

Is the Ankle-Brachial Index a Useful Screening Test for Subclinical Atherosclerosis in Asymptomatic, Middle-Aged Adults?

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ABSTRACT

Background: Measurement of the ankle-brachial index (ABI) is recommended as a screening test for cardiovascular risk prediction in individuals ≥ 50 years old; however, there is little data regarding the utility of the ABI as a screening test in individuals for whom physicians actually order non-invasive testing for cardiovascular risk prediction.

Methods: This study included 493 consecutive asymptomatic patients without known atherosclerotic vascular disease who were referred by their physician for measurement of the ABI and ultrasound measurement of carotid intima-media thickness (CIMT). ABI values were classified as “reduced” (< 0.9), “normal” ($0.9-1.3$), and “increased” (> 1.3).

Results: The mean age of the patients was 55.3 (standard deviation 7.5) years. Only 1 patient had a reduced ABI (0.2%). ABI values tended to be higher in those with increased CIMT ($P=0.051$); however, CIMT was not significantly different between those with normal and increased ABI values ($P=0.802$). There were no significant differences in the prevalence of traditional cardiovascular risk factors or carotid plaque presence among the ABI groups.

Conclusions: Despite recommendations, the ABI is not sensitive as a screening tool for detecting subclinical atherosclerosis in asymptomatic middle-aged individuals.

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INTRODUCTION

The American Heart Association Prevention Conference V described the ankle-brachial index (ABI) test as a “simple, inexpensive, noninvasive measure” of peripheral arterial disease (PAD) and stated that an abnormal ABI “provides incremental coronary and all cardiovascular disease (CVD) risk assessment information.”¹ Measurement of the ABI has been recommended to improve cardiovascular risk assessment in individuals ≥ 50 years old or in individuals at “intermediate or higher risk of CVD on the basis of traditional risk factor assessment.”¹ Although several studies have demonstrated that an ABI < 0.9 predicts future CVD and mortality, there is little data regarding the utility of the ABI as a screening test in individuals for whom physicians actually order non-invasive testing for cardiovascular risk prediction.²⁻⁷ As part of the University of Wisconsin Vascular Health Screening Program, we evaluated the prevalence of an abnormal ABI and its associations with cardiovascular risk factors and carotid intima-media thickness (CIMT), an established marker of subclinical atherosclerosis, in young and middle-aged patients referred to our program.

METHODS

Study Protocol

Data were obtained from consecutive patients without clinical evidence of atherosclerotic vascular disease who were referred by their physicians to the University of Wisconsin Vascular Health Screening Program, a primary CVD prevention screening program, for clinical determination of ABI and CIMT from August 2001 through August 2004. Risk factors for CVD that were assessed included cigarette smoking (current, past, never), hypertension (systolic blood pressure ≥ 140 mmHg or taking antihypertensive medication), hyperlipidemia (low-density lipoprotein cholesterol [LDL-C] ≥ 130 mg/dl or tak-

