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

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Abstract

Objective—To evaluate the risk of incident physical disability and the decline in gait speed over a six 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; or Allegheny County, Pennsylvania.

Participants—4705 older adults, 58% women and 17.6% black, participating in the Cardiovascular Health Study were included.

Measurements—The AAI was measured in 1992–93 (baseline). Self-reported mobility disability, activities of daily living (ADL) and instrumental activities 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 ½ mile and ADL/IADL disability

was defined as any difficulty with 11 specific ADL/IADL tasks. Individuals with mobility and/or ADL/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. These associations were partially explained by clinical cardiovascular disease (CVD), diabetes and interim CVD events for mobility disability and by clinical CVD and diabetes for ADL/IADL disability. Individuals with AAI < 0.90 had on average a mean decrease in gait speed of 0.02 m/s/year or a decline of 0.12 m/s over the 6 year follow-up. This decrease was partly explained by prevalent CVD but not further attenuated by interim CVD events.

Conclusions—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.

Keywords

Peripheral arterial disease; disability; cardiovascular disease

INTRODUCTION

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 by the six 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 AAI < 0.60) increased the risk for developing severe disability (the inability to walk ¼ mile) over a three year period compared to 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 non-disabled, 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, 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. Individuals with PAD are at high risk for cardiovascular events^{9,10} and individuals with CVD are at increased 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 ankle-arm index (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 included 5888 adults, aged 65 and older, recruited from a random sample of Medicare enrollees. This included 5201 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 Cardiovascular Health Study design and recruitment have been published elsewhere.^{12,13} Briefly, participants were recruited from a random sample of the Health Care Finance Administration Medicare eligibility lists in four US 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 currently under treatment for cancer.

Data collected in 1992–93 was considered baseline for these analyses. Of the original 5888 participants, 4988 were examined in 1992–93. Of the 4988 participants 283 were excluded from the analyses because AAI was not measured (n=238), the participant had either lower extremity revascularization (n=7) or angioplasty (n=2) or the AAI was greater than 1.5 (n=36), leaving 4705 potential participants. Of the 4705 participants, 3048 were included in the incident mobility disability analyses (excluded 1597 with disability at baseline and 60 with no response post baseline regarding disability), 2555 were included in the incident activities of daily living/instrumental activities of daily living (ADL/IADL) disability analyses (excluded 2094 with ADL/IADL disability at baseline and 56 with no response post baseline regarding disability), and 4344 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 post baseline).

Measures

Ankle Arm Index (AAI)—The AAI is the ratio of the ankle to arm systolic blood pressure and is reduced when there is atherosclerotic obstruction from the heart to 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 < 0.90 is 95% sensitive and 99% specific for angiographically significant PAD.¹⁴

The AAI was measured in 1992–1993 by trained technicians according to a standard protocol, previously described.¹⁵ The systolic pressures of the brachial and posterior tibial arteries were measured with a Doppler stethoscope (8 MHz, Parks Electronics, Aloha, OR). Measurements have been shown to be reliable between observers, stable over time, and highly correlated between right and left legs.¹⁵

Performance-based and Self-report Measures of Physical Disability—

Performance-based and self-report measures of physical disability were collected by trained technicians during the 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 or getting out of a bed or chair), instrumental activities of daily living (IADL; heavy housework, light housework, shopping for personal items, preparing their own meals, paying their bills or managing their money), and walking ½ 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 ½ mile.

