Incident Physical Disability in People with Lower Extremity Peripheral Arterial Disease: The Role of Cardiovascular Disease

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OBJECTIVES: To evaluate the risk of incident physical disability and the decline in gait speed over a 6-year follow-up associated with a low ankle-arm index (AAI) in older adults.

DESIGN: Observational cohort study.

SETTING: Forsyth County, North Carolina; Sacramento County, California; Washington County, Maryland; and Allegheny County, Pennsylvania.

PARTICIPANTS: Four thousand seven hundred five older adults, 58% women and 17.6% black, participating in the Cardiovascular Health Study.

MEASUREMENTS: AAI was measured in 1992/93 (baseline). Self-reported mobility, activity of daily living (ADL), and instrumental activity of daily living (IADL) disability and gait speed were recorded at baseline and at 1-year intervals over 6 years of follow-up. Mobility disability was defined as any difficulty walking half a mile and ADL and IADL disability was defined as any difficulty with 11 specific ADL and IADL tasks. Individuals with mobility, ADL, or IADL disability at baseline were excluded from the respective incident disability analyses.

RESULTS: Lower baseline AAI values were associated with increased risk of mobility disability and ADL/IADL disability. Clinical cardiovascular disease (CVD), diabetes mellitus, and interim CVD events partially explained these associations for mobility disability and clinical CVD and diabetes mellitus partially explained these associations for ADL and IADL disability. Individuals with an AAI less than 0.9 had on average a mean decrease in gait speed of 0.02 m/s per year, or a decline of 0.12 m/s over the 6-year follow-up. Prevalent CVD partly explained this decrease but interim CVD events did not further attenuate it.

CONCLUSION: Low AAI serves as marker of future disability risk. Reduction of disability risk in patients with a low AAI should consider cardiovascular comorbidity and the prevention of additional disabling CVD events. **J Am Geriatr Soc 56:1037–1044, 2008.**

Key words: peripheral arterial disease; disability; cardiovascular disease

Peripheral arterial disease (PAD) in the lower extremities or a low ankle—arm index (AAI) is related to physical disability and decline in physical function over time.[1–6] Recently, baseline PAD and the nature of leg symptoms was shown to predict decline in physical function as measured using the 6-minute walk test and gait speed over a 2-year follow-up.[1] Also, in a sample of older women who were disabled at baseline, the presence of severe PAD at baseline (defined as an AAI < 0.60) resulted in a greater risk for developing severe disability (the inability to walk one-quarter of a mile) over a 3-year period than in women without PAD.[3] Both studies examined the association between PAD and function or disability in a sample of people with clinically diagnosed PAD. It is unknown whether nondisabled, community-dwelling older adults with a low AAI, an indicator of PAD, would be at risk for incident disability.

The mechanisms underlying the association between PAD and physical disability are not completely understood. The local effects of PAD have been shown to contribute to physical disability, including claudicating leg pain, muscle weakness, and impaired peripheral nerve function.[4,7,8] Existing cardiovascular disease (CVD) and incident cardiovascular events may also contribute to physical disability.

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Individuals with PAD are at high risk for cardiovascular events,[9,10] and individuals with CVD are at high risk for physical disability.[11] The goal of this study was to evaluate the risk of incident physical disability and the decline in gait speed associated with the presence and severity of a low AAI, a marker of PAD, in a population of community-dwelling older adults and to explore the potential role that cardiovascular comorbidity and interim CVD events might play in these associations.

METHODS

The Cardiovascular Health Study (CHS) included 5,888 adults aged 65 and older recruited from a random sample of Medicare enrollees. This included 5,201 examined between June 1989 and June 1990 and an additional 687 African-American participants recruited in 1992/93 who underwent the same baseline examination. Details of the CHS design and recruitment have been published elsewhere.[12,13] Briefly, participants were recruited from a random sample of the Health Care Finance Administration (now called Centers for Medicare and Medicaid Services) Medicare eligibility lists in four U.S. communities: Forsyth County, North Carolina; Sacramento County, California; Washington County, Maryland; and Allegheny County, Pennsylvania. Subjects were excluded if they were living in an institution, were wheelchair-bound in the home, or were currently under treatment for cancer.

Data collected in 1992/93 were considered baseline for these analyses. Of the original 5,888 participants, 4,988 were examined in 1992/93. Of the 4,988 participants, 283 were excluded from the analyses because AAI was not measured (n = 238), the participant had lower extremity revascularization (n = 7) or angioplasty (n = 2), or the AAI was greater than 1.5 (n = 36), leaving 4,705 potential participants. Of the 4,705 participants, 3,048 were included in the incident mobility disability analyses (excluded 1,597 with disability at baseline and 60 with no response postbaseline regarding disability), 2,555 were included in the incident activity of daily living and instrumental activity of daily living (ADL/IADL) disability analyses (excluded 2,094 with ADL/IADL disability at baseline and 56 with no response postbaseline regarding disability), and 4,344 were included in the change in gait speed analyses (excluded 75 with no gait speed measure at baseline and 286 with no gait speed measure postbaseline).