Table 1. Subject Characteristics

	Reduced ABI (<0.9)	Normal ABI (0.9-1.3)	Increased ABI (>1.3)
N(%)	1 (0.2)	446 (90.5)	46 (9.3)
Age, years	54 (-)	55.3 (7.3)	55.8 (9.1)
Male, N(%)	1 (100)	234 (52.5)	27 (58.7)
Tobacco use, N(%)	0	30 (6.7)	2 (4.3)
Diabetes Mellitus, N(%)	0	17 (3.8)	1 (2.2)
Family history of CAD, N(%)	1 (100)	214 (48.0)	23 (50.0)
2 or more risk factors, N(%)	1 (100)	287 (64.3)	27 (58.7)
3 or more risk factors, N(%)	1 (100)	116 (26.0)	8 (17.4)
Lipids			
Total cholesterol, mg/dL	229	209.5 (86.0)	197.7 (58.5)
Triglycerides, mg/dL	317	129.8 (78.2)	123.8 (91.6)
High-density lipoprotein cholesterol, mg/dL	50	58.2 (17.7)	58.8 (19.9)
Low-density lipoprotein cholesterol, mg/dL	116	122.2 (38.9)	113.8 (48.6)
Total: high-density lipoprotein cholesterol ratio, mg/dL	4.6	3.9 (2.74)	3.6 (1.2)
Systolic blood pressure, mmHg*	171	128.8 (16.0)	119.5 (15.2)
Fasting glucose, mg/dL	111	87.9 (29.1)	82.7 (34.0)
Body mass index, kg/m ²	23.1	26.9 (5.7)	26.4 (5.6)
Metabolic Syndrome, N(%)	1 (100)	52 (11.7)	2 (4.3)
Lipid-lowering treatment, N(%)	1 (100)	200 (44.8)	22 (47.8)
Antihypertensive treatment, N(%)	1 (100)	102 (22.9)	8 (17.4)
Ankle-brachial pressure index†	0.75	1.15 (0.08)	1.34 (0.05)
Carotid intima-media thickness, mm	0.822	0.786 (0.172)	0.780 (0.172)
Presence of carotid plaque, N(%)	1 (100)	253 (56.7)	21 (45.7)

All values means (standard deviation) unless otherwise noted.

* $P < 0.001$

† $P = 0.051$

ing lipid-lowering medication), high-density lipoprotein cholesterol (HDL-C) <40 mg/dl, family history of coronary artery disease in a male first degree relative <55 years old or a female first degree relative <65 years old, and chronological age ≥ 45 years in men or ≥ 55 years in women.⁸ Metabolic syndrome was diagnosed using the definition from National Cholesterol Education Program Adult Treatment Panel Guidelines.⁸ Blood pressure was measured in both arms and the values were averaged. Fasting laboratory tests used standard serum enzymatic techniques. This study was reviewed by the Institutional Review Board for the University of Wisconsin Medical School and granted “exempt” status.

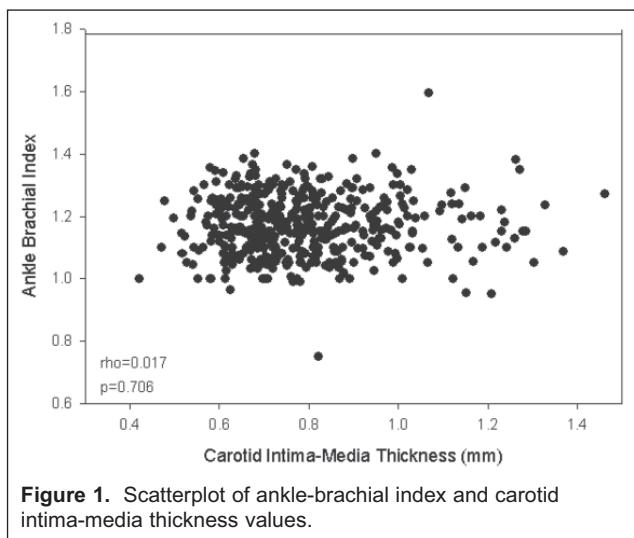
Measurement of the Ankle-Brachial Index

Using Doppler ultrasonography, the brachial artery systolic blood pressure was measured in each arm, then both the dorsalis pedis and posterior tibial pressures were measured in each ankle (Parks Flo-Lab 2100, Parks Medical Electronics, Inc.). The right and left ABI values were calculated by dividing the higher of the ankle pressures in each leg by the higher of the brachial pressure in each arm.⁹ All ABI measurements were interpreted by 1 cardiologist. Based on 34 blinded, repeated studies,

the coefficient of variation for reproducibility of ABI measurements was 5.8%.