Cardiovascular Disease (CVD)—Cardiovascular diseases, which may explain the pathway from AAI < 0.9 to functional decline, were considered categorically as a potential mediator. Prevalent CVD was defined as the presence of myocardial infarction (MI), angina, stroke, congestive heart failure (CHF), PAD (defined as self report of a physician diagnosis of peripheral arterial disease or intermittent claudication or by 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, stroke, congestive heart failure, hospitalized PAD, and transient ischemic attack between the baseline and follow-up clinic visits. The presence of the conditions was ascertained at each of follow-up years (1994–95, 1995–1996, 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 we accounted for the following potentially confounding factors: demographics (age, gender, race and education), positive Rose questionnaire for intermittent claudication, other non-CVD chronic conditions (diabetes, 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 intermittent claudication (IC) was assessed using a modified Rose questionnaire and analyzed separately from baseline self-report of PAD.²⁴ Diabetes was defined according to the American Diabetic Association guidelines of 1997; diabetes was considered present if the participant uses insulin or oral hypoglycemics or if glucose level exceeded 126 mg/dL (7.0 mmol/L).²⁵ Arthritis was assessed by self-report. Depression symptoms were assessed using the modified Center for Epidemiologic Studies Depression (CES-D) scale of 0–30.²⁶ In this analysis, a participant with a score of 10 or higher was considered to have “Depression”.²⁷ Smoking history was assessed by self-report of current or past use and the number of pack-years was calculated as the analytic variable for exposure. Relative body weight was assessed using body mass index, calculated as weight in kilograms over height in meters squared (kg/m²).

Statistical Analysis

Baseline characteristics for individuals with and without an AAI < 0.90, and stratifying by gender were compared using t-tests for continuous variables or chi square analyses for categorical variables. Severity was then considered by examining four groups based on AAI values (AAI > 1.0, 0.9–1.0, 0.8–0.9, and < 0.8).

Cox proportional hazards regression models were used to test whether those 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 among those free of disability at baseline, assessed by self report at 1 year intervals over approximately 6 years of follow-up.

Interim CVD events was used as explanatory time-dependent variables 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 prior to 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 six year follow-up (dependent variables). Each confounding factor was entered into the regression model and the marginal model, together with AAI, in order to assess the degree to which each confounder attenuates the relationship between AAI and both mobility and ADL/IADL disability and change in gait speed.

RESULTS

Peripheral arterial disease, defined as an AAI < 0.90, was found in 11.8% of the women and 15.8% of men (Table 1). In both men and women, individuals with AAI < 0.9 were older, had a lower BMI, and smoked more than those individuals with AAI ≥ 0.9. Compared to individuals without, a greater percentage of individuals with AAI < 0.9 were black, and were more likely to have prevalent CVD, arthritis, diabetes, and depression. Most of the prevalent CVD was due to co-existing angina or history of MI in the AAI < 0.9 group. In both men and women, individuals with AAI < 0.9 performed poorer on measures of physical function at baseline and were more likely to report prevalent ADL/IADL and walking difficulty compared to individuals with AAI ≥ 0.9 (Table 1).

Table 2 shows the association between severity of AAI < 0.9 and incident mobility disability. Of the 3048 individuals included in the analyses of incident mobility disability, 149 had an AAI < .8, 120 had an AAI between .8 and .9, 269 had an AAI between .9 and 1.0 and 2510 had an AAI > 1.0. In the unadjusted models, there was a dose response relationship with the risk for mobility disability increasing as the AAI decreased (also see Figure 1). After adjusting for demographics, intermittent claudication, prevalent CVD and other risk factors the association between AAI < 0.9 and incident mobility disability was attenuated, especially for the lowest AAI group (i.e. AAI < 0.80). After adjustment, individuals with an AAI < 0.80 were 1.55 times as likely to have mobility disability compared to individuals with an AAI > 1.0. The high prevalence of concurrent clinical CVD and diabetes were the major factors attenuating the association, when adjusting for concurrent clinical CVD and diabetes the univariate change in the HR was 0.30, $p < 0.0005$ and 0.16, $p < 0.0005$, respectively. This association was further attenuated by interim CVD events (HR for AAI < 0.80 went from 1.55 to 1.43). Interim CVD events were significantly related to mobility disability (HR 1.99; 95% CI 1.70, 2.34). The association between AAI and mobility disability was not further attenuated by interim non-CVD hospitalizations (data not shown).