Measures

Ankle Arm Index

The AAI is the ratio of the ankle to arm systolic blood pressure; it is low when there is atherosclerotic obstruction between the heart and the leg. In adults without atherosclerotic obstruction, the ratio of the ankle to arm systolic blood pressure is greater than 1.0. A participant was classified as having a low AAI if either leg had an ankle-to-arm systolic blood pressure ratio of less than 0.90. an AAI less than 0.9 is 95% sensitive and 99% specific for angiographically significant PAD.[14]

Trained technicians measured the AAI in 1992/93 according to a standard protocol, previously described.[15] The systolic pressures of the brachial and posterior tibial arteries were measured using a Doppler stethoscope (8 MHz, Parks Electronics, Aloha, OR). Measurements have been shown to be reliable between observers, to be stable over time, and to be highly correlated between the right and left legs.[15]

Performance-Based and Self-Report Measures of Physical Disability

Trained technicians collected performance-based and self-report measures of physical disability during annual visits. The time to walk 15 feet at the individual's usual pace (gait speed) was used as the performance-based measure.[13] Self-report questionnaires were used to assess any difficulty with ADL (bathing, dressing, eating, using the toilet, walking around the home, getting out of a bed or chair), IADL (heavy housework, light housework, shopping for personal items, preparing own meals, paying bills, managing own money), and walking half a mile.[16–18]

The endpoints were ADL/IADL disability, mobility disability, and decline in gait speed. Each type of disability was examined as a separate outcome. Participants were classified as having ADL/IADL disability if they reported difficulty in at least one of the ADL/IADL. Mobility disability was defined as reporting difficulty in walking half a mile.

Cardiovascular Disease

CVDs, which may explain the pathway from an AAI less than 0.9 to functional decline, were considered categorically as a potential mediator. Prevalent CVD was defined as the presence of myocardial infarction (MI), angina pectoris, stroke, congestive heart failure (CHF), PAD (defined as self-report of a physician diagnosis of PAD or intermittent claudication (IC) or as a history of lower extremity arterial bypass surgery, angioplasty, or amputation for arterial obstruction), transient ischemic attack, angioplasty, coronary bypass surgery, or atrial fibrillation at baseline. Incident CVD was defined as a new onset of MI, angina pectoris, stroke, congestive heart failure, hospitalized PAD, or transient ischemic attack between the baseline and follow-up clinic visits. The presence of the conditions was ascertained at each follow-up (1994/95, 1995/96, and 1996/97) using self-report with validation by medication records, electrocardiogram, and medical records and review and adjudication by a central committee of study physicians.[19]

Confounding Factors

While examining the association between AAI and functional decline, the following potentially confounding factors were accounted for: demographics (age, sex, race, and education), positive Rose questionnaire for IC, other non-CVD chronic conditions (diabetes mellitus, arthritis, and depression), and behavioral factors (smoking history and body mass index), which have been previously shown to be related to physical disability.[18,20–23]

The prevalence of IC was assessed using a modified Rose questionnaire and analyzed separately from baseline self-report of PAD.[24] Diabetes mellitus was defined according to the American Diabetes Association guidelines of 1997; diabetes mellitus was considered present if the participant used insulin or oral hypoglycemics or if glucose level exceeded 126 mg/dL (7.0 mmol/L).[25] Arthritis was assessed according to self-report. Depression symptoms were assessed using the modified Center for Epidemiologic Studies Depression (CES-D) scale of 0 to 30.[26] In this analysis, a participant with a score of 10 or higher was considered to have depression.[27] Smoking history was assessed according to self-report of current or past use, and the number of pack-years was calculated as the analytical variable for exposure. Relative body weight was assessed using body mass index, calculated as weight in kilograms over height in meters squared (kg/m^2).

Statistical Analysis

Baseline characteristics for individuals with and without an AAI less than 0.9 and stratifying according to sex were compared using *t*-tests for continuous variables and chi-square analyses for categorical variables. Severity was then considered by examining four groups based on AAI values ($\geq$1.0, 0.9–<1.0, 0.8–<0.9, and <0.8).

Cox proportional hazards regression models were used to test whether subjects with a low AAI experienced incident disability earlier than those with a normal AAI, with the outcome variable defined as the first onset of incident disability in those free of disability at baseline, assessed according to self-report at 1-year intervals over approximately 6 years of follow-up. Interim CVD events was used as an explanatory time-dependent variable and was indicated by the first interim stroke, CHF, or the first occurrence of any CVD event after baseline, regardless of whether there had been an event before the onset of disability risk. Marginal models with robust standard error estimates were used to assess the association between the four-category AAI variable (independent variable) and changes over time in mean gait speed assessed annually over the 6-year follow-up (dependent variables). Each confounding factor was entered into the regression model and the marginal model, together with AAI, to assess the degree to which each confounder attenuated the relationship between AAI and mobility disability, ADL/IADL disability, and change in gait speed.

