37.5%</td>
<td>25.3%</td>
<td>34.3%</td>
<td>0.462</td>
</tr>
<tr>
<td>Any difficulty raising arms up over head</td>
<td>22.9%</td>
<td>24.7%</td>
<td>22.3%</td>
<td>0.708</td>
</tr>
</tbody>
</table>

Continuous and ordinal variables are reported as mean (SD). For measurement scales, the highest score represents best functioning. P values represent \( \chi^2 \) test for trend for categorical variables.
Our data showed that asymptomatic PAD is measurably and independently associated with impaired lower extremity functioning. Decreasing ABI levels were associated with progressively poorer lower extremity functioning. Our findings are consistent with previous data showing that patients with PAD have atrophic muscles, fewer muscle fibers, and demyelination of peripheral nerves compared with patients without PAD. Lower extremity arterial ischemia may directly cause muscle atrophy and muscle fiber loss in the legs because of insufficient blood flow. Alternatively, PAD-related exertional leg symptoms may lead to inactivity, resulting in lower extremity muscle atrophy. Restriction of activity in adaptation to PAD-related leg symptoms may be an important cause of functional decline and mobility loss among women with PAD.

To minimize confounding by a greater burden of cardiovascular disease and comorbidities among participants with PAD, we adjusted analyses for comorbidities. Our results showed that ABI predicts lower extremity functioning independent of comorbidities among women without exertional leg pain. Additionally, we reasoned that if PAD is associated with impaired functioning because of PAD-related comorbidities, then PAD might be associated with impairment in both lower and upper extremity functioning. Our finding that PAD was not associated with poorer upper extremity functioning suggests that PAD-associated leg functioning impairment is not due to the high burden of comorbid illness and coronary and cerebrovascular atherosclerosis commonly associated with PAD. We did not compare cardiopulmonary fitness between the lower and upper extremities. Although it would be of interest to compare, for example, the relation between ABI level and 6-minute walk versus arm ergometry, we did not have measures assessing cardiovascular fitness by exercising the upper extremities.

To our knowledge, no previous studies have assessed the relation between PAD and functioning among individuals without exertional leg pain. Vogt et al. studied 1492 women in the Study of Osteoporotic Fractures. Participants were white, with a mean age of 71 years. Eighty-two (5.5%) had ABI ≤0.90, consistent with PAD. In analyses including both symptomatic and asymptomatic study participants and adjusting for age, comorbidities, and other predictors of functioning, PAD was associated independently with walking difficulty, fewer blocks walked per day, a lower likelihood that a woman left her neighborhood once or more per week, poorer lower extremity strength, and a lower frequency of exercise or work intense enough to work up a sweat. PAD was not associated independently with walking velocity or balance. Our data build on the work by Vogt et al by demonstrating a measurable relation between ABI level and lower extremity functioning among women ≥65 years of age without exertional leg pain.

| TABLE 3. Associations Between ABI and Measures of Upper and Lower Extremity Functioning Among Women ≥65 Years of Age Without Exertional Leg Pain |
| Subjective measures of lower extremity function | Unadjusted Linear Regression Coefficient (β) or OR for ABI, per 0.40 ABI Units | Adjusted Regression Coefficient (β) or OR for ABI, per 0.40 ABI Units* | P for Multiple Regression Analyses |
| Any difficulty walking one-quarter mile (yes vs no) | OR = 0.47 † | OR = 0.53 | 0.001 |
| Any difficulty walking up 10 steps without resting (yes vs no) | OR = 0.73 † | OR = 0.89 | 0.494 |
| Score for No. of city blocks walked per week, 0–3 scale | β = 0.32 † | β = 0.18 | 0.026 |
| Score for No. of stair flights climbed per week, 0–3 scale | β = 0.21 † | β = 0.11 | 0.164 |
| No. of times per week subject leaves neighborhood (continuous scale) | β = 0.81 † | β = 0.29 | 0.153 |
| No. of times per week subject leaves home (continuous scale) | β = 1.17 † | β = 0.11 | 0.156 |
| Objective measures of lower extremity function | | | |
| Usual paced 4-m walking velocity, m/s | β = 0.09 † | β = 0.03 | 0.089 |
| Fastest paced 4-m walking velocity, m/s | β = 0.15 † | β = 0.07 | 0.016 |
| Time for 5 chair stands, s | β = −1.33 † | β = −0.91 | 0.024 |
| Standing balance score, 0–4 scale | β = 0.41 † | β = 0.21 | 0.016 |
| Summary performance score, 0–12 scale | β = 1.15 † | β = 0.55 | 0.008 |
| Subjective measures of upper extremity function | | | |
| Any difficulty using fingers to grasp (yes vs no) | OR = 1.15 | OR = 1.06 | 0.742 |
| Any difficulty raising arms up over head (yes vs no) | OR = 0.96 | OR = 0.97 | 0.853 |
| Objective measures of upper extremity function | | | |
| Grip strength, kg | β = 0.03 | β = −0.07 | 0.868 |
| Upper extremity strength, 0–3 scale | β = 0.17 † | β = 0.07 | 0.304 |

*In each analysis, the dependent variable is the functional outcome measure and ABI is an independent variable. For each measurement scale, the highest score represents the best functioning. Multivariate analyses adjusted for age, black race, cigarette smoking, angina, myocardial infarction, heart failure, knee arthritis, hip arthritis, spinal stenosis, disk disease, rheumatoid arthritis, hip fracture, diabetes mellitus, pulmonary disease, Parkinson’s disease, and cancer. Analyses with dichotomous outcomes used logistic regression, and the OR for ABI is presented. All other analyses use linear regression.

†P < 0.05.
‡P < 0.01.
functioning specifically among women without exertional leg pain. The WHAS cohort is also more racially diverse.

WHAS participants represent the one-third most disabled women in Baltimore. Further study is necessary to determine whether our findings are generalizable to nondisabled persons. However, it is conceivable that differences in functioning between individuals with versus those without PAD would be greater in a population including nondisabled participants, since the range of mobility would be greater than that reported here.

We controlled for the higher prevalence of comorbidities in PAD in 2 ways, by adjusting for comorbidities in multivariable regression analyses and by comparing both upper and lower extremity functioning between participants with and those without PAD. While both analyses supported an independent association between PAD and lower extremity functioning, it is not possible to completely overcome the potential confounding of greater comorbidity burden (both symptomatic and asymptomatic) between PAD and non-PAD participants. Importantly, congestive heart failure was associated independently with poorer performance on objective measures of both upper and lower extremity functioning. Thus heart failure appears to have a more globally deleterious effect on functioning than PAD.

Our findings show that asymptomatic PAD affects more than one third of community-dwelling disabled women. On the basis of this high prevalence of PAD, clinicians should consider ABI screening among community-dwelling, disabled older women. Clinicians should be cognizant of the independent association between PAD and cardiovascular morbidity and death.2,16 As men and women live longer with chronic diseases, clinicians will be increasingly concerned with maintenance of functioning and prevention of disease-associated disability in older persons. On the basis of our findings, in addition to preventing cardiovascular morbidity and death, future studies should focus on improving functioning and preventing disability among individuals with asymptomatic PAD.

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