In unadjusted models, AAI was also related to ADL/IADL disability (Figure 1 and Table 3). Of the 2555 individuals included in the analyses of incident ADL/IADL disability, 161 had an AAI < .8, 99 had an AAI between .8 and .9, 232 had an AAI between .9 and 1.0 and 2063 had an AAI > 1.0. Once again there was a clear dose response relationship between severity and risk for ADL/IADL disability. However, 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 between 0.8 and 0.9 were 1.33 times as likely to develop ADL/IADL disability compared to individuals with an AAI > 1.0. Again, prevalent CVD and diabetes were the major factors that attenuated the associations, with a univariate change in the HR of 0.16, $p < 0.0005$ for prevalent CVD and a univariate change in HR of 0.09, $p < 0.0005$ for diabetes. Though interim CVD events was related to ADL/IADL disability (HR 1.89, 95% CI 1.61, 2.24), the association between AAI < 0.9 and ADL/IADL disability was not explained by the interim CVD events (HR for AAI 0.8–0.9 went from 1.33 to 1.36; Table 3, Model 3). The association between AAI and ADL/IADL disability was not further attenuated by interim non-CVD hospitalizations (data not shown).

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

Table 4 shows the association between baseline AAI and decline in gait speed. The mean length of follow-up was 4.96 years. Of the 4344 individuals included in the analyses of decline in gait speed, 356 had an AAI < .8, 190 had an AAI between .8 and .9, 439 had an AAI between .9 and 1.0 and 3359 had an AAI > 1.0. After adjusting for baseline performance, demographics, prevalent and incident CVD, and other risk factors, individuals with an AAI < 0.90 had a greater annual decline in gait speed than individuals with an AAI > 1.00. On average individuals with an AAI < 0.90 had a mean decrease in gait speed of 0.02 m/s/year or a decline of 0.12 m/s over the 6 year follow-up. The association between AAI and change in gait speed was partly explained by prevalent CVD and was not further attenuated by interim CVD events or by interim non-CVD hospitalizations (data not shown).

DISCUSSION

In a large cohort of community-based older adults, the presence of AAI < 0.9 was associated with a higher risk of incident mobility (difficulty walking ½ mile) and ADL/IADL (any difficulty with 11 specific ADL or IADL) disability over a 6 year follow-up. Individuals with an AAI < 0.80 had a 43% increased risk of developing mobility disability compared to individuals with an AAI of > 1.0 even after adjusting for a number of confounding factors. In previous studies that have examined the association between PAD and worsening mobility disability, the increased risk was only apparent in those women with the most severe PAD (AAI < 0.6).⁵ We found a dose response relationship with more impaired AAI that was apparent at levels of AAI just below the normal range of <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. The higher risk for ADL/IADL disability was explained by these factors.

Our finding that individuals with an AAI < 0.90 had on average a decline in gait speed of 0.02 m/s/year is consistent or even slightly greater than the 0.02 to 0.03 m/s/2year follow-up reported previously.¹ A decline of 0.02 m/s/year over the six 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 AAI < 0.9 are at high risk for new CVD events such as stroke, heart failure, and myocardial infarction.^{9,10} In the present study, a large part of the association of AAI < 0.9 with disability was related to other cardiovascular co-morbidity and diabetes. New CVD events explained some but not all of the association between AAI and incident mobility disability. Cardiovascular comorbidity and new cardiovascular events most likely have an impact on cardiovascular endurance which plays a significant role in walking extended distances and a much lesser role in completing ADL/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. This might be explained in part by survival bias in that those who completed the performance based tasks were a smaller survival subgroup.

These findings make it clear that the impact of AAI < 0.9 on disability is largely, but not completely explained by cardiovascular comorbidity. Thus, a critical way to prevent mobility disability in individuals with AAI < 0.9 would be to manage overall cardiovascular risk and to prevent new CVD events such as stroke, CHF, angina and MI. Both cross-sectional and longitudinal studies have shown that in individuals with PAD, those who take statins have less physical disability and functional decline than people who do not take statins.^{2,29} Diabetes was also a major factor explaining part of the impact of AAI < 0.9 and also independently related to disability, this is another important target to reduce risk of disability in the older adults in the community with PAD. More effort is needed to encourage clinicians to recognize that a low ankle arm index is often asymptomatic but represents substantial systemic atherosclerosis.³⁰

In spite of accounting for both prevalent and incident CVD in these analyses, a low AAI remained independently predictive of disability. This supports other studies in PAD patients showing that they have significant local disabling affects of disease in muscle strength and nerve function as well.⁷ These direct effects have been shown to be best managed by 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 3 or more times per week had a smaller decline in physical performance compared to individuals with PAD who walked less often.³¹ Several investigators have shown the benefits of an exercise program for individuals with symptomatic PAD.^{32–34} However, 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 or muscle strength and may also impact overall cardiovascular risk as well.