RESULTS

PAD, defined as an AAI less than 0.9, was found in 11.8% of women and 15.8% of men (Table 1). Men and women with an AAI less than 0.9 were older, had a lower BMI, and smoked more than those with an AAI of 0.9 or greater.

Table 1. Baseline (1992/93) Characteristics According to Sex and Ankle Arm Index (AAI) Less Than 0.9

	Men			Women		
Characteristic	AAI <0.9 (n = 309)	AAI ≥0.9 (n = 1,645)	*P*-Value*	AAI <0.9 (n = 325)	AAI ≥0.9 (n = 2,426)	*P*-Value*
Demographic						
Age, mean ± SD	77.4 (6.1)	74.8 (5.3)	<.001	77.4 (6.2)	74.3 (5.0)	<.001
Black, n (%)	72 (23.3)	233 (14.2)	<.001	104 (32.0)	417 (17.2)	<.001
>High school education, n (%)	126 (40.8)	863 (52.6)	<.001	117 (36.0)	1,043 (43.1)	.02
Behavioral						
Body mass index, kg/m^2, mean ± SD	25.9 (3.8)	26.6 (3.8)	.001	26.4 (5.4)	27.1 (5.2)	.04
Alcohol (drinks/wk), mean ± SD	2.7 (7.5)	3.2 (6.6)	.35	1.4 (4.3)	1.3 (3.8)	.80
Smoking (pack-years), mean ± SD	33.3 (34.1)	23.3 (29.2)	<.001	17.7 (24.3)	11.3 (2.6)	<.001
Health						
CVD, n (%)	185 (59.9)	521 (31.7)	<.001	146 (44.9)	485 (20.0)	<.001
Myocardial infarction, n (%)	79 (25.6)	161 (9.8)	<.001	36 (11.1)	113 (4.7)	<.001
Angina pectoris, n (%)	88 (28.5)	274 (16.7)	<.001	75 (23.1)	269 (11.1)	<.001
Peripheral arterial disease, n (%)†	45 (14.6)	17 (1.0)	<.001	18 (5.5)	9 (0.4)	<.001
Congestive heart failure, n (%)	23 (7.4)	49 (3.0)	<.001	21 (6.5)	56 (2.3)	<.001
Stroke, n (%)	28 (9.0)	67 (4.1)	<.001	27 (8.3)	42 (1.7)	<.001
Transient ischemic attack, n (%)	16 (5.2)	51 (3.1)	.07	16 (4.9)	38 (1.6)	<.001
Intermittent claudication, n (%)	20 (6.6)	11 (0.7)	<.001	25 (7.9)	17 (0.7)	<.001
Arthritis, n (%)	126 (41.3)	694 (42.7)	.66	192 (6.0)	1,369 (57.0)	.30
Diabetes mellitus, n (%)	79 (27.1)	270 (17.0)	<.001	74 (24.5)	284 (12.3)	<.001
Center for Epidemiologic Studies Depression Scale score >10, n (%)	5.5 (4.5)	4.5 (4.3)	<.001	6.9 (5.6)	5.8 (5.1)	<.001
Depression, n (%)	61 (19.9)	211 (12.9)	.001	80 (24.8)	476 (19.7)	.03
Interim CVD, n (%)	224 (72.5)	757 (46.0)	<.001	187 (57.5)	928 (38.3)	<.001
Gait speed, m/s, mean ± SD	0.84 (0.23)	0.95 (0.23)	<.001	0.73 (0.24)	0.88 (0.24)	<.001
Self-reported difficulty, n(%)						
ADL	35 (11.3)	115 (7.0)	.009	73 (22.5)	278 (11.5)	<.001
IADL	106 (34.3)	276 (16.8)	<.001	136 (41.9)	683 (28.2)	<.001
ADL or IADL	113 (36.6)	303 (18.4)	<.001	144 (44.3)	736 (30.3)	<.001
Mobility	114 (37.3)	221 (13.6)	<.001	152 (48.6)	551 (23.1)	<.001

* Two-sample *t*-test for unequal variances for continuous measures and chi-square tests for categorical variables.

† Self-report of a physician diagnosis of peripheral arterial disease or intermittent claudication or a history of lower extremity arterial bypass surgery, angioplasty, or amputation for arterial obstruction.

SD = standard deviation; CVD = cardiovascular disease; ADL = activity of daily living; IADL = instrumental activity of daily living.