Carotid Ultrasound Imaging

The standardized protocol from the Atherosclerosis Risk in Communities (ARIC) study was used to acquire images of the common, bifurcation, and internal segments of each carotid artery.^{10,13} Ultrasound images were acquired using an 8.0 MHz linear array transducer (Acuson Sequoia, Siemens Medical Solutions) and recorded digitally using a Camtronics Vericis acquisition module (Camtronics Medical Systems). Composite CIMT was calculated as the average of mean far wall CIMT measurements from all measurable segments (maximum of 6). All ultrasound examinations were interpreted by a single reader. Reproducibility (mean [standard deviation]) of scan images and CIMT measurements, determined by blinded, duplicate image acquisition and measurement was 0.004 (0.087 mm) ($r=0.98$, $P < 0.001$).¹⁰ The coefficient of variation for CIMT measurements was 3.1%.¹¹ Carotid plaque was defined as an echogenic thickening of the intimal reflection that encroached on the arterial lumen, with a minimal intimal + medial thickness of >1.2 mm.¹²



Statistical Techniques

Sigma Stat 3.0.1 (SPSS, Inc.) was used for all analyses. Continuous variables were described by mean (standard deviation) or median (range) values. ABI values were classified as “reduced” (<0.9), “normal” (0.9-1.3), and “increased” (>1.3).⁹ An “abnormal” ABI was defined as an ABI \leq 0.9 in either leg. When used as continuous variables, the right and left ABI values were averaged. Because of the unexpectedly low prevalence of “abnormal” ABI, separate analyses were performed to compare the normal and “increased” ABI groups, to evaluate associations with “non-compressible” arteries.⁹ CIMT was considered “elevated” if greater than the 80th percentile for age, sex, and race in the ARIC study.¹³ T-tests were used to identify differences in variables between ABI categories. The χ^2 test was used to identify differences among categorical variables. Pearson correlations and logistic regression were used to characterize relationships between ABI, risk factors, CIMT, and carotid plaque.

RESULTS

Subject Characteristics

Subjects included 493 asymptomatic individuals, referred by their physicians for measurement of ABI and CIMT to improve cardiovascular risk prediction (Table 1). The mean age of the entire cohort was 55.3 (7.5) years (range 26-76 years). There were 278 (56.4%) subjects \geq 50 years old. The median number of cardiac risk factors was 2 (range 0-4). There was a high prevalence of use of lipid-lowering medication (45.2%). Increased CIMT and carotid plaque were present in 205 (41.6%) and 275 (55.8%) subjects, respectively.

Ankle-Brachial Index Measurements

There were 446 individuals with a normal ABI and 46

with increased ABI. Only 1 subject had a reduced ABI—this individual was a 54-year-old male who had hypertension, hyperlipidemia, a family history of premature coronary artery disease, and Metabolic Syndrome. His right ABI was 0.79 and his left ABI was 0.71. On further questioning after the test, it was determined that he had intermittent claudication and was not truly asymptomatic. His composite CIMT was increased at 0.822 mm (61-70th percentile). He had a 1.6 mm plaque in his right carotid bulb.

The 10-year estimated cardiovascular risk was 5.1% in the group with normal ABI and 4.6% in the group with increased ABI >1.3 group ($P=0.575$). The mean CIMT in subjects with increased ABI was 0.780 (0.172). This was similar to those with normal ABI (0.786 [0.172], $P=0.802$). Systolic blood pressure was lower among individuals with an elevated ABI ($P<0.001$) than among those with normal ABI. The mean ABI (1.15 [0.09] versus 1.17 [0.09]) tended to be higher in those with increased CIMT ($P=0.051$). ABI was not significantly different in the 55.8% of subjects with carotid plaque compared to the 44.2% without plaque ($P=0.557$). The correlation between ABI and CIMT was weak and not statistically significant ($r=0.017$, $P=0.706$) (Figure 1).

DISCUSSION

In our cohort of 493 patients referred by their physician for non-invasive testing to improve cardiovascular risk prediction, only 1 patient had an ABI <0.9. On further questioning, this patient had intermittent claudication. On average, subjects in our study had at least 2 CVD risk factors and were middle-aged with a high prevalence of non-occlusive carotid plaque. The ABI was a poor screening test for the presence of subclinical atherosclerosis, considered to be present if there was increased CIMT (sensitivity <0.1%; 0/205) or the presence of non-occlusive plaque (sensitivity <0.1%; 1/275), established markers of increased cardiovascular risk in middle-aged adults.¹⁴⁻¹⁶