When examining our findings a few limitations must be considered. First, incident mobility disability was assessed by 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 by 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 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.

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Figure 1.

Figure 1a: Kaplan Meier function of mobility disability* by AAI category, unadjusted.

Figure 1b: Kaplan Meier function of ADL/IADL disability by AAI category, unadjusted.

Abbreviations: AAI, ankle-arm index; ADL, activities of daily living; IADL, instrumental activities of daily living.

P<.005, Log Rank Test for mobility disability and ADL/IADL disability.

Table 1
Baseline (1992–93) characteristics by sex and the presence of an ankle arm index (AAI) < 0.9.

	Men		Women		p-value *	p-value
	AAI < 0.9 (n=309)	AAI ≥ 0.9 (n=1645)	AAI < 0.9 (n=325)	AAI ≥ 0.9 (n=2426)		
Demographics						
Age, mean (SD)	77.4 (6.1)	74.8 (5.3)	77.4 (6.2)	74.3 (5.0)	<.001	<.001
Black, n (%)	72 (23.3)	233 (14.2)	104 (32.0)	417 (17.2)	<.001	<.001
More than high school education, n (%)	126 (40.8)	863 (52.6)	117 (36.0)	1,043 (43.1)	<.001	0.02
Behavioral						
BMI (kg/m ²), mean (SD)	25.9 (3.8)	26.6 (3.8)	26.4 (5.4)	27.1 (5.2)	0.001	0.04
Alcohol (drinks/wk), mean (SD)	2.7 (7.5)	3.2 (6.6)	1.4 (4.3)	1.3 (3.8)	0.35	0.80
Smoking (pack years), mean (SD)	33.3 (34.1)	23.3 (29.2)	17.7 (24.3)	11.3 (20.6)	<.001	<.001
Health						
CVD, n (%)	185 (59.9)	521 (31.7)	146 (44.9)	485 (20.0)	<.001	<.001
MI, n (%)	79 (25.6)	161 (9.8)	36 (11.1)	113 (4.7)	<.001	<.001
Angina, n (%)	88 (28.5)	274 (16.7)	75 (23.1)	269 (11.1)	<.001	<.001
PAD, n (%)	45 (14.6)	17 (1.0)	18 (5.5)	9 (0.4)	<.001	<.001
CHF, n (%)	23 (7.4)	49 (3.0)	21 (6.5)	56 (2.3)	<.001	<.001
Stroke, n (%)	28 (9.0)	67 (4.1)	27 (8.3)	42 (1.7)	<.001	<.001
TIA, n (%)	16 (5.2)	51 (3.1)	16 (4.9)	38 (1.6)	0.07	<.001
IC n (%)	20 (6.6)	11 (0.7)	25 (7.9)	17 (0.7)	<.001	<.001
Arthritis, n (%)	126 (41.3)	694 (42.7)	192 (60.0)	1,369 (57.0)	0.66	0.30

	Men			Women		
	AAI < 0.9 (n=309)	AAI ≥ 0.9 (n=1645)	p-value *	AAI < 0.9 (n=325)	AAI ≥ 0.9 (n=2426)	p-value *
Diabetes, n (%)	79 (27.1)	270 (17.0)	<.001	74 (24.5)	284 (12.3)	<.001
CES-D, 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)	0.001	80 (24.8)	476 (19.7)	0.03
Interim CVD, n (%)	224 (72.5)	757 (46.0)	<.001	187 (57.5)	928 (38.3)	<.001
Physical Function						
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)	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

Abbreviations: BMI, body mass index, defined as weight in kilograms divided by the square of height in meters; CVD, cardiovascular disease; MI, myocardial infarction; PAD, history of documented peripheral arterial disease, defined as 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; CHF, congestive heart failure; TIA, transient ischemic attack; IC, intermittent claudication by Rose Questionnaire; CES-D, Center for Epidemiologic Studies Depression scale, n (%) number of individuals with a score 10 indicating depression; ADL, activities of daily living; IADL, instrumental activities of daily living.