Table 2. Attenuation of the Relationship Between Ankle Arm Index (AAI) and Mobility Disability*

Risk Factors	Incidence Rate (per 100 Person-Years)	Model 1†	Model 2‡	Model 3§
		Hazard Ratio (95% Confidence Interval)		
AAI				
≥1.0	7.0	Reference	Reference	Reference
0.9–<1.0	10.3	1.54 (1.27–1.86)	1.25 (1.00–1.54)	1.20 (0.97–1.49)
0.8–<0.9	11.3	1.66 (1.27–2.17)	1.27 (0.95–1.70)	1.31 (0.98–1.75)
<0.8	15.7	2.45 (1.95–3.07)	1.55 (1.19–2.01)	1.43 (1.10–1.85)
Age	—	—	1.08 (1.06–1.09)	1.07 (1.06–1.09)
Male	—	—	0.77 (0.67–0.89)	0.74 (0.64–0.86)
Black	—	—	1.26 (1.06–1.49)	1.26 (1.06–1.50)
>High school education	—	—	0.97 (0.85–1.10)	0.95 (0.84–1.09)
IC according to Rose Questionnaire	—	—	1.21 (0.61–2.42)	1.29 (0.65–2.56)
Prevalent CVD	—	—	1.41 (1.22–1.64)	1.27 (1.09–1.47)
Arthritis	—	—	1.17 (1.03–1.33)	1.16 (1.02–1.32)
Diabetes mellitus status				
Impaired fasting glucose	—	—	1.01 (0.82–1.26)	1.01 (0.81–1.25)
Diabetes mellitus	—	—	1.62 (1.36–1.93)	1.54 (1.29–1.83)
Depression	—	—	1.05 (1.03–1.06)	1.05 (1.03–1.06)
Pack-years	—	—	1.00 (1.00–1.01)	1.00 (1.00–1.00)
Smoking status				
Quit >1 year before	—	—	1.13 (0.96–1.34)	1.16 (0.98–1.36)
Quit <1 year before	—	—	1.98 (1.43–2.73)	2.02 (1.46–2.79)
Current	—	—	1.32 (0.99–1.77)	1.37 (1.02–1.83)
Alcohol, drinks/week	—	—	0.99 (0.98–1.01)	1.00 (0.98–1.01)
BMI, kg/m^2	—	—	1.06 (1.04–1.07)	1.05 (1.04–1.07)
Interim CVD	—	—	—	1.99 (1.70–2.34)
Likelihood-ratio test‖				$P<.001$

* Any reported difficulty walking half a mile.
† Unadjusted.
‡ Adjusted for age, sex, race, education, intermittent claudication (IC) according to Rose Questionnaire, prevalence of cardiovascular disease (CVD), arthritis status, diabetes mellitus status, pack-years of smoking, smoking status, alcohol use, and body mass index (BMI).
§ Adjusted for all factors in Model 2 plus interim CVD.
‖ Likelihood-ratio test comparing Model 3 with Model 2.

Subjects with an AAI less than 0.9 were more likely to be black and to have prevalent CVD, arthritis, diabetes mellitus, and depression. Most of the prevalent CVD was due to coexisting angina pectoris or history of MI in subjects with an AAI less than 0.9. Men and women with an AAI less than 0.9 performed poorer on measures of physical function at baseline and were more likely to report prevalent ADL/IADL and walking difficulty than individuals with an AAI of 0.9 or greater (Table 1).

Table 2 shows the association between severity of PAD and incident mobility disability. Of the 3,048 individuals included in the analyses of incident mobility disability, 149 had an AAI less than 0.8, 120 had an AAI between 0.8 and less than 0.9, 269 had an AAI between 0.9 and less than 1.0 and 2,510 had an AAI of 1.0 or greater. In the unadjusted models, there was a dose–response relationship, with the risk of mobility disability increasing as AAI decreased (also see Figure 1). After adjusting for demographics, IC, prevalent CVD, and other risk factors, the association between an AAI less than 0.9 and incident mobility disability was attenuated, especially for the lowest AAI group (<0.8). After adjustment, individuals with an AAI less than 0.8 were 1.55 times as likely to have mobility disability as individuals with an AAI of 1.0 or greater. The high prevalence of concurrent clinical CVD and diabetes mellitus was the major factor attenuating the association; when adjusting for concurrent clinical CVD and diabetes mellitus, the univariate change in the hazard ratio (HR) was 0.30 ($P<.001$) and 0.16 ($P<.001$), respectively. Interim CVD events further attenuated this association (HR for AAI<0.8 fell from 1.55 to 1.43). Interim CVD events were significantly related to mobility disability (HR = 1.99, 95% confidence interval (CI) = 1.70–2.34). Interim non-CVD hospitalizations did not further attenuate the association between AAI and mobility disability (data not shown).

In unadjusted models, AAI was also related to ADL/IADL disability (Figure 1 and Table 3). Of the 2,555 individuals included in the analyses of incident ADL/IADL disability, 161 had an AAI less than 0.8, 99 had an AAI between 0.8 and less than 0.9, 232 had an AAI between 0.9 and less than 1.0, and 2,063 had an AAI of 1.0 or greater. Once again, there was a clear dose–response relationship between severity and risk of ADL/IADL disability, although in the adjusted models (Table 3, Models 2 and 3), the dose–response relationship was no longer apparent. In the adjusted model (Table 3, Model 2), individuals with an AAI