The ABI is a good test for PAD with a sensitivity and specificity of approximately 90% and 98%, respectively.² The prevalence of PAD in patients hospitalized at the University of Wisconsin Hospital and Clinics on the cardiology service was substantial, with 60% of patients having reduced ABI.¹⁷ In hospitalized patients with coronary artery disease, the ABI may be a useful screening test; however, among outpatients referred for cardiovascular risk assessment, the prevalence of reduced ABI is much lower. In the National Health and Nutrition Examination Survey, the prevalence of a reduced ABI in individuals \geq 40 years was 4.3%.¹⁸ When

high-risk individuals such as those with known CVD or chronic heart failure were excluded from analysis, only 2.9% had an abnormal ABI.¹⁸ Studies that reported higher prevalence rates screened higher risk populations. The PARTNERS study, which included 6979 patients in 350 primary care practices, found that 29% of patients had PAD.¹⁹ The PARTNERS study was limited to patients who were >70 years or 50-69 years old with a history of cigarette smoking or diabetes mellitus. The Minnesota Regional Peripheral Arterial Disease Screening Program, which recruited patients from the media, senior health fairs, retirement homes, and a lipid clinic, found that 26.5% of patients had an ABI ≤ 0.85 .⁷ The mean age was 73 years and a significant number of those with PAD were current smokers (18.9%) or had diabetes mellitus (19.6%).

Although previous studies have demonstrated wide ranges of PAD prevalence, it appears that in middle-aged patients at low to intermediate risk who often are referred for cardiovascular screening tests, the prevalence of reduced ABI is low, as shown in our study. Therefore, the usefulness of the ABI as a screening test for subclinical atherosclerosis in asymptomatic intermediate risk patients does not seem to warrant widespread implementation. Screening most patients ≥ 50 years old or intermediate risk patients may not yield a significant number of positive results given the low prevalence of asymptomatic PAD in patients <70 years old without a history of smoking or diabetes mellitus. In the current study, advanced subclinical atherosclerosis was characterized by increased CIMT and was present in 41.6% of subjects. Although some studies have shown an association between advanced CIMT and low ABI, the results have been inconsistent.²⁰⁻²² We were unable to demonstrate a significant relationship between ABI and CIMT or the presence of carotid plaque—2 established surrogates for CVD.¹⁴⁻¹⁶ Of note, the individual with reduced ABI also had increased CIMT (although not above the 80th percentile) and carotid plaque. The current study demonstrated that a significant number of patients with advanced subclinical atherosclerosis may be missed if the ABI is the only screening tool offered to patients with multiple risk factors.

Limitations

As above, our subjects on average were middle-aged and only 56% were >50 years old. Nevertheless, in the 278 subjects who were >50 years old, only 1 subject (0.36%) had reduced ABI. Of the 290 subjects who were at intermediate risk (2 or more risk factors), only 1 (0.34%) had reduced ABI. The prevalence of reduced ABI may have been higher if more subjects smoked cigarettes or

had diabetes mellitus. Many subjects did, however, have at least 2 risk factors for CVD and many were receiving lipid- and blood pressure-lowering medications, indicating that their physicians considered them to be at either intermediate or higher risk and likely to have an abnormal test. Also, almost half had a family history of premature coronary artery disease.

CONCLUSIONS

In asymptomatic middle-aged adults, ABI was not a useful screening test, as only 1 individual had an ABI <0.9. There were no significant associations between ABI and CIMT or carotid plaque presence, well-established screening tools for determining cardiovascular risk. Similarly, increased ABI was not a sensitive predictor of subclinical atherosclerosis. Although there may be a role for ABI as a screening tool in older patients or those with a history of tobacco abuse or diabetes mellitus, it does not appear to be a sensitive screening tool in middle-aged asymptomatic adults in whom physicians desire additional assessment of cardiovascular risk using non-invasive imaging. Given our findings, we do not recommend the ABI as a screening tool for subclinical atherosclerosis in asymptomatic, low and intermediate risk individuals.

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