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

Table 2

Attenuation of the relationship between ankle arm index (AAI) and mobility disability

	Incidence rate (per 100 person-years)	Model 1 Hazard Ratio (95% CI)	Model 2 Hazard Ratio (95% CI)	Model 3 Hazard Ratio (95% CI)
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)
More than a HS education	--	--	0.97 (0.85,1.10)	0.95 (0.84,1.09)
IC by 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)
ADA Diabetes				
IFG	--	--	1.01 (0.82,1.26)	1.01 (0.81,1.25)
Diabetic	--	--	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 ago	--	--	1.13 (0.96,1.34)	1.16 (0.98,1.36)
Quit < 1 year ago	--	--	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

Abbreviations: Mobility disability defined as any reported difficulty walking ½ mile; CI, confidence interval; HS, high school; IC, intermittent claudication by Rose Questionnaire; CVD, cardiovascular disease; ADA, American Diabetes Association; IFG, impaired fasting glucose; BMI, body mass index, defined as weight in kilograms divided by the square of height in meters;

* Likelihood-ratio test comparing model 3 to model 2

Model 1 – unadjusted.

Model 2 – adjusted for age, gender, race, education, IC by Rose Questionnaire, prevalence of CVD, arthritis status, diabetes status, pack-years of smoking, smoking status, alcohol use and BMI.

Model 3 – added interim CVD to all those variables in model 2.

Table 3

Attenuation of the relationship between ankle arm index (AAI) and ADL/IADL disability

	Incidence rate (per 100 person- years)	Model 1 Hazard Ratio (95% CI)	Model 2 Hazard Ratio (95%CI)	Model 3 Hazard Ratio (95% CI)
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)
More than a HS education	--	--	1.24 (1.09,1.40)	1.22 (1.08,1.39)
IC by 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)
ADA Diabetes				
IFG	--	--	0.98 (0.81,1.20)	0.97 (0.80,1.19)
Diabetic	--	--	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 yr ago	--	--	1.17 (1.00,1.37)	1.18 (1.01,1.38)
Quit < 1 yr ago	--	--	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

Abbreviations: ADL, activities of daily living; IADL, instrumental activities of daily living; CI, confidence interval; HS, high school; IC, intermittent claudication by Rose Questionnaire; CVD, cardiovascular disease; ADA, American Diabetes Association; IFG, impaired fasting glucose; BMI, body mass index, defined as weight in kilograms divided by the square of height in meters;

Model 1 – unadjusted.

Model 2 – adjusted for age, gender, race, education, IC by rose questionnaire, prevalence of CVD, arthritis status, diabetes status, pack-years of smoking, smoking status, alcohol use and BMI.

Model 3 – added interim CVD to all variables in model 2.

Table 4

Gait speed (15 foot walk) change over six years of follow-up in relation to ankle arm index (AAI).

	Mean Performance		Coefficients reflecting change in the slope (95% CI)	
	Baseline (m/s)	Mean change (m/s/year) No.	Model A	Model B
AAI				
> 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, −0.003)	−0.008* (−0.013, −0.003)
< 0.8	0.77	−0.018	−0.008* (−0.012, −0.005)	−0.008* (−0.012, −0.005)
Test for trend			p<.001	p<.001

Abbreviations: CI, confidence interval; CVD, cardiovascular disease; MI, myocardial infarction, CHF, congestive heart failure; TIA, transient ischemic attack.

No. Mean change, adjusting for baseline performance.

* A significant difference in the change compared to reference category, at the 0.05 level.

Model A - Adjusted for baseline performance, demographics (age, gender, race, and education), intermittent claudication, prevalent CVD, other risk factors (arthritis, diabetes, depression, smoking history, and body mass index).

Model B –Adjusted for any interim CVD (MI, stroke, CHF, angina, TIA or claudication) as well as variables in Model A.