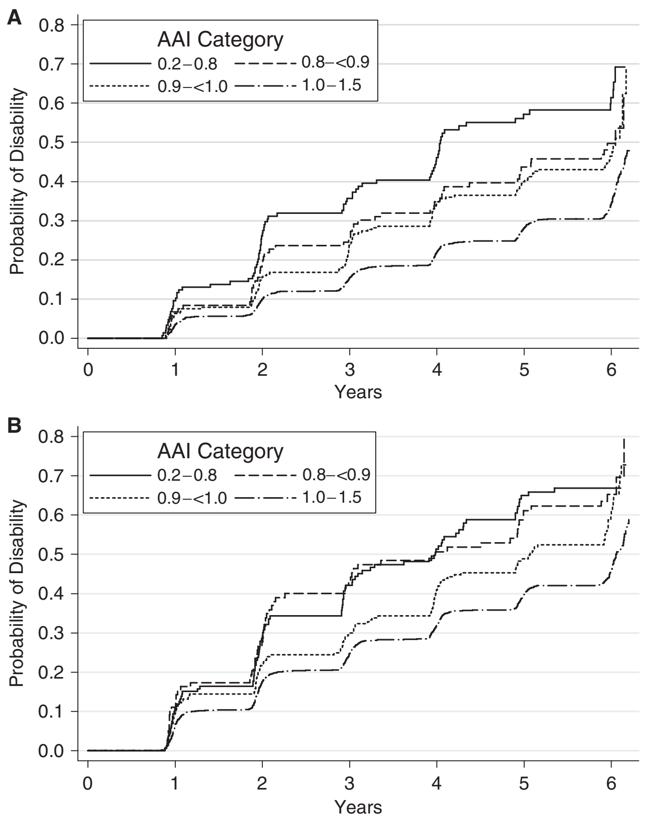

Figure 1. (A) Kaplan-Meier function of mobility disability* according to ankle arm index (AAI) category, unadjusted. (B) Kaplan-Meier function of activity of daily living (ADL)/instrumental activity of daily living (IADL) disability according to AAI category, unadjusted. $P<.005$, log-rank test for mobility disability and ADL/IADL disability. *Mobility disability defined as any reported difficulty walking half a mile.

between 0.8 and 0.9 were 1.33 times as likely to develop ADL/IADL disability as individuals with an AAI of 1.0 or greater. Again, prevalent CVD and diabetes mellitus were the major factors that attenuated the associations, with a univariate change in the HR of 0.16 ($P<.001$) for prevalent CVD and a univariate change in HR of 0.09 ($P<.001$) for diabetes mellitus. Although interim CVD events were related to ADL/IADL disability (HR = 1.89, 95% CI = 1.61–2.24), the interim CVD events did not explain the association between an AAI less than 0.9 and ADL/IADL disability (HR for AAI 0.8–0.9 went from 1.33 to 1.36; Table 3, Model 3). Interim non-CVD hospitalizations did not further attenuate the association between AAI and ADL/IADL disability (data not shown).

The associations between AAI and incident mobility or ADL/IADL disability were also examined in models stratified according to sex. The results were similar; therefore the models were not stratified according to sex; instead sex was included as a covariate in the models. Interactions between AAI and sex were also not significant.

Table 4 shows the association between baseline AAI and decline in gait speed. The mean length of follow-up was 5.0 years. Of the 4,344 individuals included in the analyses of decline in gait speed, 356 had an AAI less than 0.8, 190 had an AAI between 0.8 and less than 0.9, 439 had an AAI between 0.9 and less than 1.0 and 3,359 had an AAI of 1.0 or greater. After adjusting for baseline performance, demographics, prevalent and incident CVD, and other risk factors, individuals with an AAI less than 0.9 had a greater annual decline in gait speed than individuals with an AAI of 1.0 or greater. On average, individuals with an AAI less than 0.9 had a mean decrease in gait speed of 0.02 m/s per year, or a decline of 0.12 m/s over the 6-year follow-up. Prevalent CVD partly explained the association between AAI and change in gait speed, which interim CVD events and interim non-CVD hospitalizations did not further attenuate (data not shown).

DISCUSSION

In a large cohort of community-based older adults, the presence of an AAI less than 0.9 was associated with a higher risk of incident mobility (difficulty walking half a mile) and ADL/IADL disability (any difficulty with 11 specific ADLs or IADLs) over a 6-year follow-up. Individuals with an AAI less than 0.8 had a 43% greater risk of developing mobility disability than those with an AAI of 1.0 or greater, even after adjusting for a number of confounding factors. In previous studies that have examined the association between PAD and worsening mobility disability, the greater risk was apparent only in women with the most severe PAD (AAI < 0.6).[5] The current study found a dose–response relationship with more-impaired AAI that was apparent at levels of AAI just below the normal range of less than 1.0 and progressed with further decrements related to higher risks for mobility disability. This was partly explained by, but independent of, other comorbid CVD and diabetes mellitus. These factors explained the higher risk for ADL/IADL disability.

The finding that individuals with an AAI less than 0.9 had an average decline in gait speed of 0.02 m/s per year is consistent with or even slightly greater than the 0.02 to 0.03 m/s over a 2-year follow-up reported previously.[1] A decline of 0.02 m/s per year over the 6 years of follow-up translates to a average change of 0.12 m/s. This degree of decline has been shown to be a significant and meaningful decline in gait speed in that it is perceived as disabling change in function.[28]

Individuals with an AAI less than 0.9 are at high risk for new CVD events such as stroke, heart failure, and MI.[9,10] In the present study, a large part of the association between an AAI less than 0.9 and disability was related to other cardiovascular comorbidity and diabetes mellitus. New CVD events explained some but not all of the association between AAI and incident mobility disability. It is likely that cardiovascular comorbidity and new cardiovascular events affect cardiovascular endurance, which plays a significant role in walking extended distances and a much lesser role in completing ADL and IADL. Prevalent baseline CVD played a greater role in the attenuation of the association between AAI and change in gait speed than interim CVD events. Survival bias might explain this in part, in that those who completed the performance based tasks were a smaller survival subgroup.

These findings make it clear that cardiovascular comorbidity largely, but not completely, explains the effect of an AAI less than 0.9 on disability. Thus, a critical way to prevent mobility disability in individuals with an AAI less than 0.9 would be to manage overall cardiovascular risk and to prevent new CVD events such as stroke, CHF, angina pectoris, and MI. Cross-sectional and longitudinal studies

Table 3. Attenuation of the Relationship Between Ankle Arm Index (AAI) and Activity of Daily Living and Instrumental Activity of Daily Living Disability

	Incidence Rate (per 100 Person-Years)	Model 1*	Model 2†	Model 3‡
		Hazard Ratio (95% Confidence Interval)		
AAI				
≥1.0	10.1	Reference	Reference	Reference
0.9–<1.0	13.9	1.42 (1.18–1.71)	1.13 (0.92–1.39)	1.09 (0.89–1.34)
0.8–<0.9	17.6	1.79 (1.39–2.31)	1.33 (1.01–1.76)	1.36 (1.03–1.79)
<0.8	17.4	1.84 (1.49–2.28)	1.17 (0.91–1.51)	1.11 (0.86–1.4)
Age	—	—	1.07 (1.06–1.09)	1.07 (1.06–1.09)
Male	—	—	0.67 (0.58–0.76)	0.65 (0.57–0.74)
Black	—	—	1.35 (1.15–1.57)	1.34 (1.14–1.57)
>High school education	—	—	1.24 (1.09–1.40)	1.22 (1.08–1.39)
IC according to Rose Questionnaire	—	—	1.21 (0.73–2.01)	1.11 (0.97–1.85)
Prevalent CVD	—	—	1.49 (1.29–1.72)	1.39 (1.20–1.61)
Arthritis	—	—	1.34 (1.18–1.51)	1.35 (1.19–1.52)
Diabetes mellitus status				
Impaired fasting glucose	—	—	0.98 (0.81–1.20)	0.97 (0.80–1.19)
Diabetes mellitus	—	—	1.43 (1.20–1.70)	1.36 (1.14–1.62)
Depression	—	—	1.04 (1.03–1.06)	1.04 (1.03–1.06)
Pack-years	—	—	1.00 (1.00–1.00)	1.00 (1.00–1.00)
Smoking status				
Quit >1 year before	—	—	1.17 (1.00–1.37)	1.18 (1.01–1.38)
Quit <1 year before	—	—	1.42 (1.03–1.96)	1.46 (1.06–2.01)
Current	—	—	1.29 (0.98–1.70)	1.32 (1.00–1.74)
Alcohol, drinks/week	—	—	1.00 (0.99–1.01)	1.00 (0.99–1.02)
BMI, kg/m^2	—	—	1.03 (1.01–1.04)	1.03 (1.01–1.04)
Interim CVD	—	—	—	1.89 (1.61–2.24)
Likelihood-ratio test				$P<.001$

* Unadjusted.
† Adjusted for age, sex, race, education, intermittent claudication (IC) according to Rose Questionnaire, prevalence of cardiovascular disease (CVD), arthritis status, diabetes mellitus status, pack-years of smoking, smoking status, alcohol use, and body mass index (BMI).
‡ Adjusted for all factors in Model 2 plus interim CVD.

have shown that individuals with PAD who take statins have less physical disability and functional decline than those who do not.[2,29] Diabetes mellitus was also a major factor explaining part of the effect of an AAI less than 0.9 and was independently related to disability; this is another important target to reduce risk of disability in older adults in the community with PAD. More effort is needed to encourage clinicians to recognize that a low AAI is often asymptomatic but represents substantial systemic atherosclerosis.[30]

Table 4. Gait Speed (15-Foot Walk) Change over 6 Years of Follow-Up in Relation to Ankle Arm Index (AAI)

	Mean Performance		Coefficients Reflecting Change in the Slope (95% Confidence Interval)	
AAI	Baseline (m/s)	Mean Change (m/s per Year)	Model A*	Model B†
≥1.0	0.92	−0.009	Reference	Reference
0.9–<1.0	0.83	−0.009	0.0004 (−0.003–0.003)	0.0004 (−0.003–0.003)
0.8–<0.9	0.80	−0.019	−0.008 (−0.013 to −0.003)‡	−0.008 (−0.013 to −0.003)‡
<0.8	0.77	−0.018	−0.008 (−0.012 to −0.005)‡*	−0.008 (−0.012 to −0.005)‡
Test for trend			$P<.001$	$P<.001$

Mean change, adjusting for baseline performance.
* Adjusted for baseline performance, demographics (age, sex, race, and education), intermittent claudication (IC), prevalent cardiovascular disease (CVD), and other risk factors (arthritis, diabetes mellitus, depression, smoking history, and body mass index).
† Adjusted for variables in Model A plus interim CVD (myocardial infarction, stroke, congestive heart failure, angina pectoris, transient ischemic attack, or IC).
‡ A significant difference in the change compared with reference category, at the .05 level.

In spite of accounting for prevalent and incident CVD in these analyses, a low AAI remained independently predictive of disability. This supports other studies in patients with PAD, showing that they have significant local disabling effects of disease in muscle strength and nerve function as well.[7] These direct effects have been shown to be best managed using exercise. Exercise interventions to improve muscle strength may be appropriate to prevent functional decline in people with PAD. In an observational cohort study, individuals with PAD who walked for exercise three or more times per week had a smaller decline in physical performance than those who walked less often.[31] Several investigators have shown the benefits of an exercise program for individuals with symptomatic PAD,[32–34] although the effectiveness of an exercise program to improve physical function and prevent incident mobility disability in individuals with predominantly subclinical PAD such as those examined here has not been established. A walking program may prevent functional decline by improving circulation, cardiovascular endurance, and muscle strength and may affect overall cardiovascular risk as well.

While examining these findings, a few limitations must be considered. First, incident mobility disability was assessed according to self-report. Older adults who are starting to decline in physical function may fail to report that they are having difficulty with functional tasks, thus possibly underestimating the incidence of physical disability.[35] The performance-based outcome of gait speed may have been an underestimate of the true change in that this measure may not have been completed in the frailest of subjects. Also, the majority of the individuals with PAD in this study had mild PAD; thus care must be taken when generalizing the results to individuals with more-severe PAD. Strengths include the large sample size of individuals with predominantly subclinical or undiagnosed PAD and careful ascertainment of cardiovascular comorbidity and subsequent cardiovascular events.

A low AAI is not only a strong marker of cardiovascular and mortality risk, but also serves as a marker of future disability risk. Reduction of disability risk in individuals with a low AAI requires attention to the high prevalence of cardiovascular comorbidity and the prevention of additional disabling CVD events. Individuals with undiagnosed PAD can easily be identified using an AAI test, which can serve as a useful factor to consider when targeting programs for older adults at high risk for physical disability.

CONCLUSION

Low AAI serves as a marker of future disability risk. If the goal is reduction of disability risk in patients with a low AAI, healthcare providers should consider cardiovascular comorbidity and the prevention of additional disabling CVD events.

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REFERENCES

1. McDermott MM, Liu K, Greenland P et al. Functional decline in peripheral arterial disease: Associations with the ankle brachial index and leg symptoms. JAMA 2004;292:453–461.
2. McDermott MM, Guralnik JM, Greenland P et al. Statin use and leg functioning in patients with and without lower-extremity peripheral arterial disease. Circulation 2003;107:757–761.
3. McDermott MM, Ferrucci L, Simonsick EM et al. The ankle brachial index and change in lower extremity functioning over time: The Women's Health and Aging Study. J Am Geriatr Soc 2002;50:238–246.
4. McDermott MM, Liu K, Guralnik JM et al. The ankle brachial index independently predicts walking velocity and walking endurance in peripheral arterial disease. J Am Geriatr Soc 1998;46:1355–1362.
5. McDermott MM, Fried L, Simonsick EM et al. Asymptomatic peripheral arterial disease is independently associated with impaired lower extremity functioning: The Women's Health and Aging Study. Circulation 2000;101:1007–1012.
6. Vogt MT, Cauley JA, Kuller LH et al. Functional status and mobility among elderly women with lower extremity arterial disease: The Study of Osteoporotic Fractures. J Am Geriatr Soc 1994;42:923–929.
7. McDermott MM, Guralnik JM, Albay M et al. Impairments of muscles and nerves associated with peripheral arterial disease and their relationship with lower extremity functioning: The InCHIANTI Study. J Am Geriatr Soc 2004;52:405–410.
8. McDermott MM, Mehta S, Greenland P. Exertional leg symptoms other than intermittent cluadication are common in peripheral arterial disease. Arch Intern Med 1999;159:387–392.
9. Newman AB, Shemanski L, Manolio TA et al. Ankle-arm index as a predictor of cardiovascular disease and mortality in the Cardiovascular Health Study. Arterioscler Thromb Vasc Biol 1999;19:538–545.
10. Resnick HE, Lindsay RS, McDermott MM et al. Relationship of high and low ankle brachial index to all-cause and cardiovacular disease mortality: The Strong Heart Study. Circulation 2004;109:733–739.
11. Pinsky JL, Jette AM, Branch LG et al. The Framingham Disability Study: Relationship of various coronary heart disease manifestations to disability in older persons living in the community. Am J Public Health 1990;80:1363–1368.
12. Tell GS, Fried LP, Hermanson B et al. Recruitment of adults 65 years and older as participants in the Cardiovascular Health Study. Ann Epidemiol 1993;3:358–366.
13. Fried LP, Borhani NO, Enright P et al. The Cardiovascular Health Study: Design and rationale. Ann Epidemiol 1991;1:263–276.
14. Fowkes FGR. The measurement of artherosclerotic peripheral arterial disease in epidemiological surveys. Int J Epidemiol 1988;17:248–254.
15. Newman AB, Siscovick DA, Manolio TA et al. Ankle-arm index as a marker of atherosclerosis in the Cardiovascular Health Study. Circulation 1993;88:837–845.

16. Fitti JE, Kovar MG. National Health Interview Survey. Vital Health Stat 1987;21:1–115. Publication DHHS (PHS) 87–1323.
17. Katz S. Assessing self maintenance: Activities of daily living, mobility, and instrumental activities of daily living. J Am Geriatr Soc 1983;31:721–727.
18. Ettinger WH, Fried LP, Harris T et al. Self-reported causes of physical disability in older people: The Cardiovascular Health Study. J Am Geriatr Soc 1994;42: 1035–1044.
19. Mittelmark MB, Psaty BM, Rautaharju PM et al. Prevalence of cardiovascular diseases among older adults. The Cardiovascular Health Study. Am J Epidemiol 1993;137:311–317.
20. Seeman TE, Charpentier PA, Berkman LF et al. Predicting changes in physical performance in a high-functioning elderly cohort: MacArthur Studies of Successful Aging. J Gerontol: Med Sci 1994;49:M97–M108.
21. Brach JS, VanSwearingen J.M., Fitzgerald S et al. The relationship between physical activity, obesity, and physical function in community-dwelling older women. Prev Med 2004;39:74–80.
22. Launer LJ, Harris T, Rumpel C et al. Body mass index, weight change, and risk of mobility disability in middle-aged and older women: The epidemiologic follow-up study of NHANES I. JAMA 1994;271:1093–1098.
23. Jensen GL, Friedmann JM. Obesity is associated with functional decline in community-dwelling rural older persons. J Am Geriatr Soc 2002;50:918–923.
24. Rose G, McCartney P, Reid DD. Self-administration of a questionnaire on chest pain and intermittent claudication. Br J Prev Soc Med 1977;31:42–48.
25. Wahl PW, Savage PJ, Psaty BM et al. Diabetes in older adults: Comparisons of 1997 American Diabetes Association classification of diabetes mellitus with the 1985 WHO classification. Lancet 1998;352:1012–1015.
26. Radloff LS. The CES-D Scale: A self-report depression scale for research in the general population. Appl Psychol Meas 1977;1:385–401.
27. Andresen EM, Malmgren JA, Carter WB et al. Screening for depression in well older adults: Evaluation of a short form of the CES-D (Center for Epidemiologic Studies Depression Scale). Am J Prev Med 1994;10:77–84.
28. Perera S, Studenski S, Chandler JM et al. Magnitude and patterns of decline in health and function in 1 year affect subsequent 5-year survival. J Gerontol Med Sci 2005;60A:894–900.
29. Giri J, McDermott MM, Greenland P et al. Statin use and functional decline in patients with and without peripheral arterial disease. J Am Coll Cardiol 2006;47:998–1004.
30. Hirsch AT, Criqui MH, Treat-Jacobson D et al. Peripheral arterial disease detection, awareness, and treatment in primary care. JAMA 2001;286:1317–1324.
31. McDermott MM, Liu K, Ferrucci L et al. Physical performance in peripheral arterial disease: A slower rate of decline in patients who walk more. Ann Intern Med 2006;144:10–20.
32. Gardner AW, Katzel LI, Sorkin JD et al. Improved functional outcomes following exercise rehabilitation in patients with intermittent claudication. J Gerontol Med Sci 2000;55A:M570–M577.
33. Gardner AW, Katzel LI, Sorkin JD et al. Exercise rehabilitation improves functional outcomes and peripheral circulation in patients with intermittent claudication: A randomized controlled trial. J Am Geriatr Soc 2001;49:755–762.
34. Hiatt WR, Regensteiner JG, Hargarten ME et al. Benefit of exercise conditioning for patients with peripheral arterial disease. Circulation 1990;81:602–609.
35. Brach JS, VanSwearingen JM, Newman AB et al. Identifying early decline of physical function in community-dwelling older adults: Performance-based and self-report measures. Phys Ther 2002;82:320–328.